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The International Society of Biological and Environmental Repositories presents Abstracts from their Annual Meeting

Keeping Step in an Evolving Global Research Environment: Biobanking for Now and for the Future

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The abstracts that follow demonstrate the broad range of timely issues addressed in the contributed oral and poster presentations at ISBER's 13th Annual Meeting.

ISBER Abstracts

HOT TOPICS (HT)

HT 01. Victorian Brain Bank Network - Developing and Introducing a Cost Recovery Model

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Background: The Victorian Brain Bank Network (VBBN) is part of the Australian Brain Bank Network (ABBN) which was formed in 2003. Building on previous grants, an Australian National Health and Medical Research Council (NHRMC) Enabling grant scheme (2004–2014) transformed a group of Australian brain banks into a national and comprehensive network supporting neuroscience research. Our aim has been to achieve a level of financial sustainability through cost recovery for services associated with accessing tissue.

Method: In 2005 the VBBN took part in a national review of the costs associated with the collection, processing, characterization, storage and distribution of tissue in order to develop a cost recovery model.

Results: In 2005 the ABBN Management Committee approved a cost recovery model for services associated with fulfilling tissue applications. Cost recovery did not commence in Victoria until 2007 because time was required to inform and educate researchers of the policy and to allow researchers to factor this cost into future grant applications. Cost recovery has generated 10% of the VBBN's income over the last 5 years and has shown a gradual increase from when first introduced in 2007 of 3% to 14% in 2011.

Conclusion: The implementation of the cost recovery model has shown a level of success and researchers in general have understood the need for this policy. Cost recovery is an important aspect of financial sustainability and if this is not achieved, then revenues must come from other sources to maintain this valuable resource.

HT 02. Insufficient Reporting of Pre-analytical Variables For Biospecimens, IRB decisions, and IC Procedure by Both Academic and Industry Authors in the Scientific Literature

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Background: Little is known about pre-analytical variable reporting in scientific literature, though submission of approval by institutional review boards (IRBs) and patient's informed consent (IC) were introduced 20 years ago. This impacts the quality of the biospecimen, scientific validity, and integrity.

Methods: A PubMed search was done using the key words "biomarker discovery, human, English." Open source papers published in 2004 and 2009 were analyzed based on a) the affiliation (academic center vs. industry) for the first author of the paper and b) concerning information on IRBs and IC.

Results: The number of publications on biomarker discovery (open source/total) increased from 31/266 in 2004 to 94/742 in 2009. Papers with academic/industry authors did not include any information on pre-analytical variables in 42.9%/70.0% (2004) and 53.5%/87.5% (2009) of their submissions. In 2004/2009 only 35.5%/41.4% of papers mentioned anything about IRBs. ICs were mentioned in 32.3% of all papers in 2004 and in 50.0% of all papers in 2009.

Conclusions: Our data shows that information regarding the reporting of pre-analytical variables in scientific papers is low in both academia and industry. Information regarding IRBs and IC is surprisingly low as well. This deficit of information makes it very difficult to correctly interpret scientific results. Tools like the recently published SPREC (Standard PREanalytical Code) and BRISQ (Biospecimen Reporting for Improved Study Quality) could help remedy these deficiencies.

HT 03. Comprehensive Sample Management: Outsourced, Onsite and Hybrid Approach

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Research organizations are increasingly turning to specialized outsourcing service providers to manage their sample inventories and biorepository operations to save costs and improve research efficiencies. Hybrid approaches to outsourced biospecimen management are developing where inventories are stored onsite, but are dictated by standard operating procedures and data management technology provided by an outsourced provider. In addition, some companies are using complete onsite service models in which people, processes and technology from an outsourcing sample management company are brought in and leveraged to manage sample assets.

The presenter will use real-world case studies to highlight efficiencies resulting from organizations bringing outsourced operations on site to their research facilities. Specific topics that will be outlined include:

- Best practices for integrating an outsourced team into existing onsite biorepository operations
- Considerations for evaluating the need and benefit of onsite management of biomaterials
- How to build a single, centralized sample management database
- Establishing metrics to evaluate the proficiency of biorepository operations

HT 04. Preservation of Morphology and Biomolecules within Tissue Stored for Three Years at −80°C in PAXgene Tissue Stabilizer Reagent

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Background: For biomolecule preservation current standard practice is snap freezing in liquid nitrogen and storage at −80°C. While tissue morphology is damaged during freezing, it is preserved in formalin fixed, paraffin-embedded (FFPE) tissue for decades. The PAXgene Tissue System is a non-crosslinking formalin substitute consisting of a tissue fixative and a tissue stabilization reagent. After fixation and transfer into the stabilizer, tissues can be stored at −80°C.

Methods: Rat tissue specimens were fixed in PAXgene Tissue Fixative for 3 hours, transferred into PAXgene Tissue Stabilizer and stored in the Stabilizer at −80°C. After 3 years of storage, specimens were processed and embedded in paraffin. Nucleic acids were purified from sections of paraffin embedded tissue using the corresponding PAXgene Tissue kits. Purity, yield, integrity and performance in qPCR and qRT-PCR were measured. Quality of morphology was analyzed by H&E staining.

Results: Morphology from PAXgene Tissue specimens stored at −80°C was well preserved and comparable to FFPE specimens. Nucleic acids were of high purity with RNA integrity values >6 and DNA fragments between 20 and 10 kb in length. Performance in qPCR and qRT-PCR, was comparable to nucleic acids isolated from snap frozen tissue.

Conclusion: For rat liver, kidney, spleen, intestine and lung specimens after three years storage at −80°C in PAXgene Tissue Stabilizer, morphology and biomolecules are still preserved.

For research use only. Not for use in diagnostic procedures. No claim or representation is intended to provide information for the diagnosis, prevention, or treatment of a disease.

HT 05. What Do Publishers of Biomedical Journals Do to Improve the Information about Pre-Analytical Variables of Biospecimens?

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Background: We have shown that in selected scientific papers focusing on biomarker discovery in more than 50% of cases there was no information about pre-analytical variables. We concluded that one of the major stakeholders dealing with this issue should be publishers and reviewers of biomedical journals.

Methods: We developed a short questionnaire of how reviewers are approaching papers with missing or insufficient information about pre-analytical variables. This questionnaire was sent to several biomedical journals.

Results: Publishers and/or editor-in chiefs of 60 journals (6 biomarker research, 1 biobanking, 15 pathology, 5 laboratory medicine, 7 cancer, and 26 journals of major importance) received the questionnaire by email. The impact factors of these journals were between 0.848 and 94.262 (mean 9.634; median 4.043). Only 9 (15%) journals responded and none were willing to participate in the survey. The 12 reasons (multiple mentioned) for not participating were: no interest (4), no time (2), publishers stated that reviewers are not willing to participate (2), internal process to pre-screen papers with missing pre-analytical information before peer-review (2), technically too time consuming to forward questionnaire to reviewers (1), paper with missing pre-analytical information not rejected for first review (1)

Conclusion: This issue is of low interest to publishers and/or editors-in-chief as only a small percentage responded and all declined to participate to this survey. Therefore it will be the task of biobankers to improve this situation by implementing the recently introduced SPREC (Standard PREanalytical Code) and BRISQ (Biospecimen Reporting for Improved Study Quality) guidelines into their quality management systems.

HT 06. Precise Nucleic Acid Quantification Using Lab-On-A-Chip Spectroscopy and the cDROP Quantificiation Algorithm

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Precise quantification and quality control of isolated genomic DNA is critical for success of downstream processing prior to functional nucleic acid analysis including next generation sequencing. Traditionally, two quantification methods are used: (1) UV/Vis based quantification which can lack specificity due to contribution of co-purified substances to A260 absorbance in poorly processed samples. (2) Fluorescence-based assays which intercalate double stranded DNA. This presentation describes cDrop quantification which extends the capabilities of UV/Vis spectroscopy by employing advanced algorithms to decompose UV/Vis spectral data into contributing reference spectra from molecules present in complex DNA samples. This allows DNA fraction quantification with high specificity and quantification of contributing quantities of co-purified substances including RNA, phenol and others present in the sample.

A comprehensive comparison between three DNA quantification methods is presented. Differences between the two traditional methods was studied as a function of the physical state of the DNA samples. Observations were verified using cDrop in a three-phased approach; A) Commercially available highly pure DNA samples are quantified and compared for accuracy, precision, reproducibility and bias of agreement; B) known contaminants like RNA or salts were spiked into DNA samples to measure accuracy and specificity of sample quantitation; C) A large number of real-life samples were analyzed for deviations between the three quantification methods. This enables assessment of correlation factor quality between traditional quantification methods and verified robustness of the cDrop method making UV/Vis the nucleic acid quantification method of choice given the dynamic range, ease of use and operational efficiency.

HT 07. An Innovative Approach to Biospecimen Storage that Conserves Energy and Facility Space

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The Division of Cancer Epidemiology and Genetics (DCEG) of the U.S. National Cancer Institute stores over 11 million biospecimens in support of studies designed to understand the etiology of cancer. Approximately 2/3 or 7.8 M of these biospecimens are stored at ultra-low temperatures (-80 °C) either in mechanical chest or upright freezers. To address rising costs for biospecimen storage and to identify energy-efficient biospecimen storage environments, DCEG conducted market research on ultra-low walk-in freezers. Evaluation criteria included a request for a single storage chamber with temperature variations within ±5 °C, efficient use of repository space with reduced energy requirements, redundant power sources, ability to be dismantled and reassembled at a new location, if needed, and delivered by a manufacturer with a proven track record for these units.

Bahnson Environmental Specialties, LLC (Raleigh, NC) was identified as a supplier who could meet all criteria and a 2,500 cu. ft. walk-in storage environment was purchased and installed at

the NCI-Frederick Central Repository for DCEG. Following the design and procurement of a unique system of shelving for biospecimen storage, transfer of material from existing freezers was initiated. During the initial filling, 48 upright freezers and 33 chest freezers were emptied, resulting in a reduction of storage space by ~50% and a reduction in energy consumption by at least 50%. As specimen consolidation efforts continue, savings in space and energy are expected to increase. Implications for cost savings for centralizing repository services are described.

HT 08. A New Niche: A Tissue Bank Rotation in Pathologists' Education

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Introduction: Tissue Banking is vital to the practice of Surgical Pathology and, with the growth of molecular diagnostic techniques, has become even more pertinent. Typically, Pathologists' Assistants are charged with the collection of tissue. Further, a "niche" has been identified as private biorepositories and biotechnology corporations have increased; Pathologists' Assistants are being utilized to collect, catalog, manage tissue and tissue banks in these companies.With this recognition, training in the proper collection of tissue, regulations and management of the tissue bank is now relevant to the training of a Pathologists' Assistant. To this end, West Virginia University has collaborated with the University of Pittsburgh Health Sciences Tissue Bank at UPMC Shadyside in Pittsburgh, PA (UPHS-TB) to provide a rotation experience in the clinical training year of Pathologists' Assistants (PAs).

Methods: Pathologists' Assistants receive graduate level didactic training in subjects such as Human Anatomy and Physiology, dissection and description methods specific to Anatomic Pathology, Microbiology and Immunology, Disease Mechanisms, and Pathologic Processes in the first year of course work. The UPHS-TB is uniquely situated to provide students with this experience and knowledge. Demonstration of patient consenting, tissue procurement, transport and storage and management of tissue, and crucial regulations and standards will be part of the student learning.

Result: Assessment of collected post-rotation and post-graduate evaluations and surveys will be reviewed for outcomes.

Conclusion: We propose that the Tissue Bank Rotation will become integral to the education of a Pathologists' Assistant.

HT 09. Development and Application of Creative Tools to Accomplish Rapid Transfer of Specimens from Traditional Freezers into a Dense Storage Collection

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Background: Biorepositories are looking for innovative dense storage solutions that minimize footprint and energy use while maximizing specimen storage and temperature stability. Fisher BioServices under subcontract to SAIC-Frederick was tasked with the rapid transfer of over 2 million specimens from traditional −80°C mechanical storage into a Division of Cancer Epidemiology and Genetics (DCEG), National Cancer Institute provided 2,500 cu. ft. walk-in/reach-in storage environment.

Methods: This process involved identification and training of oversight and key staff, personnel safety risk assessment and mitigation for work within space that can reach −40°C, selection and prioritization of specimens to be placed into the space, and development and modification of work flows and processes for access and input.

Results: Staff accomplished 80% filling of the space in less than five months. Challenges, solutions and lessons learned in the effort to maximize fill rate efficiency are described. Among these is development of a database tool for rapid update of specimen location, container and vial type data, as well as the design, testing and production of a customized cart cooled by dry ice in which boxes could be staged for placement in the space.

HT 10. Collaborative Models to Facilitate Exchange Between Biospecimen and Electronic Repositories Supporting Biomedical Data Research

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Background: This presentation contributes to an emerging debate over how to best define biomedical information found in publicly available survey data. The collection of biomedical information is an increasingly important element of research for both the biological and social sciences. Evidencing the importance of publicly available data containing biomarker information is the growing research literature that uses this information drawn from secondary data sources. What remains lacking is acceptable cross-disciplinary terminology that defines different categories of biomedically descriptive variables.

Methods: The presentation will introduce an organizational framework initiated as part of the NACDA data repository at the University of Michigan that differentiates between simple body measurement, the identification of chemical markers and summary measures of both types found in secondary sources.

Results: The presented approach offers incentives for cross-archival collaboration. Metrics of success use both the number of specimens distributed and the use of specimens in original research both in primary and secondary applications. The investment in time in developing cross-archival linkages is offset by the competitive advantage of better outcome measures. The approach allows the biorepository to better identify or to prioritize investment in the preservation of specific specimens as it provides concrete measures of specimen use beyond the initial snip, slice or slide.

Conclusions: The creation of information resources that reflect not only the presence of biospecimens, but their use and contributions to science offers great promise for the future. It requires a multidisciplinary approach but it will ultimately add considerable marginal value collections in biospecimen repositories.

HT 11. Well Structured Chaos: Tools for Creating Accessible, Open Source Metadata Records to Identify Biospecimen Availability, Use and Analysis Across Repositories

J. W. McNally[1], M. I. Sayre[1]

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Background: There is ongoing interest in developing seamless metadata linkages that relate biospecimen inventories with associated external information resources emerging from the use of

these specimens. The creation of "metadata", or "data about data", is well established among researchers operating repositories. Metadata also includes "data results" emerging from the use of biospecimens in research such as essays or experimentation as well as in publications. When these various metadata are maintained in unrelated collections this limits their potential value to the research community.

Methods: This presentation builds on previous work examining the state of the archival sciences and the multiple databases that catalog the existence of biospecimen inventories, data records and publications that report analysis of biospecimen data. Examples include models such as the RAND RD-HUB, NACDA, PubMed and the NIGMS Collections. The presentation focuses on emerging open source XML/DDI tools that are now organizing these independent sources of information into an integrated resource.

Results: The potential for integrated systems clearly exists. Several examples show this process already being done for individual research projects. New open source metadata management tools being developed at NACDA show how this process can be extended to cross-reference multiple collections housed and maintained at multiple independent sites.

Conclusions: The creation of information resources that reflect not only the presence of biospecimens, but their use and contributions to science offers great promise for the future. It requires a multidisciplinary approach but it will ultimately add considerable marginal value collections in biospecimen repositories.

NATIONAL & INTERNATIONAL BIOBANKING NETWORKS (NIBN)

NIBN 01. Pharmacogenomics Research in Africa: Challenges in Setting up Research-Based Biorepositories

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Background: Research in genomics is advancing at a very fast pace due to new technologies with increased sensitivity and precision in biomarker and novel targets discovery. One area of genomics that is receiving a lot of attention is pharmacogenomics. Polymorphism in genes coding for drug metabolizing enzymes have been shown to differ both quantitatively and qualitatively in different populations. Thus, a single phenotype may be caused by different polymorphisms in different ethnic or racial groups, making it difficult to extrapolate from one population to another. The objective is to form a pharmacogenomics research consortium in Africa by bringing together interested research groups and then sharing samples and data to decode the genetic variability among African populations and its effects on response to drug treatment. However, numerous problems are encountered.

Methods & Results: Groups interested in pharmacogenomics research have signed up to the formation of the research consortium. There are challenges with respect to research funding (for costs associated with acquisition, storage and preparation of samples), ELSI (e.g. data collection from communities with different cultural values, data sharing, prospective benefit and clearance of the research protocols by ethics with different rules) and the inclusion of these samples in biorepositories for future use. Suggestions will be made on how these challenges will be met.

Conclusion: By coming together, the researchers are discussing how to overcome the different challenges in order to accelerate genomics research in Africa.

NIBN 02. Pediatric Specimens for Research: The Cooperative Human Tissue Network Experience

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Background: The Cooperative Human Tissue Network (CHTN) is comprised of six academic institutions funded by NCI to provide remnant human tissue to researchers throughout the United States and Internationally. The Pediatric Division of the CHTN (pCHTN), located within the Biopathology Center at the Research Institute of Nationwide Children's Hospital, has a unique relationship with The Children's Oncology Group (COG). COG specimens are distributed via pCHTN following evaluation of scientific value of the request and subsequent approval by the applicable COG Disease Committee(s).

Methods: Investigators complete an application, provide a summary of the project for tissue use and signs an agreement regarding biohazards and commercial use. Patient identity cannot be provided to investigators to ensure patient confidentiality. Copy of an approval of the research from the investigator's local institutional review board (IRB or human use) is also required.

Results: The pCHTN ensures the proper collection, storage, and availability of high quality, well annotated human specimens, collected from pediatric patient populations. A fee for service per sample applies. Tissue microarray slides are available for 13 pediatric cancers.

Conclusions: The role of the pCHTN is the primary provider of pediatric tumors and normal pediatric cases to investigators. To maximize the number of pediatric cases available to investigators, the pCHTN has a well-established relationship with the COG. Additional contributions by pCHTN to the Network is to provide services to CHTN investigators (especially the ones who are conducting molecular studies), such as nucleic acid extractions, Tissue Microarrays (TMA), and virtual images of stained slides.

NIBN 03. The Need for a Joint ESBB –ISBER Working Group on Metadata: "ESBBperanto"

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Background: Modern research projects require large numbers of biomaterials and associated data to produce meaningful results. Most biobanks cannot individually provide the required numbers leaving researchers to approach multiple biobanks to address their needs. Biobank registries are useful to identify sample availability. MIABIS (Minimum Information About BIobank data Sharing) provides a mechanism for standardizing biobank catalogues. However, query results are often a heterogeneous mix of information and definitions. This is compounded in Europe where cultural and linguistic differences affect data.

Methods: The problem of heterogeneity of information needs to be addressed for retrospective and prospective data. For prospective collections, a minimum data set must be defined. Definitions and nomenclatures are needed to describe data items. Biospecimen Reporting for Improved Study Quality (BRISQ) (Moore et al. Cancer Cytopathology 2011;119:92–101) has provided a tiered list of items and a first step could be assigning nomenclatures to the first tier. Retrospective collections require a mapping system to the defined minimum data set. A system

similar to the Unified Medical Language System (UMLS) or National Institutes of Health, might be considered.

Results: Biobanks and researchers would benefit from standardized information on biomaterials. General concepts should be established and adapted to various biobanking fields, biomedical and environmental.

Conclusion: The biobanking community would benefit from a dedicated working group with experts from different biobanking fields, dedicated to harmonizing definitions and languages. They could present white papers on relevant biobank metadata. This ESBBperanto working group will enable comparability of biomaterials and data across different biobanks and countries.

NIBN 04. An Attempt to Establish a Network of Bioresource Facilities in Japan

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Background: Recently, demands for human samples have been increasing. As a result, many biobanks have been established not only in the US but also in other areas of the world including Japan. This increasing number of biobanks pushes them to communicate with each other and to establish a network among them. Although various networks have been established, most of the existing networks are aimed to share catalogue information of stored samples. This in a sense puts biobankers in a frustrating situation. Right now, biobankers are exposed to a flood of information evaluating outcomes of biobanking. Biobanking themselves should have appropriate support. This demand requires sharing information not only of availability of stored samples but also of biobank operations and their governance. Participants: Initially, nine bioresource facilities near Tokyo participated in a voluntary study group meeting. In addition to this, an expert in ethical and policy issues of biobanks, and also an expert in cryobiology participated.

Methods: This attempt is at the beginning phase where we introduce our activities to each other. All the representatives have exchanged their experiences in the meeting. We will continue to meet regularly and strengthen our ties.

Future Plan: Our plan is to evaluate various quality assessment methods in accordance with a variety of samples, and then provide the methods and references not only for participating facilities but also new-comers to the bioresource research community. Eventually, we would like to set up a central physical site to provide timely assistance regarding biobank operation and governance.

NIBN 05. Networking Benefits Dissected in Seperate Win-Win Situations within Eurocan Platform Biobanking

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Sharing samples between hospital integrated biobanks is needed for doing medical research with high impact on patient care. However, sharing samples is seen as a "no go" area for most investigators, afraid to lose on their institutional and departmental investment of resources. Biobanks have tried to set up networks enabling scientists to find samples they might be interested in. However, the enthusiasm to upload sample data is not always shared happily without knowing the benefits in advance.

Since the aim of the European project EurocanPlatform is to set up a European translational cancer research platform, biobanking has become one of the work packages.

Motivation and even influencing the environment of primary investigators and collectors have become key targets in the work package.

Making an inventory of possible benefits for both parties was one of the activities within the group. This resulted in a list of possible win-win situations beneficial for both collector stakeholders and scientists looking for (more) samples outside their institute. Mostly, the items on the list show situations where the collector receives either raw data for further analyses, technical skills, opportunity to use new techniques as a guest, reimbursement of costs, or opportunities to contribute to the research resulting in co publication in turn of the use of their samples. In addition, conditions are added to the specific win-win situations. Publication of the list on the Internet especially on biobank network websites and in literature could contribute to the motivation of sharing.

NIBN 06. New Innovative Technology in the Field of Repository of Cervical Cell Samples by Liquid Based Cytology

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Background: The Swedish national biobanking infrastructure, BBMRI.se (BioBanking and Molecular Resource Infrastructure of Sweden), has initiated a project for the improvement and national harmonization of biobanking procedures in clinical cytology. In Sweden, cervical screening takes place every three to five years between the ages of 23–60, primarily using cytological procedures followed by HPV testing. Liquid-based cytology is the norm.

Methods: Cervical cells are collected into a preservative medium in bar-coded glass vials and sent for diagnosis. In our new process a portion of the cell suspension is transferred to a microtiter plate format with removable tubes marked with 2D-matrix codes. This can be done very efficiently with a liquid handling robotic station. The samples are stored at −25°C.

Results & Conclusions: The preservative medium does not freeze at this temperature, which is a significant advantage for cytodiagnosis. The sample and data flow is fully tracked with a commercial Laboratory Information Management System (LIMS)

and provides a robust platform for sample management and compliance with national regulation and ethical rules.

NIBN 07. Promoting the Use of High-Quality Biospecimens for Medical Research: Integrating Quality Coding Standards for Pre-Analytical Treatment in the German Biobank Registry

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Background: Pre-analytical factors significantly influence the reproducibility of biomarker research with human biospecimens from biobanks. As generally consented evidence-based molecular assays are still missing to track biospecimen quality-states, it remains a critical first step that information regarding the handling of biospecimens stored in biobanks is made visible to researchers in an accepted and standardized manner.

Methods: (i) Integration of the 1st version of the "Standard PREanalytical Code" (SPREC) into the registering workflow of the German Biobank Registry (DBR). SPREC identifies main pre-analytical variables for fluid and solid biospecimens, e.g. in clinical settings, prior to their storage (Betsou et al., 2010; ISBER Biospecimen Science Working Group).

(ii) Preparing for automatic implementations of further extensions related to SPREC, and importantly, for future evidence-based molecular assay-based biospecimen quality-state controls.

Results: The DBR (www.biobanken.de) represents a web-based interactive nation-wide registry displaying an up-to-date overview on types of biospecimens, sample sizes and disease orientations as well as ethical issues of diverse medically relevant biobanks from Germany. Integration of SPREC helps researchers to trust in and select appropriate biobank samples for research in the first instance. However, future visions on control of the quality-state of stored biospecimens aim at relying eventually on molecular evidence-based standards.

Conclusion: National and international biobank registries must strongly support world-wide efforts to introduce coding standards for biospecimen quality-states – first being of descriptive nature and eventually being based on molecular evidence - by integrating them into their biobank registering workflows.

NIBN 08. The Project Portal for the German Biobank Registry: A Case-Specific National Biospecimen Locator

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Background: For research in translational and personalized medicine, Web-based query tools for high-quality biobanks as well as for specific cases and samples are urgently required to enable trans-institutional research access to human biospecimens and data and statistical validity of results.

Methods: By integrating a project portal (PP), the German Biobank Registry (GBR; www.biobanken.de) is complemented with an underlying metabiobank regularly importing up-to-date data from the connected local biobanks by the semi-automated CRIP protocol. Over a web-based interactive user interface, the PP enables queries on a case-by-case and sample-by-sample basis and conveys the user's search criteria as csv-file to the biobanks holding suitable specimens and data.

Results: With the PP in the GBR, a user-friendly and scalable web-based "showcase" is set up for all types and sizes of German biomedical research biobanks. Out of the 101 German biobanks registered in the GBR, so far 5 biobanks have connected to the PP: BioPsy, ColoNet, KompNet HIV/AIDS, Pediatric Diabetes Biobank, and popgen. They display up-to-date information on their samples, data, and services, and receive project requests on-line enabling them to immediately select the requested material. The PP is in full compliance with all relevant ethical and legal standards.

Conclusion: The PP for the GBR is a case-specific German biospecimen locator and a "hub" in the global biobanking infrastructure.

NIBN 09. DNA Bank Network: Information Architecture for a Global Network of Biodiversity for DNA and Tissue Banks

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Ready access to correctly identified specimens, tissue and DNA is crucial for biodiversity research, phylogenetics, biomedicine as well as for biotechnology. Having such resources available is an asset for users in all areas of basic and applied research who lack time or expertise to create them on their own. Dedicated DNA and tissue banks have been established or are being developed worldwide differing widely in accessibility of both samples and respective documenting data.

The DNA Bank Network developed a generic information infrastructure for specimen based DNA and tissue banks facilitating online access to such resources and data via a shared webportal. Data transfer is accomplished using the decentralized BioCASe information architecture, which is also in use by the Global Biodiversity Information Facility (GBIF). Data are automatically encoded using the ABCDDNA data schema, a new standard to structure and transfer DNA data via XML.

The open source DNA Module is designed to manage information characterizing each DNA sample. It enables DNA providers to reference these samples dynamically with voucher data recorded in GBIF compliant locally administrated databases and with sequence data stored in databases such as EMBL, GenBank or BOLD. Accessible voucher specimens are the only reliable basis to verify the species identity of genetic samples as well as inferred sequence data mostly specified by voucher numbers and taxon names.

Here we discuss the IT principles the DNA Bank Network is built on, the Network's generic data architecture, the DNA Module and ABCDDNA and the requirements for becoming a partner of the Network.

NIBN 10. The Belgian Virtual Tumourbank, a Tool for Translational Cancer Research

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Cancer is one of the leading causes of death worldwide. Over the last decades, tremendous biological and technological advances have been observed and to some extent translated into clinical practice. Access to human samples to look for new therapeutic targets and/or assess how the new discoveries could impact patient care is of paramount importance. In this respect, tumorbanks are valuable tools. However, the availability of tumor samples in single research institutions is often limited, especially for rare disease entities. To avoid this scattering of samples amongst different institutions, clinical and technical data from the available tumor samples from all major university hospitals in Belgium are being centralized in one central database, the so-called Belgian virtual tumourbank. This Tumourbank can be consulted via an electronic catalogue tool, allowing scientists to query a copy of this database, containing only non-identifiable data, and trace the samples they are interested in to conduct their research. The use of the national registry number as a unique identifier allows linkage with other databases. This linkage of data, available in the biobanks, with clinical information from the Cancer Registry assures not only completeness of the dataset but also an optimal quality of the data being registered and used for research purposes. Furthermore linkage with longitudinal databases (e.g. on survival, treatment or exposure) offers a rich potential source of information for scientists, allowing progress in the knowledge of the mechanism, the diagnosis and the treatment of cancer, which is beneficial for all future cancer patients.

NIBN 11. 30th Anniversary of the UCSF Aids Specimen Bank

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Background: Thirty years ago the acquired immune deficiency syndrome (AIDS) was first described in a report from the US Centers for Disease Control (CDC). Investigators and physicians at the University of California, San Francisco (UCSF) were alarmed at seeing patients that were wasting, had Kaposi's sarcoma lesions, lymphadenopathy, fungal and viral infections, etc. In order to understand what the infectious agent that was causing this disease, it was determined that a specimen bank had to be created in order to store tissues and blood samples for research purposes.

Methods: The UCSF AIDS Specimen Bank (ASB) was created in response to this epidemic in late 1982. Dr. John Greenspan organized and designed ASB and began to receive specimens from pathologists and clinicians. Request for serum and tissue samples came from investigators throughout the world. The specimens were used to help identify the causative agent of AIDS.

Results & Conclusions: Since 1982, ASB has grown from a one-person, 2-freezer operation to a large enterprise, which is comprised of 7 staff, 25 ultra-low, and 11 liquid nitrogen freezers. ASB processes over a 100 specimens (from HIV and non-HIV participants) daily and has sent out over 450,000 specimens worldwide. ASB is one the largest HIV repositories on the west coast of the United States.

NIBN 12. Korea National Research Resource Center (KNRRC): Past, Present and Future

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Biological resources are the source material for scientific investigation, leading to many of the discoveries on which biotechnology is founded. Ensuring the proper maintenance and exchange of biological resources is essential to the future advancement of biotechnology. Korea Ministry of Education, Science and Technology (MEST) and National Research Foundation of Korea (NRF) have been supporting the 'Research Resources Center' project since 1995. The Korea National Research Resource Center (KNRRC) consists of 36 research resource banks (RRBs) located in 25 universities, 5 core centers (human-originated resources, plants, animals, microorganisms, and fusion-matters) and a central office. Its collection includes microorganisms, plants, animals, human specimens, and non-biologic materials. The total inventory of KNRRC RRBs is over 14 million items. Among these, 206,309 items have accession numbers with full information in the DB and is open to the public. In 2010, 109,478 resources were distributed to scientists in universities, research institutes and industry.

The KNRRC headquarters provide a total management system for the RRBs. The KRMS (KNRRC Resource Management System) includes the homepage, DB, and inventory system for each RRB. The standard data set (SDS) and characteristics of the resources were collected and stored in the database which makes online database search, online deposition and distribution possible.

KNRRC provides educational programs for RRB staff and working on standardization and harmonization of resources in order to provide Authenticated, Customer-oriented resources with Easy access (ACE). Currently, KNRRC is serving as the head office of Asian Network of Research Resource Centers (ANRRC).

NIBN 13. Returning Genetic Research Results to Individuals: The International Cancer Genome Consortium Experience

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Disclosure of individual research results to participants has emerged as a complex and contentious issue. Approaches and practices of research investigators, funding bodies and human research ethics committees are diverse. The development and approval of ethically justified policies regarding the disclosure of results is important as genetic research is increasingly prevalent, and the focus has shifted from studying rare diseases to determining the role of genetics in common disorders such as cancer. This is the main aim of the International Cancer Genome Consortium (www.icgc.org); to elucidate comprehensively the genomic, transcriptomic and epigenomic changes present in many forms of cancers that are of clinical and societal importance across the globe.

Ethical principals of beneficence, respect and reciprocity provide justification for routinely offering certain results to research participants. The Australian Pancreatic Cancer Genome Initiative (APGI), the Australian arm of the ICGC, has employed a result-evaluation approach to returning results, which assesses the information and the context of the study in order to decide if results should be offered. Using this approach the analytical validity and clinical utility of results are considered and help determine what information is disclosed, at what time point and to whom. We present 3 cases where results were returned to participants based on this approach, and discuss the process, issues and outcomes.

NIBN 14. The Future of Biobanking in Australia? – Network, Network, Network

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Background: Clinical Biobanking in Australia has followed similar trends to other developed nations. Early beginnings of researchers assembling cohorts for specific studies, advanced to larger scale assembly of material and data, collected under open access agreements. This evolution was expedited by the National Health and Medical Research Council of Australia (NHMRC) recognizing that investment in biobanking was necessary to enable supply of quality material to the burgeoning field of "omics" research. In 2004 the NHMRC Enabling Grant (EG) scheme was introduced. The EGs provided an essential avenue of funding leading to the establishment of what are now key national resources, with the remit of being open access and having clear and transparent governance mechanisms. Over recent times increased awareness of expenditure and 'value for money' has extended to scientific research and, inevitably, biobanks. Funding streams from all avenues – local, state and national have approached the economics of biobanking with vigor, many organizations undertaking independent surveys.

Outcomes: Almost without exception, conclusions have been that the best operational framework is establishment of networks. In order to attract and maintain funding, a networked solution has to be accomplished. Several existing models worldwide have been scrutinized and the merits considered. It is likely that a combination, encompassing the best features of existing structures, will be adopted but the final model is as yet unclear and its integration into health and research realms.

Conclusions: Biobanking is posed with many challenges and a networked solution is being imposed by those financing the activities. Whether the outcomes meet the expectations remains to be seen.

NIBN 15. Connecting with International Biobank Networks: Open Innovation is a Driver for Global Harmonization of Patient-Focused Research for Individualized Medicine

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Background: The Irish Biobank Network was started by Biobank Ireland Trust in 2008. We examined how open innovation from international biobank networks has influenced biobanking practice and government funding strategy.

Methods: The main elements of the Irish biobank network - funding, main biobank focus, buy-in strategy, international involvement, consent, hospital staff involvement, biobank and network management, data handling, SOPs, Quality Control, policy-making, researcher access, attitudes, communication - were contrasted with former practice/conditions.

Results: A 4-hospital Irish biobank network has developed "bottom-up" without direct government support. Funds materialize from various sources, and 11 pharma/biotech companies have provided modest unrestricted grants. Open innovations emanating from international biobank network leaders have transformed Irish biobanking. Harmonization of SOPs, QC, (generic) patient consent and sample release was established with help from patient groups and the Data Protection Commissioner. Pathologists and other hospital staff play a central role. Researchers, prospectively biobanking, share samples/data with the network. Researchers trained in biobanking can provide cover for biobank personnel: this promotes an understanding of *quid pro quo*, sharing and recognition of a bigger picture than "my project." Multiple samples/data from over 1100 patients are available. Media coverage has increased public awareness.

Conclusions: The network's strength is that people (patients, hospital medical staff and management, pathologists and biobank personnel, pharma/biotech, patient groups, the public, government agencies and media) work together. Each hospital biobank is at a different developmental stage. Government agency funding must be lightly administered and carefully allocated to leverage translational biomedical research in Ireland.

NIBN 16. Comprehensive Biospecimen Resource for the caHUB and the National Institutes of Health's Common Fund Genotype Tissue-Expression (GTEx) Program

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Background: The Cancer Human Biobank (caHUB) includes biospecimen source sites (BSS), a comprehensive biospecimen resource (CBR), a pathology resource center (PRC), and a comprehensive data resource (CDR) to implement the collection and management of high quality biospecimens for the NIH Common Fund's Genotype-Tissue Expression (GTEx) program. GTEx will study human gene expression and regulation in multiple normal tissues, providing valuable insights into mechanisms of gene regulation compared to disease-related perturbations.

Methods: VARI's Program for Biospecimen Science (PBS) was selected as the CBR for the caHUB. Using a stringent Quality Management Program and standard operating procedures (SOPs) the CBR produces biospecimen kits for the collection of up to 32 tissue types from each organ procurement or rapid autopsy case. Tissues are placed in a fixative (PAXgene) to maintain nucleic acid quality then shipped to VARI via overnight express shipment.

Results: The GTEx program is fully operational, collecting up to 11 cases per month with generation of genomic data by the Broad Institute. Sixty-five patient cases ($n = 1200$ specimens) have been collected (May to December of 2011) resulting in good quality RNA. The collection, processing, and pathology review and shipment of biospecimens to the Broad Institute are completed within 9 days.

Conclusions: The caHUB's CBR management of biospecimen collections has a proven track record for the NIH's GTEx project for normal tissue. The BSSs, CBR, PRC, and CDR as designed by the caHUB with the NCI-SAIC-Frederick are a well-organized system to acquire process and manage high quality tissues and data for research.

NIBN 17. Challenges of Linking Disparate Biobank Databases – A Case Study: Linking the Gynaecological Oncology Biobank at Westmead (WGOB) into the Australasian Biospecimen Network - Oncology Tissue Specimen Locator

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Background: The Australasian Biospecimen Network-Oncology (ABN-Onc) comprises eight biobanks that collect biospecimens for research. ABN-Onc has developed a web-based Tissue Specimen Locator (TSL) which allows researchers to interrogate a national database for available biospecimens (www.abrn.net/abnweb/OncologySearchPage.aspx). The challenge was linkage to the TSL of disparate databases on diverse IT platforms.

Method: The TSL was designed to allow linkage of databases via a minimum data set; 'Primary Cancer Site', 'Broad Morphology' and 'Type of Sample'. In this paper we present a case study describing obstacles that were overcome in the process of linking in WGOB. WGOB is a gynecological cancer-specific bank, based in a health care facility, with a Mac FileMaker Pro database.

Results: Two project teams, the central ABN-Onc hub and an on-site team at Westmead, (including a dedicated project manager, pathologist and IT professional per site) worked together to address issues related to:

- the data dictionary for data mapping
- coding of data stored within the WGOB database
- mode of data transfer, ensuring patient confidentiality considering firewall barriers
- TSL data QC and ongoing maintenance

Conclusion: The WGOB database was able to share information regarding biospecimens available for research via the TSL. The data linkage protocols developed included clear communication strategies and focus on risk mitigation. The TSL project facilitates the process for new oncology biobanks to list their collections on the TSL, increasing and promoting access to biospecimens for oncology research while enabling biobanks to retain custodianship of specimens and maintenance of their current database.

NIBN 18. The Prostate Cancer Biospecimen Network (PCBN)

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Background: Recent acceleration on new technological platforms increased demands on biospecimens used for post-genomics research projects. This coincided with a shift in the banking of biospecimens as variability can be attributed to processing history rather than intrinsic differences, resulting in limited availability of biospecimens useful optimally for research. The Prostate Cancer Biorepository Network (PCBN), a collaboration between Johns Hopkins School of Medicine (JHU), New York University School of Medicine (NYU), and Department of Defense (DOD), was developed in recognition of this need. Although prostate cancer (PCa) biospecimens are available at many institutions, they often represent convenience samples, lack detailed annotation and are collected and processed without uniform protocols.

Method: PCBN procures clinically-annotated fresh-frozen and formalin-fixed prostate tissues, fluids and derived analytes, in a systematic, reproducible fashion under stringent conditions. PCBN conducts biospecimen science research to annotate critical parameters in the biospecimen "life cycle" and evaluate their impact on molecular integrity and biomarker findings.

Results: The biospecimens offered include large, comprehensively-annotated cohorts that accurately represent the spectrum of PCa. Tissue microarrays (TMAs) are constructed for rapid biomarker discovery studies and verified for adequate fixation. Analytes are derived with maximal recovery from samples with known hypoxic and thermal histories to ensure comparable molecular profiles.

Conclusions: Clinical translation of promising biomarker research is hampered by lack of availability of high-quality, well characterized prostate specimens and lack of understanding of the impact of pre-analytical variation on biomarker test results. The PCBN will provide critical resources and biospecimen science to enhance the validity and translation of PCa biomarker research.

RETURN OF RESULTS (ROR)

ROR 01. Biospecimen Resource for the Multiple Myeloma Research Foundation CoMMpass-SM Study

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Background: The Multiple Myeloma Research Foundation (MMRF) launched a genomics study, CoMMpassSM in collaboration with Translational Genomics Research Institute (TGen), Van Andel Research Institute (VARI) and Spectrum Health Medical Center (SHMC). The primary aim of CoMMpassSM is to collect biospecimens from 1,000 multiple myeloma (MM) patients. The goal is to integrate genomic changes associated with major clinical events, including treatment response and disease progression. Comprehensive reports will inform physicians of potentially actionable results, such as, evidence of minimal residual disease, rational selection of therapies and clinical trial eligibility. The biospecimen resource will fuel discovery of new therapeutic targets, drug development and biomarker validation.

Methods: Biospecimen kits are designed by VARI for collection of bone marrow aspirate and peripheral blood. Kits are tracked from design through shipment and use. Kits maintain biospecimens between 2–8°C during shipment to SHMC for characterization by flow cytometry and BRAF sequencing in a clinical diagnostic laboratory. VARI isolates CD138+ tumor cells and nucleic acids for molecular sequencing and analysis at TGen.

Results: CoMMpassSM biospecimen management includes kit design, distribution, tracking, processing and biobanking. Since Q2'11, 25 patient cases have been processed. Flow cytometry

confirms diagnosis and tumor purification. Here we present the number and integrity of MM cells necessary to achieve high quality sequencing.

Conclusions: Comprehensive biospecimen collection and genomic characterization is key to implement personalized medicine initiatives. The MMRF, in partnership with VARI, SHMC and TGen, establishes a network through CoMMpassSM study to identify new drug targets and biomarkers for MM patients.

ENVIRONMENTAL REPOSITORIES (ER)

ER 01. Asian Network of Research Resource Centers (ANRRC)

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Asian countries have a diverse range of ecosystems with the vast variety of flora and animals. The plant resources are extremely extensive and the majority of them an endemic with considerable potential for resource development. An international network of Biological Resource Centers is a critical element of the infrastructure that supports advances in the biological sciences and their capacity to contribute to sustainable growth.

To promote continuous discovery of resources in Asia, KNRRC organized an ad-hoc meeting to initiate ANRRC in January 2009. At this meeting, three institutes of Japan (RIKEN BRC), China (IMCAS) and Korea (KNRRC) signed MOU for cooperation. The inauguration meeting of ANRRC was held in Seoul, Korea in the same year with more than 300 people from 12 countries participated. The second annual meeting was held at RIKEN, Tsukuba, Japan where the first and second president of ANRRC were elected for a two year term. In 2011, IMCAS (Institute of Microbiology, Chinese Academy of Science) hosted the third ANRRC meeting.

The ANRRC members comprise 69 institutes from 13 Asian countries and the numbers are expected to increase. The cooperation of Asian RRCs will facilitate the exchange of scientific, technical, environmental, and legal information; case studies; and best practices and experiences on issues relating to biosafety, biosecurity, and bioresources.

The implementation of the cross-training program of scientists will improve the quality of the management of the resource centers. KNRRC wishes to encourage Asian RRCs to explore ways of promoting mutual benefit and prosperity through shared scientific and industrial advances.

ER 02. Nontuberculous Mycobacteria Repository in Korea

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Background: Nontuberculous Mycobacteria (NTM), pathogens as acid-fast bacillous except *Mycobacterium tuberculosis* complex and M. leprae, are ubiquitously distributed in the environment. The increasing incidence of pulmonary disease by NTM has made it essential for laboratories to identify NTM species from clinical specimens. In Korea, the KMRC (Korean Mycobacterium Resource Center) has collected various NTM and has cooperated with NCCP (National Culture Collection for Pathogens in NIH) in 2009.

Methods: Recently, useful methods for identification of the diversity within the genus Mycobacterium has been introduced, such as sequence-based taxonomy from environmental and clinical isolates. In this study, we performed the identification of NTM isolates based on sequence analysis of 16S rRNA gene, rpoB gene, hsp65 gene, erm gene and 16S-23S internal transcribed spacers(ITS).

Results: We separated 44 species from clinical specimens by sequence-based identification method. Identified species are as follows: *M. abscessus, M. massilliense, M. bolletii, M. chelonae, M. marinum, M. szulgai, M. malmoense, M. lentifulavum, M. triviale, M. parascrofulaceum, M. arupense, M. obuense, M. kumamotoense, M. paraseoulense, M. celatum, M. aubagnense, M. neoarum, M. kubicae, M. shimoide, M. goodii, M.gilvum, M. timonense, M. shinjukuense, etc.*

Conclusion: Biological resources are necessary to improve the quality of the human health, agriculture and environment. Especially pathogenic resources which are used as essential materials for studying to develop diagnostic techniques, medical cures and vaccines. The Korean institute of tuberculosis (KIT) has run KMRC for supporting mycobacterial research activities. The KMRC obtained the ISO 9001 certificate and various NTM isolates are stored under systemic control.

ER 03. Continued Expansion of the Marine Environmental Specimen Bank into the U.S. Pacific Islands Region

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The National Institute of Standards and Technology (NIST) has been involved in long-term environmental specimen banking since 1979 through environmental research and monitoring programs. Today, NIST maintains an archive of marine biological and environmental specimens (i.e. marine mammal tissues, marine sediments, shellfish samples, fish tissues, bird eggs and feathers,) collected throughout the coastal continental U.S., including Alaska, in support of these programs. Samples are archived at the Marine Environmental Specimen Bank (Marine ESB), Hollings Marine Laboratory, Charleston, SC USA. In 2010, the 111th U.S Congress directed NIST to expand its biodiversity storage capabilities and resources into the Pacific region through a Pacific Islands component. NIST has developed collaborations with Federal, State, and local agencies, as well as universities and industry in this region to expand on-going projects, successfully collecting samples for the National Marine Mammal Tissue Bank and the Seabird Tissue Archival and Monitoring Project. Future projects are also being established for the collection of sea turtles as well as for coral ecosystems and mussels and oysters. These collections will help improve biological and chemical measurement capabilities in environmental health and research and address future questions regarding the effects of human-induced and natural stressors on environmental conditions and marine animal/human health in the unique ecosystems of the Pacific region. In addition, NIST is developing a 'satellite' biorepository in this region in order to maintain some samples locally as well as to provide a back-up system to store duplicate samples in separate geographic locations.

HUMAN SPECIMEN REPOSITORIES (HSR)

HSR 01. Management of an Institutional Biobank in a Tumor Center

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The Institutional Tissue Bank of Fudan University Shanghai Cancer Center was established in 2006 with the goal of serving as

a central repository for human tissue samples for cancer research and personalized medicine. The ITB's collection procedures meet global quality standards, providing high reliability of tissue samples. Quality control for morphology, RNA, DNA and protein has been set up to ensure the sample quality. The Tissue Bank occupies 500 square meters, with sufficient space for sample preparation, sample storage, data registration, data tracking/access, related equipments and monitor system. Variant samples including blood, tumor tissue, and body fluid are collected and serve as alternative permanent patient tissue records.Up until December 2011, 50,000 samples are stored dynamically.

HSR 02. From Many to One- An Initiative to Develop an Institution-wide Human Specimen Repository at an Academic Medical Center

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Background: The Oregon Health and Science University Biolibrary is an organizational umbrella for many of the human specimen repositories on campus. Its goals are standardizing the method by which specimens and related data are collected and managed, increasing the visibility and use of the repository resources and upholding the rights and wishes of donors. These goals are key to meeting the vision of building an expansive resource to support basic and translational research. Like many academic institutions, OHSU has been collecting and storing specimens for decades. Specimen data are currently managed in Excel, Access, physical files and home-built databases. Secondary specimen use is low, and we argue that this is primarily due to the lack of an informatics solution that enables cross-protocol searching. A standardized model is necessary in order to best grow and utilize biospecimen resources.

Methods: Our methods included identifying stakeholders, assessing current operations, and forming governance and advisory structures to define the vision, strategy and tactics for the initiative. We addressed consenting of specimen donors, specimen acquisition, management and utilization, community engagement, informatics solutions, and the operational model.

Results: The results section contains the operational models considered, business requirements for an informatics solution, outcomes from discussions with stakeholders and the public, and the proposed specimen management model.

Conclusion: The conclusion summarizes the key findings and next steps to implementing the infrastructure and crafting communications.

HSR 03. Biobank Certification: Development of a Program by the Canadian Tumour Repository Network (CTRNet)

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Background: One goal of CTRNet is to improve the capacity/quality of cancer biospecimens and data through standardization of biobanking processes. CTRNet achieves this by creating national standards to promote the ability of cancer researchers to utilize tumor biobanks. Two areas of focus in the past year have been the creation of a Biobank Certification Program linked to an Education Program.

Methods: CTRNet developed a Biobank Certification Program comprising two linked phases, Registration and Certification – and a supporting Biobank Education Program, both targeting the full spectrum of tumor biobanks. The program design was formulated over a period of 2 years after international landscape assessment, national consultation with a range of stakeholders, advice from leaders from the ethics and research communities, and input from working groups drawn from leaders and staff of leading Canadian biobanks interested in such a process to help ensure public confidence in biobanking and quality of biospecimens for research.

Results: The Registration phase of the Certification Program was launched at a workshop held at the Canadian Cancer Research Alliance Conference in November 2011. The elements comprise an online registration form that enables classification of the biobank and a 'basics of biobanking' online educational module (accessed through www.ctrnet.ca) which take ~15 and 60 minutes respectively to complete, based on pre-launch testing across CTRNet biobanks.

Conclusions: The benefits of deployment of a Certification program are widely accepted across biobank, research and ethics communities to foster biobank standardization, ethics review and public confidence, and increased quality in translational cancer research.

HSR 04. Collecting Blood for Research in the Asian American Community: A Collaboration Between the UC Davis Cancer Center Biorepository and the Asian American Network for Cancer Awareness, Research and Training (AANCART)

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Background: The UC Davis Cancer Center Biorepository (CCB) and AANCART conducted three blood drives and tested blood from Asian Americans with limited English proficiency for Hepatitis B infection and diabetes to create a snapshot of these conditions in this community.

Method: A specific AANCART consent form was developed, translated into Vietnamese, Hmong and Chinese and approved by the local IRB. Blood drives were organized as add-ons to events such as health fairs and special screenings. The UC Davis Department of Pathology and Laboratory Medicine provided phlebotomists and supplies. Interpreters consented participants with limited English proficiency. Participants received gift cards to local stores. Research participants were assigned study IDs and completed a one-page questionnaire in regards to age, gender, race, ethnicity and medical history such as diabetes or HEP B infection. Specimens were sent to the clinical lab for immediate testing or stored in the Biorepository −70°C freezer for future research.

Results: We collected 585 specimens from 146 subjects. Fourteen of 146 tested postive for the Hepatitis B surface antigen. Five of 59 were considered diabetic based on the hemoglobin A1C test

and thirteen showed high levels of glucose indicating an increased risk for diabetes.

Conclusions: Collaboration with AANCART to collect research specimens in the Asian American community aids in the goal to reduce cancer health disparities and promotes biospecimen collection for research. The support of the clinical laboratory and interpreters is critical for success.

HSR 05. From Institutional to National Biorepository, A Roadmap for a Rapid Expansion

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The National University Health System (NUHS) Tissue Repository (formerly NUH-NUS Tissue Repository) is a diseased-based repository with a single specimen collection site at the National University Hospital, Singapore. Since the middle of the year (2011), the repository was tasked to take over the disease and population-based collection at the Singapore Biobank, formerly Singapore Tissue Network, which houses close to a million specimen with collection sites spreading across multiple hospitals and clinics in Singapore. Here, we describe the challenges in the rapid scale up of repository in terms of (1) Storage of the specimen from a single site facility to multi-sites (2) Logistics of receiving of specimen from multiple collection sites (3) Specimen processing scale up (4) Data management. We were able to transition from a single site diseased-based biorepository to a multi-site disease and population-based biobank with an almost ten-fold collection increase within 6 months.

HSR 06. Commencement of a BioBank with V.A. Almazov Federal Center for Heart, Blood and Endocrinology

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Background: V.A.Almazov Federal Center for Heart, Blood & Endocrinology is one of the leading centers of North-West Russia specialized in cardiological/cardiosurgical, hematological and endocrinological care, fundamental and translational research. Today, V.A.Almazov Center unites a Clinical Complex (350 beds) with an outpatient dept., Rehabilitation Complex (300 beds), Perinatology Center (130 beds), hemotransfusion station, numerous auxiliary units and services.

Methods & Results: Commencing a biobank, V.A.Almazov Center accepts a dual-purpose layout: namely, Clinical BioBank section (blood, umbilical cord blood, bone marrow specimen, homografts, etc. intent for clinical applications) and Research BioBank section of mixed origin: populational and pathological (primarily, cardiovascular, hematological and endocrinological) biospecimen. Biospecimen of both low-tech processing requirements (frozen whole blood, PAXgene, serum, plasma, slides/smears, urine samples) and high-tech processing requirements (purified DNA, RNA, viable and FF PBMC & BMMC samples, etc.) are collected and stored.

Conclusions: The V.A.Almazov Center BioBank is a newly commenced human specimen repository serving longitudinal, multidisciplinary and multi-site research projects. Algorithms matched to the targeted diseases (principal and secondary timepoints, biospecimen collection and biospecimen processing particulars) are presented, as well as the BioBank structure and workflow layout (sample indexing principles, storage formats, disease-specific clinical forms, etc.).

HSR 07. Not Just a Repository - The CRI Pediatric BioBank & Analytical Tissue Core: Making an Impact on Research Studies by Offering Analytical Services to Investigators

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Background: The Pediatric BioBank & Analytical Tissue Core (PBATC) of the Children's Research Institute (CRI) at the Medical College of Wisconsin has procured over 10,000 samples since its establishment in 2008. Banked specimens include pediatric tumors and developmental malformations, as well as placenta, blood, bone marrow, and normal tissues. The PBATC additionally offers the following analytical services to provide specialized experimental support for tissue-based research:

- High-resolution slide scanning
- Quantitative image analysis
- Laser-scanning cytometry (tissue sections and adherent cells)
- DNA, RNA, and protein extraction from blood, fresh, frozen or formalin-fixed-paraffin-embedded tissue samples
- Generation of tissue micro-arrays (TMAs)
- Primary cell line generation

Some of these analytical services are also utilized for PBATC specimen quality assessment and for improvement of procurement workflows and storage protocols.

Methods: We documented usage of analytical services offered by the PBATC and correlated this usage with investigators' scientific output over a period of 12 months.

Results: In 2011 alone analytical services provided by the PBATC were utilized by >30 principal investigators from numerous local and national and one international institution. Data collected using PBATC analytical services were reported in five presentations at national and international scientific meetings, published in seven peer-reviewed journals, and used as preliminary data for four successful extramural grant applications.

Conclusions: Offering analytical services within the Pediatric BioBank & Analytical Tissue Core to facilitate tissue-based research has not only increased revenue to strengthen the PBATC, but has also helped PBATC clients to enhance their research quality and productivity.

HSR 08. Developing a First Nations Tissue Banking Framework

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Background: Indigenous peoples in Canada lack health services and experience lower health status than the general population. Lack of access to services results in underrepresentation of Indigenous peoples in medical research. It is important to include Indigenous populations but significant

violations in research ethics and institutional racism provide good reason for many First Nations to distrust the Western medical system.

Methods: Key informant interviews were performed in eleven Carrier Sekani First Nations to assess trust of the medical system, medical research and utilization of tissue samples. Iterative coding and thematic analysis identified areas of opportunity and trust/mistrust.

Results: This study identified that 52/58 participants trusted researchers, while 6 were skeptical of researchers. The majority of participants ($n=39$) had no concerns with tissue research, whereas a minority ($n=2$) indicated they did not feel comfortable with tissue research. There was a documented need for improved communication between researchers and the public ($n=32$).

Conclusions: Building on this research, a multidisciplinary team has been formed consisting of First Nations community members, Western clinicians and medical researchers. The team is developing a framework through community consultation, to determine how to perform biomedical research and tissue banking in accordance with First Nations Principles of Ownership, Control, Access, and Possession (OCAP). In the historical context of research with Indigenous populations, this framework will set the foundation upon which future biomedical and genomic research can progress, with respect for the ethical and cultural issues now expected.

HSR 09. Banking Breast Biopsies from Women Facing a Neo-Adjuvant Therapy Following Cancer Diagnosis

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Sheba Medical Center is a university-affiliated tertiary hospital that serves as Israel's national medical center in many fields, although it is not focused only on cancer patients.

The existing breast bank (established 28 months ago) already holds biospecimens of 231 patients, including:

- Tumor tissue of only 58 patients.
- 75 patients donated only blood.
- 20 patients donated ascites fluid for culturing tumor cells.

Molecular and biochemical QC tests as well as pathological evaluation, performed on representing samples, confirm that all samples are of best quality.

Only 25% of samples were of tumor tissue, due to the fact that many breast biospecimens didn't meet the rigid criteria for collection:

"Don't bank tissues under the following conditions: 1. When you don't have a proven biopsy of invasive breast cancer. 2. Where tumor size is less than 1.5–2cm. 3. DCIS patients, as the pathologist cannot assess the specimen macroscopically. 4. Patients who underwent neo-adjuvant therapy. In case 'Informed Consent Form' was signed, bank blood specimens only."

Therefore, we recently decided to establish the first Israeli tissue bank for breast biopsies from cancer-diagnosed women facing a neo-adjuvant therapy. Following IRB approval, we started collecting breast biopsies for the new bank on 08-2011.

These samples are being collected when the patient arrives to mark the tumor prior to neo-adjuvant treatment. So far we collected biospecimens of 18 patients (out of 23 relevant cases). In this manner we anticipate collecting biospecimens of $\sim$70 patients a year.

HSR 10. Comparison of Biospecimen Collection Methods from a Large Geographical Region: A BC Generations Project Perspective

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Background: The British Columbia Generations Project (BCGP) aims to recruit 40,000 British Columbia residents aged 35 to 69 for its prospective study that includes acquiring biological specimens on each enrolled participant. Participants are recruited from all regions within BC, Canada's third largest province with a land mass of 947,800 km^2. This large geographical region presents some challenges when collecting biological samples.

Methods: Participants to our first assessment center (AC) were able to donate their blood and urine specimen on-site during the time of their visit. Subsequent ACs have had participants donate their specimens at a nearby private laboratory. For participants joining via the at-home enrollment package, a lab requisition is provided for a local private laboratory (if available) while those who live more than two hours from the nearest available laboratory, a saliva kit which could be mailed to their home, was offered.

Results: Of the 4,609 participants who attended our first AC, 4,590 provided a biological sample (>99%). Participants attending subsequent ACs (N=4) have donated samples 88% - 94% of the time. Only 44% of samples have been obtained from mailed lab requisitions and 22% of invited participants provided a saliva sample.

Conclusion: Obtaining biological samples from participants is most successful when you can link it with an assessment center visit. For those individuals joining from home, more effort will be needed to collect their samples.

HSR 11. Development of a Biobank Resource Centre (BRC) by the Office of Biobank Education and Research (OBER) and the Canadian Tumour Repository Network (CTRNet)

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Background: The Office of Biobank Education and Research (OBER) is a provincial initiative of the Department of Pathology and Laboratory Medicine, University of British Columbia. OBER's goals are: 1) to promote certification of B.C. tumor and non-tumor biobanks in order to enhance quality through standardization and foster public confidence in biobanks; 2) to facilitate adoption of best practice-based standards through education; and 3) to provide active support for new and established biobanks. To address our third goal, OBER created a Biobank Resource Centre (BRC) in collaboration with the Canadian Tumour Repository Network.

Methods & Results: The BRC consists of: 1) live biobank support and 2) a needs/issue assessment strategy and online tool, 3) a fit-for-purpose document library, "tool-kit", and services intended to support all phases of biobanking. Documents include process maps, plans, procedures, equipment and performance catalogue, and facilities design plans. Tools include a biobank user fee costing tool; and Biospecimen Reporting for Improved Study Quality (BRISQ) tool. Services include a biobank

pathology annotation and analysis service, and biobank business plan development.

Conclusions: OBER has been established as a center to communicate common standards and policies amongst biobanks and between biobanks and the public through education, training and support in the form of the BRC.

HSR 12. Epstein-Barr Virus Transformed Human Lymphoblastoid Cell Lines: A Practical Perspective on the Effect of Donor Age and Gender on Transformation Efficiency

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Background: Genetic Repositories Australia provides a national facility for the processing, storage and distribution of human genetic samples including DNA and lymphoblastoid cell lines (LCLs). The current study examined factors that predicted successful transformation.

Methods: *In vitro* transformation of human B-lymphocytes with Epstein Barr virus lead to the establishment of permanently growing (immortalized) LCLs. The effect of donor age, gender and sample cryopreservation on the efficiency of transformation was investigated.

Results: LCLs were successfully established across all age groups and cohorts. 978 of 991 samples were transformed into LCLs (fresh lymphocytes 829/841, 98.57% efficiency, cryopreserved 149/150, 99.33% efficiency), a transformation success rate of 98.69% overall. The effect of gender on transformation has not previously been reported. In this study, males transformed sooner than females (median = 34 vs. 36 days to transform respectively, $p < 0.001$). The number of days to transform cryopreserved lymphocytes was less than fresh lymphocytes (median = 34 vs. 35 days respectively, $p < 0.001$). As donors increased in age, so did time in culture ($p < 0.001$) although, interestingly, donors >90 years transformed in the same time as the younger adults (20–64years).

Conclusion: This study provides a practical perspective on factors affecting transformation efficiency and shows LCLs can be successfully transformed irrespective of age or disease status. Overall, males and cryopreserved lymphocytes transformed sooner however these effects fell out when donor age was considered. A prospective randomized study will examine these specific effects in detail. Establishment of LCLs are a valuable component of any human biobank, this study demonstrates there are no intrinsic barriers to their successful production.

HSR 13. Unique Challenges and Opportunities of a 'Prostate' Specific Tissue Bank

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Background: The Australian Prostate Cancer BioResource (APCB) vision is to provide a unique, quality assured facility for the collection, storage and access to tissue to support research into the treatment and cure of prostate cancer. The APCB is a federated tissue bank comprised of four nodes located in Brisbane, Sydney, Melbourne and Adelaide. The APCB is a 'not-for-profit' entity, funded jointly by the NHMRC (National Health and Medical Research Council) and the Prostate Cancer Foundation of Australia (PCFA).

Methods: Key to the establishment of the APCB was strong drive and leadership from principle investigators from each node. This included having a clear vision, goals, objectives and strategies established to ensure nodes were aligned to the common purpose. Some key challenges were the development of best practice standardized protocols for biobanking tissue across the four nodes. Node ICT (Information and Communications Technology) capability needs to align despite varying databases requiring specialist operational knowledge. Cost increases in the face of the Global Financial Crisis have impacted the ability for coordinators and management to meet face to face and have also driven dependency on ICT to maintain communication.

Federating biobanks into a national entity has enabled many opportunities. Larger and specific cohorts can be built which aids research discovery, facilitates validation of biomarkers and enables participation in large scale consortia.

Processes have been harmonized across nodes and economies of scale regarding consumables and equipment are utilized.

Results: To date the APCB has collected 15,171 samples from 3,519 men and has distributed 1,724 samples to researchers.

Conclusions: To federate existing tumor banks clear vision, streamlined processes and strong governance structure is vital.

HSR 14. Standardization and Quality Control of Protein Samples of Biorepositories for Gastrointestinal Cancers in Japan

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Biobanks are a critical resource for recent clinical research and medicine as they generate a high quantity of genotypic and phenotypic data. Combining the genetic and molecular information with clinical data or patients' records will help us to understand disease mechanism at the molecular level. The ultimate goal of biobanks is to develop new targeted diagnostics and therapies to promote so-called 4P medicine "predictive, preventive, personalized and participatory" medicine. For this purpose, we applied proteomics procedures to discover novel biomarkers for gastrointestinal cancer diagnosis or treatment, and found the storage conditions of sera and plasma is critical for future usage. So far we have collected a large amount of sera and plasma from gastrointestinal cancer patients and is stored centrally at −80°C in Chiba University Hospital, Japan. Fresh-frozen tumor materials are also stored. Our biobank is a rich resource for gastrointestinal cancer patient-related tissues (sera, fresh-frozen and paraffin-embedded tumor tissue, DNAs and RNAs) for future translational research. In this study, standardization and quality control of sera samples for biobanking will be presented and discussed.

HSR 15. Potentials and Pitfalls in Establishing a Global Network for Bio-Specimens of Neurological and Mental Rare Diseases

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Background: Neurological disorders affect the brain, spinal cord and nerves of the central and peripheral nervous systems. While many neurological and mental disorders are common, others occur infrequently and are recognized as rare disorders. The scientific research community and pharma companies are desperately in need of such specimens. Our biorepository faces specific difficulties to recruit donors, due to the small numbers and the lack of patient's organizations.

Methods: The rare neurological and mental disorders we collect include Alexander's disease, Kluver-Bucy Syndrome, Charcot-Marie-Tooth Disease, Creutzfeldt-Jakob Disease, Guillain-Barré syndrome, Kuru and Capgras delusion.

To recruit donors we use patient registries, contacts with neurologists and nursing homes and work on the following:

1. Harmonization of standard operating procedures (SOP's).
2. Setting the legal and ethical Code of Conduct.
3. Stimulate the search for Biomarkers of these diseases.
4. Set up consensus on Global Regulations for Biobanking.
5. Set up a Global infrastructure for a digital inventory/D-base of available specimens.
6. Formulate strategies to increase collaboration/exchange of specimens/data for research.

Conclusions: Global exchange/collaboration of specimens of neurological/mental rare disease would greatly benefit from an increased number of biorepositories, working closely together. Currently, there is little collaboration and there are no inventories, or accessible D-bases. Adapting the National Cancer Institute model of the Specimen Resource Locator and the NIH RD-hub (National Institutes of Health Rare Disease-HUB) model may facilitate specimen availability and ISBER can play a major role in this globalization process.

HSR 16. The SWAN Biorepository Model

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Background: The SWAN Repository is the biological specimen bank of the Study of Women's Health Across the Nation. SWAN is a multi-site, longitudinal study of the natural history of the midlife including the menopausal transition. The goal is to describe the chronology of the biological and psychosocial characteristics that occur during midlife. SWAN describes the effect of the transition and its associated characteristics on health and risk factors for age-related chronic diseases. SWAN was designed to collect and analyze information on demographics, health and social characteristics, reproductive history, pre-existing illness, physical activity, and health practices of mid-life women in multi-ethnic, community-based samples; elucidate factors that differentiate symptomatology; utilize biomarkers of the aging ovarian-hypothalamo-pituitary axis and relate these to alterations in menstrual cycle characteristics; and explain factors that differentiate women susceptible to long-term pathophysiological consequences of ovarian hormone deficiency.

Methods: SWAN has seven clinical sites recruited in 1996–97 and consists of 3302 women (Hispanic, Japanese, Chinese, Caucasian and African American) groups. The biological specimen bank can be linked to data collected in the Core SWAN protocol that includes epidemiological, psychosocial, physical, and biomarker data.

Results: The SWAN Repository includes over 1.8 million samples of serum, plasma and urine from annual visits. The DNA collection contains extracted and diluted DNA from 1538 participants (except Hispanic). Samples are free of identifiers and collected under consents that allow a broad range of activities related to women's health.

Conclusion: These samples are available to researchers who wish to study the midlife menopausal transition.

HSR 17. Eastern Maine Medical Center BioRepository (EMMCB)

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Background: The state of Maine leads the USA with the highest age adjusted cancer incidence rate for both men and women. Eastern Maine Medical Center (EMMC) and its oncology department CancerCare of Maine recognized the need, opportunity, and challenge to contribute to basic and translational research by developing a biorepository of well annotated human specimens in the current financial climate of limited resources.

Methods: In late 2010, oncologists, surgeons, pathologists, key administrators, clinical laboratory and research professionals came together to develop the EMMC BioRepository (EMMCB). To circumvent the need for study specific protocol and consent approval by the local IRB for each specimen request, a general collection protocol was created that allows prospective, retrospective, and ad-hoc banking of a variety of human specimens (i.e. blood, bone marrow, residual tissue) from consented participants (patients with malignancies and controls). The EMMCB protocol and consent are subject to regular IRB review and comply with the federal mandate of the protection of human subjects in research as well as with HIPAA. To review, grant, and regulate end-user specimen and data access, a multidisciplinary EMMCB Specimen Allocation Committee was created to evaluate each end-user request.

Results & Conclusion: By the end of 2011 and within 8 months of operation, EMMCB has consented more than 160 individuals for specimen collection (blood and/or tumor tissue) and has provided an equal amount of annotated biological specimens to qualifying researchers. We are preparing to expand and improve our physical banking facilities and to add new disease sites to our collection.

HSR 18. Biospecimen Use and Emerging Techniques in Cancer Research

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Background: The average cohort size for tissue biospecimens used in cancer research studies has increased >3-fold over 20 years. To understand some of the factors behind changes in biospecimen use we hypothesized that emergence of specific techniques assaying certain products drive these observed biospecimen trends.

Methods: We assessed 378 publications using tissue biospecimens, representative of all papers from 1988 to 2010 in the journal Cancer Research. Publications were categorized by biospecimen utilization, format type (Frozen, formalin-fixed paraffin-embedded (FFPE) and fresh), extract type (RNA, DNA, protein, cells and molecules) and research techniques performed.

Results: We observed changes in techniques, biospecimen formats and products assayed, but no significant changes in the number of techniques performed per paper. There was an increase in use of FFPE format biospecimens and also the proportion of techniques assaying RNA products from biospecimens of all formats. The ratio of RNA:DNA products assayed has increased >10 fold for both frozen and FFPE formats over the past 17 years.

Conclusions: While specific techniques such as the tissue microarray analysis have clearly driven changes in requirements there is an overall trend towards focusing on gene expression across all formats of biospecimens. Since pre-analytical variables influence gene expression more than gene structure, recognition of this research trend is important for biobanks and their decisions around priorities for optimal biospecimen preservation format and annotation.

HSR 19. Working Toward a Common Purpose: The Building of a Shared Biorepository for Demyelinating Disease Research

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Background: Multiple sclerosis (MS), neuromyelitis optica (NMO), transverse myelitis (TM), and acute disseminated encephalomyelitis (ADEM) are severely disabling inflammatory demyelinating diseases of the central nervous system. Currently, the causes and mechanisms of each are poorly understood and treatments are only partly effective.

Methods: To accelerate progress in curing these diseases, three nonprofit organizations have collaboratively created an open-access multi-disciplinary blood sample and data repository for studying these disorders individually and jointly. Each organization – Accelerated Cure Project (ACP), Guthy-Jackson Charitable Foundation (GJCF), and Transverse Myelitis Association (TMA) – while focused on separate disorders, recognized the opportunity to achieve operational and scientific benefits by creating a common resource.

Results: The repository has to date enrolled 2,231 subjects with demyelinating diseases and 613 controls. Most were enrolled through a network of 10 participating clinics. However, creative strategies were developed to enhance the enrollment of patients with rare diseases such as NMO and TM. For instance, GJCF provides financial support for a traveling registered nurse to collect samples and data from NMO subjects in remote locations. Also, temporary enrollment stations have been established at several patient meetings and camps sponsored by GJCF and TMA.

Conclusions: The repository has been operating successfully since 2005 and has supported 60 studies, including several that have investigated similarities and differences among the diseases. By pooling together not only their financial resources, but also their scientific expertise, problem-solving skills, and patient outreach channels, three organizations have built a much richer resource than they could have developed alone.

HSR 20. The Impact of Preanalytical Variables on Biomarker Research

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The scientific efforts on biomarker discovery research in the past five years have resulted in numerous potential biomarker candidates. These biomarkers, however, require further investigation by verification and validation in the clinical setting prior to specific application. One major hurdle in the transition from the research lab to the clinical lab is preanalytical variability, most notably, time and temperature, which have significant impact on analyte stability. This presentation will discuss the potential impact of sample handling on protein and peptide stability and how this variability can be controlled through the use of protease inhibitors. Specifically, the presentation will discuss the stabilization of Glucagon-like peptide-1 (GLP-1), Gastric inhibitory polypeptide (GIP), Glucagon, and Ghrelin, four plasma peptides of particular interest in metabolic disorder research, especially diabetes drug research. The extremely short half-life of these metabolic peptides in blood provides a challenge for accurate analysis; therefore, preservation of proteomic sample integrity is vital. Some of the methods to minimize instability in these samples will also be examined including:

- The use of time-course mass spectrometry to characterize the kinetic digestion of each incretin peptide caused by active plasma endogenous enzymes;
- Incorporation of a cocktail of protease inhibitors in blood collection tubes (e.g., BD™ P800 blood collection system) to minimize variability/instability.

Stabilization of the aforementioned peptides enables their use in pharmacokinetic and pharmacodynamic studies. Further, stabilization of proteins and peptides could improve the success rate of transitioning biomarker candidates from discovery research to clinical applications.

HSR 21. How to Effectively Build Process Efficiencies for Long-Term Sample Lifecycle

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Today, biomaterials such as whole blood, human tissue, DNA and RNA serve as the foundation for translational research that holds the promise of bringing personalized medicine from bench to bedside. As such, these materials must be closely monitored at every point - from patient collection until they reach the end of their lifecycle. This process can sometimes span several decades and involve extensive sample testing, complex transportation of samples between research laboratories and protein extractions from preserved samples, all of which requires dedicated human and technological resources. However, by taking a holistic approach to sample management, in which every component of the sample lifecycle is considered during upstream planning, the biorepository can be leveraged to accelerate drug development and bring novel medicines to market.

The presenter will give an in-depth, step-by-step overview of every component included in the sample lifecycle and highlight specific processes that can increase efficiencies in biorepository operations. Specific topics that will be discussed include:

Registration processes that help ensure efficient inventory management throughout the complete sample lifecycle

Standardized protocols for sample preparation techniques to reduce pre-analytical variables

Cold chain processes that ensure sample integrity on a global scale

Good storage practices to protect sample assets

Standard operating procedures for proper disposal of research samples

HSR 22. Experience of Establishing and Organizing the First ICMR National Tumour Tissue Repository (INTTR) in India

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Background: The INTTR was established in 2005 to adopt standardized methods for collection, long-term storage, retrieval, and distribution of diseased as well as normal tissues and components of blood, to maintain and provide clinical information to the individual investigators while protecting the confidentiality and interests of specimen donors and to provide a follow-up record of all patients whose tissues are maintained in the biorepository.

Methods: The process of establishing INTTR was classified into various tasks viz. operational, administrative and dealing with ethical/legal issues. Standard operating procedures were established for collection, storage, reterieval and disbursement of tissues. Indigenously developed software is being used to anonymize the biospecicmens and to facilitate storage and reterieval of biospecimens. The biospecimens are collected following administration of informed consent. Disbursement of tissues is done for institutional review board approved projects. A material transfer agreement is executed for disbursement to non-institutional investigators.

Results: During the period of 6 years from May 2005 to November 2011, a total of 20,534 tissues were collected from various anatomic sites following administration of informed consent and 1205 tissues were disbursed to the principal investigators for various institutional review board approved projects. Clinical information was provided as per the investigators needs.

Conclusions: Central tissue repository has many advantages like better control of biospecimens, easy availability of various types of tissues and an increased opportunity to participate in intramural and extramural research. A biorepository can be easily implemented in a pathology laboratory and is a valuable institutional asset for translational research purposes.

HSR 23. The "North German Tumorbank of Colorectal Cancer" as Part of the Priority Program Tumor Biobanks Funded by the German Cancer Aid Foundation

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Background: The German Cancer Aid Foundation (Deutsche Krebshilfe e.V.) supports four biobank networks focusing on CNS tumors (CNS-TuBa), melanomas (MELACONSORT), breast carcinomas and colorectal carcinomas. The latter one, briefly called "ColoNet", comprises university clinical centers, private oncology practices and non-university medical centers (see above affiliations). While coordinated by surgical disciplines, ColoNet operates interdisciplinary involving surgeons, pathologists, gastroenterologists, and oncologists.

Methods: ColoNet's steering committee and task force have developed and installed the harmonization of standard operating procedures (SOPs) concerning all biobanking aspects including overall quality measures. In addition, common scientific projects have been initiated.

Results: ColoNet has harmonized SOPs for sample collection and processing of native material, DNA, RNA, miRNA and serum. Crucial steps for quality assurance have therefore been implemented and resulted in certification according to DIN EN ISO 9001. Further objectives are the expansion of the sample and clinical data collections and the construction of a web-based sample search data base accessible via http://www.northgermantumorbank-crc.de under section "Samples".

Such repository will be used for research projects in order to improve early diagnosis, therapy, follow-up and prognosis of colorectal cancer patients. Apart from the routine sample storage at −170°C, ColoNet's unique characteristic is the participation of outpatient clinics and oncologists in private practice.

Conclusion: The funding by the German Cancer Aid has already led to a closer scientific connection between the participating institutions and to a substantial collection of biospecimens obtained under highly standardized conditions.

HSR 24. The Challenge of Developing Economic and Management Tools to Pilot a Biobank

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Biobanking is an emerging activity in the era of translational research and personalized medicine. The high quality of biospecimens on one hand and the implementation of efficient processes on the other hand allow biobanks to stay at a competitive level.

An entrepreneurial approach needs to be favored even though biobanks are and have to be considered as non-profit organizations. Sustainability and cost recovery analyses should be adopted to pilot biobanks. In Switzerland, the "Biobanque de Lausanne", a state of the art biobank focused on cancer, has developed economic models to optimize price setting considering not only the cost price of sample storage and distribution, but also infrastructure maintenance costs. These models should be flexible enough to be adapted to the development of biobanking field and researcher's needs.

Biobank's promotion as well as collaborations need to be favored outside but also inside the institution to allow success of the biobank, and efficiencies of scale. In Lausanne, besides its common activity, the biobank has developed a specific service for the management of human biospecimens in the context of oncology clinical trials. This service is the reflection of a win-win collaboration throughout which the biobank was promoted and the hospital recognized as a professional and high-quality translational center for oncology patients.

The biobanking field is an exciting field where a lot has been developed, but still needs to be much more expanded and successfully implemented in Switzerland.

HSR 25. The Russian Human Radiobiological Tissue Repository: A Unique Resource for Studies of Plutonium-Exposed Workers

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Background: In 1948, the Soviet Union established a nuclear weapons production complex called the Mayak Production Association in Ozyorsk, Russia. Plutonium and other radioactive materials were released into the environment after a series of accidents and poor management practices at Mayak between 1948 and 1967, while lower level occupational exposures continued among workers for several more decades. As a result, thousands of people in this unique cohort have received significant radiation exposures.

Methods: The United States and Russian Federation agreed to establish and maintain a state-of-the-art tissue repository, funded by the U.S. Department of Energy, to serve as a resource for studies of the effects of protracted internal and external radiation exposure on human health. A major goal is to provide the key data for future reassessments of plutonium and other radiation protection standards and regulations in the United States and worldwide.

Results: The Russian Human Radiobiological Tissue Repository (RHRTR) currently contains autopsy and/or surgical tissues (including tumors) from over 1,000 registrants, including Mayak workers and residents of the general population of Ozyorsk (controls) who had never worked at Mayak. Additionally, blood specimens and extracted DNA have been acquired from nearly 5,000 registrants, including multiple members of over 170 families (comprising men who had worked in the Mayak production facilities, spouses, and children). All specimens are annotated with medical, sociodemographic, and exposure data.

Conclusions: The materials of this unique biorepository are available to interested scientists worldwide, representing an unprecedented opportunity for studies on the Mayak population.

HSR 26. Banking General Population Specimens for Biomarker Discovery and Validation: The BC Generations Project

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Background: The British Columbia Generations Project (BCGP) aims to recruit 40,000 British Columbia residents aged 35 to 69. Participants are recruited by a variety of methods including mailed invitations, media, community awareness, and referrals. Participants provide biological samples, questionnaire information and physical measurements, and give permission for follow-up through linkage to administrative health records and use of the data and specimens for research on cancer and other chronic diseases. Data and specimen collection procedures and products are harmonized with those used in other Canadian provinces with the Canadian Partnership for Tomorrow Project. BCGP participants will be followed prospectively for a minimum of 25 years.

Methods: Biological specimens are processed for subsequent long term cold storage of plasma, buffy coat, red blood cells, serum, whole blood, and urine. Samples are fully tracked using a customized laboratory information management system. Quality control and quality assurance procedures are in place and are being expanded as necessary.

Results: As of November 30, 2011 17,233 subjects have been recruited with 15,388 completing a physical measures assessment and 11,327 providing a biological sample.

Conclusion: A middle age, prospective BC population biorepository is being generated. This prospective cohort will focus primarily on the investigation of environmental and lifestyle risk factors for cancer and their interaction with genetic risk factors. In addition, identification of pre- and post- cancer biomarkers will be enhanced with the collection of additional samples at future times.

HSR 27. Development of the Cincinnati Children's Hospital Biobank

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Background: Rapid expansion, over a very short period of time, from a biobank servicing a few institutional researchers into a large regional biobank necessitated sweeping changes. These changes required a dedicated group of individuals willing to provide the visionary leadership necessary to overcome the many issues that arose.

Methods: Networking has provided informed decisions concerning the type and location of our bank, samples to collect, services to offer, and equipment required to provide the highest quality services at the lowest cost. Instrumentation, along with a robust quality assurance program, ensures high quality products. Personnel educate employees and the public about the role of biobanks and importance of pre-analytical variables to quality scientific studies.

Results: In addition to our on-site facility, an off-site facility of approximately 2700 square feet has been renovated and now houses 30 freezers with additional space for sample processing and expansion. Robotic instrumentation for DNA sample processing and quality control will allow us to save close to $90,000 in labor costs each year while processing more samples with higher quality. Education to both the public and employees has garnered a high level of confidence in our endeavors.

Conclusion: Successful expansion of the Cincinnati Biobank Core Facility has required a great network of knowledgeable and invested individuals willing to provide expertise and advice as well as listen to the needs of our target audience.

HSR 28. Accrual of Non-Malignant Tissues from Reduction Mammoplasties – A Valuable Source of Control Samples for Translational Research: The Canadian Breast Cancer Foundation (CBCF) Tumor Bank Experience

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The use of non-malignant tissues as controls is a valuable way to identify, explore and understand molecular mechanisms contributing to the state of malignancy. A major limiting factor is the availability of high-quality surgically resected non-malignant tissues that meet the same standards as tumor tissues found in biorepositories. Benign tissues resected from patients undergoing cancer-related surgeries (often referred to as "normal adjacent tissue") is not appropriate for all investigations, particularly those examining genetic factors of predisposition. Most surgeries involving the resection of non-malignant and non-diseased tissues involve traumas and biobanking is rarely feasible. The CBCF Tumor Bank, in collaboration with an Alberta plastic surgeon, launched an initiative to bank tissues from consenting reduction

mammoplasty patients. The American Society for Aesthetic Plastic Surgery reports that approximately 138,152 North American women underwent reduction mammoplasties in 2010[1], making it a common planned surgery that allows for pre-surgical identification of candidate participants. Tissues are snap-frozen within 20 minutes of devitalization and stored following the same procedures as tumor tissues. Clinical data are obtained from the study participants, including any personal or familial histories of cancer. The majority of participants have reduction mammoplasties for non-cancer related reasons such as cosmetic considerations and mammary hyperplasia causing neck and back pain. Since 2005, approximately 150 samples of non-malignant breast tissues have been accrued and subsets of these specimens have been utilized by researchers. This presentation will outline the accrual procedures, quality control aspects and the potential use of this resource of Alberta's CBCF Tumor Bank.

HSR 29. University of Colorado Skin Cancer Biorepository: Building a Better Cancer Research Biobank

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The University of Colorado Skin Cancer Biorepository was established in 2005 at the newly built Anschutz Medical Campus at the University of Colorado in the Division of Medical Oncology. The Cutaneous Oncology Clinic sees approximately 50 diagnosed skin cancer patients a week, the goal of the biorepository is to consent and collect blood from all patients and follow up specimens: resected tumors (melanoma, squamous cell carcinoma, basal cell carcinoma, and Merkel cell carcinoma) and normal tissue. The Skin Cancer Biorepository is organized into 4 essential components: first, the attending physicians and research clinical coordinators, consenting patients and obtaining blood samples. Second, is the laboratory, where the samples are processed, annotated and properly stored. Third, is further careful annotation of each de-identified sample with clinical data and laboratory data and subsequent entry into a database established exclusively for the Skin Cancer Biorepository. Fourth, is the distribution of samples to qualified investigators for studies approved by the Scientific Advisory Committee. Biospecimens collected are tissue/tumor, whole blood, serum, plasma, RNA and DNA – and the annotated "data" are the clinical information pertaining to the patient/donor of that particular biospecimen. The biorepository also includes extensive modern molecular biology capabilities to isolate and analyze the chemical components (DNA, RNA, miRNA) from tissue/tumors from over 1700 patients. The ultimate goal of the bank being not to just store human biological specimens, but rather to stimulate the discovery and validation of findings important to the detection, prognosis, and treatment of skin cancer.

PLANT/SEED REPOSITORIES (PSR)

PSR 01. Ex Situ Conservation of Short-Lived Seeds of Salicaceae: Factors Affecting Seed Viability During Mid-Term Storage and Cryopreservation Success

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Seeds of many Salicaceae species are known to be short-lived since they lose viability during storage at conventional seed bank temperatures of around −18°C. We investigated factors affecting desiccation tolerance, storability and the response to cryopreservation (−196°C) for seeds of twelve Salicaceae species collected in mountain conservation forests and of seven willow clones used in soil detoxification program. Storability of seeds was positively affected by an air-cleaning procedure which is commonly employed to Salicaceae seeds before storage. Additionally, seed storability was found to be dependent on lot provenance, vigor of the seed lot and seed water content. However, there was no direct influence of seed lot vigor on the range of safe water contents (hydration window) for cryopreservation. The hydration window was narrow for seeds of *Salix gracilistyla* (0.10-0.17 g g-1DW) regardless of viability. Low viable seeds of *S. caprea* clones had similarly narrow hydration window but at elevated water content (0.20-0.37 g g-1DW). For seeds of rare Korean willow *S. hallaisanensis*, the hydration window was determined as 0.14-0.31 g g-1DW. No critical water content was revealed for seeds of *Populus alba* × *P. glandulosa* up to 0.12-0.2 g g-1DW depending on the seed lot. With all species, germination and production of normal seedling were not affected by cryogenic storage when seeds were cryopreserved within their hydration windows. The study opens the door for routine implementation of cryopreservation for conservation of Salicaceae seeds in the seed banks and emphasizes the need to account for seed lot quality when developing cryopreservation protocols.

PSR 02. Korea Brassica Resource Bank

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The genus Brassica, phylogenetically related to *Arabidopsis thaliana*, is one of economically important crops and a botanical model of plant polyploidization and rapid phenotypic evolution. We established the Korea Brassica Genome Resource Bank (KBGRB) in order to supply basic plant materials for structural/functional genomics and breeding of Brassica. Since the establishment of KBGRB in 2004, KBGRB has supported genomic materials for Multinational Brassica Genome Sequencing Project and collected over 10,000 accessions of Brassicas from different areas in the world. KBGRB has collected seeds including inbred lines and mapping population of various Brassica species, and DNA stocks including BAC libraries and cDNA libraries of *Brassica rapa*. Moreover, all germplasms of KBGRB have been propagated, maintained, and distributed to scientists in the world. Currently, KBGRB has collected 11,041 accessions of Brassica species, 33,159 clones for cDNA libraries, and 222,336 clones for BAC libraries, and 1,398 genetic markers. KBGRB has distributed more than 621,345 clones, 280 genetic markers and 6,210 accessions of seed to researchers in over 10 countries since 2004. Information and other requests for genomic resources of Brassica are accessible at http://www.brassica-resource.org.

BIOSPECIMEN SCIENCE (BSS)

BSS 01. Room Temperature Stability of Cardiac Troponin I, B-type Natriuretic Peptide, N-terminal ProBNP and Hs-CRP Collected in Various BD™ Vacutainer® Tubes

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Background: Knowledge of *in vitro* stability of cardiac troponin (cTnI), B-type natriuretic peptide (BNP), N-terminal proBNP (NT-

[1]www.surgery.org/media/statistics

proBNP) and hs-CRP in samples collected from patients with different diseases in BD™ Vacutainer® tubes containing anticoagulants or P100, a protease inhibitor cocktail, is incomplete.

Methods: Specimens were collected from patients with acute myocardial infarction (STEMI, $n=10$ and non-STEMI, $n=10$), heart failure (HF, $n=20$) and end-stage renal disease (ESRD, $n=20$) in tubes containing no anticoagulant, EDTA, Li-Heparin or P100. Samples were centrifuged, aliquots frozen at −70°C within 15min (baseline). Remaining aliquots were incubated at room temperature (RT) for 30min, 1h, 5hr and 24h before storage at −70°C. Analyte recovery for each BD™ Vacutainer®-type was determined; trends in analyte recovery were examined by Chi-square analysis.

Results: Baseline values ranged from (0.015-39ng/mL) for cTnI, (3-2644pg/mL) for BNP, (5-32178pg/mL) for NT-proBNP and (0.35-9.48mg/L) for hs-CRP. No trend in degradation (recovery) for the disease states for any analytes over time was observed except for BNP. BNP degradation over 24 hours at RT was 13% in EDTA plasma, 38% in heparinized plasma and 60% for serum ($p=0.0014$). BNP showed no degradation in samples collected in BD™ P100 protease inhibitor tubes.

Conclusions: cTnI, NT-proBNP and hs-CRP recovered well with all Vacutainer® types after RT incubation for 24h. BNP did not recover well for serum, heparin or EDTA collections. Collection in BD™ P100 Vacutainer® tubes demonstrated high recovery for all analytes after 24h incubation at RT, including BNP. Collection of labile analytes such as BNP in BD™ P100 Vacutainer® tubes is advantageous.

BSS 02. Therapeutic Drug Target Interactions by Mass Spectrometry Proteomic Analysis of Formalin Fixed Paraffin Embedded Pediatric Brain Tumors

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Background: Proteomic platforms are emerging as an invaluable tool for personalized medicine particularly in the field of oncology. The recent availability of protocols to extract high quality proteins from archived tissue samples fixed in formalin and stored in paraffin blocks for mass spectrometry analysis opens an array of diagnostic and therapeutic possibilities.

Methods: Formalin fixed paraffin embedded (FFPE) tissue samples from 3 atypical teratoid rhabodid tumor (ATRT), 3 anaplastic astrocytoma (AA), 3 ependymoma (EP) and 3 medulloblastoma (MED) were retrieved from the pathology files. A representative block was selected for laser dissection and protein extraction per protocol (Expression Pathology). Proteins were analyzed with a ThermoScientific LTQ-Orbitrap XL mass spectrometer and peptides were matched to protein libraries (X!Tandem).

Results: The results were filtered for proteins with at least 95% confidence. Unique proteins for each tumor and associated therapeutic drug-target interactions (TDTI) were determined through software analysis (GeneGO). There was a total of 1,070 proteins and 397 were unique: ATRT (161), AA (64), EP (61) and MED (111). Nineteen TDTI were associated with these unique proteins: ATRT (5), AA (8), MED (6). No TDTI were associated with EP unique proteins.

Conclusions: Mass spectrometry now provides an opportunity for a greater array of analysis of tissue samples. The proteomic analysis of FFPE samples offers a significant potential for improved personalized medicine in pediatric oncology and should be strongly considered as an adjunct in future clinical trials involving pediatric brain tumors.

BSS 03. Controlled Analysis of Preanalytical Variables in Clinical Blood and CSF Sample Collection, Processing and Storage

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Blood and cerebral spinal fluid (CSF) sample collection, processing, handling and storage protocols are based mainly on accepted practices rather than careful comparative analysis and testing. We set out, therefore, with the support of the National Cancer Institute and the National Institute of Neurological Disorders and Stroke, to examine variables intrinsic to each step in the process of obtaining and storing clinical samples, beginning with collection of samples from healthy and diseased subjects in controlled studies. For blood, various tube types were tested including EDTA, heparin, serum and protease inhibitors. For both blood and CSF, various times on bench and temperatures of incubation were compared. The effects of freeze-thaw cycles and time in freezer were also examined. For CSF subjects, seated or recumbent collection and fasted or fed conditions were compared. Sample analysis has been performed by high resolution mass spectrometry, leading to the identification of specific proteins that are affected by the various parameters tested. While different blood collection tubes can be used with reproducible results, there is a marked difference in the protein content obtained from each type, with protease inhibitor tubes offering significant protection from changes to the proteome (of CSF, as well). Freeze thaw cycles affect only a few specific proteins and only after multiple cycles. CSF samples are robust with respect to subject condition, but are affected by temperature and time of incubation prior to freezing. A multiplexed assay is currently being assembled for the analysis of stored samples in order to determine sample integrity and utility for use in clinical research.

BSS 04. Management of a Tumor Bank and Potential Determinants of Success: Experience of Canadian Breast Cancer Foundation (CBCF) Tumor Bank

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Background: The CBCF-Tumor Bank (http://www.abtumorbank.com) is a resource for translational research. Identification of determinants for success of a tumor bank operation was attempted, including breast and ovarian cancer specimen usage and any potential correlations between rates of utilization of specimens and their clinicopathological characteristics.

Methods: Specimen accrual statistics, usage patterns and clinical data were retrieved from a relational in-house database (MySQL), called DORA (Database for Online Retrieval and Analysis).

Results: As of Dec 1st, 2011, specimens had been accrued from 5,061 cases of which 45% and 6% were breast and ovarian cancer specimens, respectively. Annual request rates from academic centers in Canada, USA and UK increased linearly over five years

(2007-2011). Utilization of specimen types to-date were germline DNA from buffy coat cells ($n=1553$) > tumor tissues ($n=709$) > serum ($n=114$). One hundred percent utilization for germline DNA was noted from breast cancer specimens. We observed a linear correlation between published median five-year survival rates and rates of utilization for the cancer types examined. Specimens of poor prognosis categories (metastatic or triple negative in breast cancer), and ovarian high-grade serous carcinomas showed higher utilization rates. Ease of access (time between initial request by a researcher and the shipment of the materials), may also play a critical role in the overall success of the tumor bank.

Conclusions: Similar analysis is recommended for all tumor types to justify and align resources available within tumor banking programs. Funding: CBCF-Prairies/NWT Region, Alberta Cancer Foundation, and Alberta Cancer Prevention and Legacy Fund/Alberta Innovates-Health Solutions.

BSS 05. Impact of Shipment and Storage Conditions on Cell Viability and Function Assessed by Different Testing Methods

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Collaboration between biobanks may accelerate research, but numerous factors can affect biological specimen integrity throughout this process. Logistics and sample transport can introduce significant preanalytical bias. Many variables can influence the sample integrity during the logistics process, including: temperature, packaging, sample type, seasons, customs, and transit time/ship days. Most critical samples to be sent are those samples which must remain viable during and after shipment.

In our study we have focused mainly on the impact of two critical factors: (1) shipping temperatures, and (2) different applied preservation media. Therefore, two different sample types, peripheral blood mononuclear cells (PBMCs) and Jurkat cells, have been analyzed using different techniques before and after shipping at different temperatures (room/ambient temperature, dry ice, and liquid nitrogen), as well as before and after storage in different preservation media (serum with cryoprotectant, cryopreservation solution, and room temperature transport medium).

Sample quality was measured by determining levels of viability and apoptosis, whereas sample functionality was assessed by ELISPOT. The viability parameters were assessed by trypan blue dye exclusion, flow cytometry and CASY counter.

Our results showed that certain shipment conditions, especially the room temperature transport media, dramatically affected the integrity of the sample during the shipment at various temperatures and in different preservation media. Therefore the analytical results were differently affected according to the specific method used.

The obtained results suggest specifications of the optimal conditions for viable cell samples' shipment and downstream assays.

BSS 06. Development of a Unique Human Cancer Xenograft Model: Essential Role for the UC Davis Cancer Center Biorepository

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Background: The NSG mouse, developed by Jackson Laboratories (JAX), lacks mature B and T cells and functional NK cells making it a unique, immunodeficent model for human tumor xenografts. Since September 2009, our biorepository (CCB) has provided 133,220 fresh human tumor samples for immediate engraftment utilizing our pre-operative consenting protocol which ensures absolute patient confidentiality by providing only coded specimens to investigators.

Methods: Informed consent is obtained by surgeons during a pre-operative visit. CCB is notified immediately of patient consent. On the day of surgery, the specimen is delivered fresh to pathology where the pathologist determines the availability of "remainder tissue" for research. Any "remainder tissue" is placed in RPMI solution, coded by CCB and transferred to JAX. Tumor is engrafted into the NSG mice within 1-2 hours of surgical resection and monitored for tumor development. Tumors are harvested within 4-6 months of engraftment at 1cm size with samples submitted for genomic analysis, histopathology and re-engraftment.

Results: To date, sixty patient derived xenografts (PDX) models of diverse tumor types including 20 lung, 10 glioblastoma and 10 pancreatic tumors have been established successfully. Morphologic comparison of the patient and mouse tumors has demonstrated remarkable fidelity. Genomic analysis for EGFR and KRAS mutations has shown excellent correlation in 10 lung samples to date.

Conclusions: Following OHRP guidelines for informed consent and patient confidentiality, the biorepository has become an effective resource for providing fresh human tumor tissue to JAX for immediate engraftment.

BSS 07. Linking Biospecimens to Patient Clinical Information to Advance Rare Diseases Research

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Background: Although there may be few patients diagnosed with a given rare disease in a single country or around the globe, their cumulative public health burden is significant, with great unmet medical needs collectively. In the United States, it is estimated that there are about 25 million people suffering from rare diseases. To help rare disease patients, and to better understand the underlying pathogenesis of rare diseases, linking patient data and medical information to donated biospecimens is essential.

Methods:

1. Establish a Global Rare Diseases Patient Registry and Data Repository-GRDR.
2. Aggregate patient information using Common Data Elements (CDEs).
3. Establish Rare Disease Human Biospecimens (RD-HUB).
4. Link biospecimens to patient de-identified information: using coded voluntary Global Unique Identifiers (GUID) Interfacing with RD-HUB.

Results: The Office of Rare Diseases Research (ORDR), in collaboration with PatientCrossroads, Children's Hospital of Philadelphia and Medscape have:

1. Launched a pilot project to establish the GRDR http://grdr.info to collect de-identified patient clinical data for research.
2. Developed a set of Common Data Elements (CDEs) for patient data entry to collect and aggregate data in a meaningful manner http://www.grdr.info/index.php/common-data-elements.

3. Established a web-based database/website for rare disease biorepositories and biospecimens, RD-HUB http://biospecimens.ordr.info.nih.gov/ to locate biospecimens and to interface with GRDR.

Conclusion: By aggregating de-identified patient clinical information through a data repository using ORDR CDEs and linking to biospecimens, the GRDR will serve the rare disease community and its investigators conducting research, initiating natural history studies, developing clinical trials and eventually developing treatments for the rare disease patients.

BSS 08. Long Term Storage of Fluorescent *In Situ* Hybridization (FISH) Slides

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Background: Molecular cytogenetic diagnostic test of FISH technology is an important methodology for evaluation of and/or predicting breast cancer patients. The HER2 FISH test is one of the critical tests in this field for selection of therapeutic agents such as trastumab. Although the FISH technology is adequate, there is a drawback. The FISH technology utilizes fluorescent signals, and these signals would fade out relatively rapidly even stored at −20°C.

Materials: Multiple HER2 stained FISH slides derived from 10 different cases were used for this study.

Methods: The stripping procedures were done, such as removing cover glass, fluorescent probe, and diamidino-2-phenylindole. Then the slides were stored at room temperature, 4°C, −20°C, and −80°C for 11 days, 31 days, and 101 days respectively. Following these storages, each slide was stained under routine FISH procedure. As a control, one slide was stored at −20°C in a regular fashion. Evaluation was done by using an automatic signal count program of MetaCyte software.

Results: Under −80°C and −20°C storage up to 101 days, no remarkable signal fadeout was observed. So far no noticeable fadeout has been observed even in control slides stored at −20°C. Under room temperature, and 4°C storage, remarkable signal fadeout was observed.

Conclusions: Although this study is preliminary, once stained FISH slides can be stored long term under −80°C, and −20°C after stripping. This stripping and re-probing technology can be applicable on special occasions.

BSS 09. Standardizing Surgical Pathology Summaries for Biorepository Specimens

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Background: Surgical pathology reports are examined and used to assist in the management of patients routinely in clinical care. However, the ability to search for discrete information within these reports can be difficult and may impede the transfer of the associated pathological information to investigators using banked samples for research.

Methods: The University of Florida CTSI Biorepository is working with pathologists and basic science researchers throughout the institution to develop standardized pathology confirmation reports by anatomical site that can then be provided to researchers requesting banked specimens from the library.

Results: Pathology confirmation reports for seventeen anatomical sites have been created with the assistance of consulting pathologists. Basic scientists, who are actively using tissue from the various anatomical sites in their studies, are also being consulted to ensure that the reports capture information relevant to their research. The CTSI Biorepository will then work to capture the information into the database for standardized reporting purposes.

Conclusions: The goal is to capture relevant information from the reports in an easily searchable and reportable way outlining the pathological status for each tissue sample at the time samples are requested. We propose that the time it takes researchers to find samples that meet their research needs will be substantially reduced by eliminating the need to review pathology reports for all samples of interest before selecting those that meet their research criteria.

BSS 10. Analysis of Genomic DNA Stored in QIAsafe DNA and GenTegra™ DNA Biostabilization Storage Matrices

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Background: Currently, biological materials such as nucleic acids are shipped and maintained in cold environments (4°C, −20°C, −80°C) to preserve sample integrity. Exposure to elevated temperatures (for example: during shipping delays) and to freeze-thaw cycles can degrade samples. This study evaluates two technologies for stabilizing DNA at room temperature.

Methods: Whole blood genomic DNA (two donors) was isolated, normalized, and aliquoted. DNA was stored in QIAsafe DNA (QIAGEN or Biomatrica® as DNAstable®) and GenTegra™ DNA (IntegenX) matrices according to the manufacturers' protocols. Stability through real time, accelerated stress (37°C and 76°C), and multiple cycles of freeze/thaw or dehydration/rehydration was compared to dried DNA or DNA stored at −80°C. DNA recovery was assessed by quantitating the rehydrated or thawed DNA by PicoGreen assay. DNA quality was analyzed by agarose gel electrophoresis and PCR amplification.

Results: Real time stability studies show that DNA recovery and quality are stable for 32 months in both QIAsafe and GenTegra stabilization systems (real time studies are ongoing). Both systems protect DNA at 37°C for up to 8 weeks; QIAsafe DNA shows some degradation at 76°C. Up to four dehydration/rehydration cycles were performed with no reduction in DNA quantity, quality, or integrity for either system.

Conclusion: Both QiaSafe and GenTegra stabilize DNA at room temperature. Hydration and recovery of DNA is easier with QiaSafe, but GenTegra provided better stabilization at 76°C. Both systems appear suitable for biobanking and shipping samples at room temperature, reducing costs without compromising sample quality and consistency.

BSS 11. The Integrity Study Phase I: Measuring the Impact of Sample Preparation Techniques and Storage Temperatures on the Integrity

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Background: The presenter will highlight data collected during the first six months of a 24-month longitudinal research project that evaluates the affect various sample preparation methods, different aliquoting schema and storage temperatures have on DNA and RNA. The study's targeted outcomes will be

highlighted and the first release of monthly RNA analysis will be presented.

Methods: The longitudinal study analyzes the desiccated powder storage method that requires reconstitution and frozen storage of pre-extracted samples versus extracted DNA, which require freeze/thaw cycles for processing. Five storage temperatures (4-6°C, −20°C, −70°C, −80°C and LN_2) and two aliquoting strategies are being evaluated over a 24-month period. During the study, data will be reported every six months.

Results: The poster will outline the first phase of the INTEGRITY study, which will provide data on collected RNA samples. The presenter will also outline the study design and discuss data to be obtained and reported during the remaining phases of the study. Various methods and procedures to capture and store samples for future research purposes will also be discussed.

Conclusion: The goal of the INTEGRITY study is to determine the best method and length of time and temperature for storing samples for future research analysis. With the proper protocol design and standard operating procedures in place, inconsistencies and discrepancies in sample integrity can be alleviated in a timely and efficient manner and the risk of sample loss can be mitigated.

BSS 12. Storage Form of Peripheral Blood Components Determines Quality of Extracted DNA and RNA

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Background: Post-storage quality of distributed blood component samples and their derivatives is affected by various pre-analytical as well as storage factors. The precise nature and impact of these factors has not been studied in detail. As a result, blood components are stored in many different ways to meet all researchers' needs. However, hospital integrated biobanks often only have limited volumes of blood available for storage. In search of the most versatile procedure for storage of blood components, we studied the effect of storage form on the quality of DNA and RNA extracted from frozen buffy coat (BC), red blood cell lysed white blood cell (WBC) pellets and WBC suspensions.

Methods: Peripheral blood of healthy volunteers was fractionated into BC, WBC pellets and/or WBC suspensions. These were snap-frozen in LN_2 and stored at −80°C for 6 weeks. Subsequently, DNA and RNA was extracted and the yield, integrity and real-time PCR performance was analyzed.

Results: DNA yield per 1000 WBC tends to be higher when extracted from BC compared to WBC pellets or suspension, but purity, integrity and PCR performance are comparable between the 3 storage forms. In contrast, although RNA yield per 1000 WBC is comparable, RNA integrity and PCR performance is severely affected when stored as WBC suspension. Surprisingly, storage of cells as BC does not appear to affect RNA quality.

Conclusions: Qualitative DNA and RNA can be obtained from short-term stored BCs. Studies to evaluate the application of long-term BC storage as valid RNA source are ongoing.

BSS 13. Serum vs. EDTA and Citrate Plasma for Cytokine Detection in Multiple Sclerosis (MS) Patients: Evaluation of the Better Sample for Biomarker Development

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Serum and plasma samples have long been used interchangeably in clinical research settings for various cytokine analyses. This study evaluates cytokine levels in serum, EDTA and citrate plasma from MS patients to determine the most suitable sample for biomarker studies.

Peripheral blood from 26 MS patients was collected into SST, EDTA and ACD tubes. To control the time variant these tubes were collected in a single draw, processed and stored within one hour of blood collection.

Cytokine analysis in serum, EDTA and citrate plasma from each patient was done using MSD human proinflammatory 9 PLEX ultra sensitive plates. The cytokines analyzed in this study were GMCSF, IFN-g, IL-10, IL-12p70, IL-1b, IL-2, IL-6, IL-8, TNF-α. Regardless of the cytokine being measured, EDTA plasma showed very low levels of cytokines compared to serum and citrate plasma (ACD). Serum and citrate plasma showed insignificant differences for cytokines IFN-γ, IL-10, IL-12p70, IL-2, IL-6 and TNF-α. Majority of the cytokines had similar pattern of results in serum and citrate plasma and these samples were superior to EDTA plasma for cytokine analysis using MSD multiplex kits. Future cytokine studies should consider the sample type before drawing clinically useful conclusions.

BSS 14. Comparison Study of RNA Quality and Integrity After Room Temperature Storage in Various Preservation Systems

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A multicenter study investigated quality of RNA preserved for 2 weeks in the following RNA room temperature (RT°) storage systems: RNAstable® (Biomatrica), Gentegra™ (IntegenX) and RNAshell™ (Imagene). As these systems are based on the anhydrobiosis principle, the study design included dried RNA stored at RT° and additional control conditions: liquid RNA at RT° and at −80°C. 357 RNA samples produced from 7 donors at a single center. Samples were shipped to five centers where RNA was applied to RNAstable® and Gentegra™ at five centers while RNA was applied to RNAshell™ by Imagene. Finally, the samples were shipped at ambient temperature to three testing centers. Samples were rehydrated following two weeks storage and isochronous analysis was performed. Spectrophotometry and RIN measurement showed that RNA yield and RIN values were similar for RNAstable®, Gentegra™ and RNAshell™ and comparable to samples stored at −80°C, actually RIN values were ranging from 7.2 to 8.6 and RNA yield percentages were close to 100% in all conditions. Integrity and recovery were lowest for the liquid RNA RT° samples. The fitness-for-purpose of RNA after rehydration was assessed by real-time PCR analysis. RNA stored in RNAstable® or RNAshells™ was amplifiable similarly to −80°C controls. Interestingly Cq values for −80°C controls were not significantly different from Cq values for RNA stored either liquid or dried at RT°, showing that a 2-week RT° storage did not interfere with real-time PCR analysis when the initial RNA sample was highly pure. In conclusion, RNAstable® and RNAshell™ are reliable RNA RT° storage systems.

BSS 15. Developing a Research Program to Study the FFPE Manufacturing Process

H. M. Moore[1], Therese Bocklage[2], Erin Gover[3], Howard Greenman[4], Kelly Higgins[2], Nicole Lockhart[1], Cathleen Martinez[2], Marlena Martinez[2], Neil Mucci[5], Angela Notah-Chavez[2], Nancy Roche[3], Anna Smith[3], David Tabor[3], Jake Vargas[2], Kay Washington[6], Carol Weil[1], Kerry Wiles[6], Gail Wiseman[4]

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Background: To improve the quality of patient tissue samples for medical care and research, the production of formalin-fixed, paraffin-embedded (FFPE) tissues must be standardized using evidence-based protocols. The NCI Biospecimen Research Network (BRN) has undertaken a research program to better understand the effects of different tissue fixation, processing, and storage procedures on the molecular stability of FFPE tissues. The development of experimental design, ethical and regulatory issues, biospecimen annotation, SOPs and training, logistical management, and molecular analysis will be described for the program.

Methods: A broad informed consent approach was developed within the caHUB planning process and adopted for the BRN program. More than 300 new data elements were developed to thoroughly annotate the biospecimen lifecycle. The data elements were incorporated into an OpenClinica® web-based data collection system that utilizes bar code readers to enter time stamps for various procedural steps. An experimental design was implemented that incorporates a tool for randomly assigning tissue aliquots to different downstream fixation and processing protocols. Detailed SOPs were developed to guide all procedures.

Results: The first experiments are focused on the effects of two preanalytical factors (delay time to fixation, time in formalin fixative) on molecular stability, as measured by immunohistochemistry and DNA/RNA quality. Late-breaking results of these first experiments will be reported at the meeting.

Conclusions: There are significant scientific, informatics, and operational challenges when developing rigorous biospecimen research projects. The BRN program has met these challenges with innovative approaches that will ensure high quality research data from this important study.

BSS 16. Morphological Retrieval of Fresh Tumor Tissues After RNALater® Preserved Process

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Background: Quality is the key of biorepository science. Many factors are involved in the whole biorepository process. One of the efforts is to store the tissue in RNALater® solution to get more intact RNA. But it is difficult to get morphological features after this storage step. We want to retrieve morphological features in RNALater® preserved tissues in our institutional tissue bank.

Methods: Eighty esophageal carcinomas along with normal tissues were included in the study. Morphological frozen sections for each case were prepared right after tissue collection as mirror images. RNALater® stored tissue, with different storage durations (1-48 months), were treated and embedded in OCT. H&E staining was performed to the sections from re-embedded tissues. Microdissection was performed when needed. RNA was extracted from the section and quality was checked with Agilent 2100 bioanalyzer.

Results: Morphological analysis of mirror tissue and RNALater® stored tissue matched very well. Tumor percentage and microdissection estimated in the frozen section and RNALater® stored section was similar. Around 60% of RNA earned over the RIN limit of 6. The quality of RNA extracted from microdissection was as good as the ones directly from tissue pieces from RNALater® solution. Real time PCR was performed in different miRNA and mRNA expression analysis.

Conclusions: RNALater® stored tissue can be used to keep RNA quality high. Morphological features can be kept well in RNALater® solution but special treatment is needed. Microdissection is an important step to maintain the purification of tumor cells as study materials in future research steps.

BSS 17. Ischemia Time Monitoring: Experience of the Prostate Cancer Biorepository Network

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Background: Translational research projects have increasingly relied on the use of high-quality, well-annotated and well-characterized biospecimens. Although ample biospecimens are available, they often represent convenience samples resulting in potentially uncomparable populations. For this reason, tracing pre-analytical variables that potentially affect quality and comparability are imperative in ensuring experimental differences is attributed to the pathological condition rather than a biological response to environmental changes and biological stresses introduced by biobanking. A well-known contributor of variation is ischemia. Conventionally, 30-minutes before preservation is considered the limit for conservative treatment, however, it is difficult to accept that it only takes 30-minutes between time-of-devascularization of a robotic–prostatectomy specimen and time-of-preservation.

Methods: We collected precise ischemia times for robotic-prostatectomy specimens in the setting of a tertiary-care hospital. With the assistance of surgical/OR staff, we monitored precise devascularization times in addition to acquisition, processing and preservation to calculate the total time these tissues are subjected to ischemic conditions.

Results: We found an increase in acquisition time over estimates (30mins to 2.5hr). Furthermore, we confirmed that specimens remain at 37°C, with limited-to-no blood supply for approximately 1.5hr.

Conclusions: Inaccurate estimates in acquisition times of biospecimens could potentially be detrimental to downstream applications. Research has shown resulting changes in expression profile both at the mRNA and the protein level, and has been reported in as little as 5-minutes following tissue excision. Therefore, given the under-estimation of acquisition time, standardizing protocols where possible, and precise tracing of pre-analytical variables are imperative in minimizing and accounting for experimental variance.

BSS 18. Molecular Stability Test of Aged RNA Samples from Human Lymphoblastoid Cell Lines

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Background: The RNA integrity is essential for generating high-quality experimental data in various genomics studies, especially using biobanked human cell lines and tissues. In order to assess the molecular stability of aged RNA samples, we examined transcriptomic profiles of isolated RNA samples and cell pellets in accelerated degradation conditions using four different human lymphoblastoid cell lines (LCLs).

Methods: Total RNAs were isolated from four LCL cell pellets placed on ice (Control group) or at Room Temperature (RT group) for 2hrs. Subsequently, isolated RNA samples from the control groups were subsequently heat-treated at 60°C (Heat-treated group) for 2hrs. Prior to transcriptomic microarray analysis, the RNA integrity number (RIN) value was measured to determine the RNA integrity by Agilent 2100 Bioanalyzer.

Results: RNA samples represented average RIN values of 9.6, 8.2 and 7.7 of control, heat-treated, and RT groups, respectively. In the RNA integrity analysis, the heat-treated group RNAs showed smears in the eletropherogram of the Bioanalyzer whereas the RT group RNAs showed band patterns, suggesting different mechanisms of RNA degradation. The number of degraded RNA transcripts was higher in the RT group than the heat-treated group, compared with the control group. In addition, LCL strains exhibited different numbers of differential transcripts, suggesting individual variations in the RNA stability in accelerated RNA degradation conditions. Interestingly, the RNA stability of housekeeping genes was also different in the RT-placed RNAs and heat-treated cell pellets.

Conclusions: This study suggests that different RNA transcripts may have different molecular stability in pre-analytical conditions of biobanked RNA samples.

CRYOGENICS AND CELL PRESERVATION (CCP)

CCP 01. Bone Marrow Derived Cultured Fibroblasts as a Source of Constitutional DNA

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Background: Genomic analyses now being widely applied to interrogate the mutational landscape of many hematological malignancies require a parallel sample of developmentally unrelated DNA from the same individual to distinguish acquired from inherited anomalies. Although multiple non-hematopoietic tissues have been used for this purpose, including epithelial cells present in buccal swabs or urine specimens, or fibroblasts generated *in vitro* from a skin biopsy, all of these sources have significant ethical, financial, technical or practical limitations, particularly when the patients are deceased. Here we investigated the potential of obtaining sufficient numbers and purity of cultured bone marrow fibroblasts derived from bone marrow aspirates that had been cryopreserved in DMSO for up to 18 years.

Methods: Bone marrow aspirate cells were thawed and cultured in human Long Term Culture Media (Myelocult, STEMCELL Technologies, Vancouver, BC) at 37°C, 5%CO_2 and >90% humidity with weekly media changes and a switch to 20% FCS in Iscove's medium at week 2. When confluence was achieved, the cells were trypsinized and split sequentially for up to 4 passages at which time the cells were harvested, counted and assessed by FACS for residual contaminating hematopoietic (CD45+) cells.

Results: 42 of 47 cultures (89%) produced $>5\times10^5$ fibroblasts with <2% CD45+cells after 5 to 8 weeks and this result was unrelated to the period of prior cryopreservation of the cells or the initial number available (down to $2x10^5$ cells).

Conclusion: Cryopreserved bone marrow aspirate cells can serve as a useful source of fibroblasts suitable for constitutional DNA analyses.

CCP 02. Novel Alcohol-Free Cell Cryopreservation Method Results in Higher Human Embryonic Stem Cell Viability and Function

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Mammalian cells are cryopreserved to avoid loss by contamination, to minimize genetic change, and to store cells with finite lifespan. In recent years, human stem cells have gained significant importance in the medical field. Not only have stem cells changed basic research but they have become critical to personalized medicine. Stem cells are difficult to obtain and hard to culture *in vitro* therefore adequate and reliable methods to cryopreserve these cells for short and long-term storage is vital. Current benchtop methods of cryopreservation include isopropyl alcohol containers and less controlled and less standandarized methods using polysterene boxes or towels. We present a comparison between current methods of cryopreservation and a novel CoolCell® alcohol-free highly controlled method.

RC-10, a sensitive and difficult to culture human embryonic stem (hESC) cell line was chosen for evaluation. Cryopreserving RC-10 cells in a CoolCell® resulted in a 93% increase in number of stem cells at 3 days post-thaw with high reproducibility ($p<0.0001$), while current methods yielded only a 23-57% increase. Moreover, the CoolCell® method yielded 100% viability after thawing, effectively increasing the yield of human stem cells by 40-75% providing the researcher with significantly more sample per patient.

We conclude that the BioCision CoolCell® freezing container outperforms the existing methods by demonstrating improved post-thaw cell recovery and function. This method of benchtop controlled-rate freezing of cells provides an important, more economical alternative for the standardization of cell cryopreservation.

ETHICAL, LEGAL AND SOCIAL ISSUES RELATED TO REPOSITORIES (ELSI)

ELSI 01. Pediatric Participation in Research: Lessons Learned from an Ontario Population-Based Cardiac Biorepository

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Background: Consenting minors for genetics research and biobanking involves ethical and social challenges. We examined factors influencing participation rates in a population-based biorepository for childhood heart disease.

Methods: Individuals were prospectively enrolled across 7 centers in Ontario using a standardized consent form. Individuals were approached for consent for the donation of blood/saliva (DNA), tissue, and skin from the affected individual for future genomics and stem cell research. Consent rates were compared between pediatric and adult patients and factors affecting consent were analyzed using multivariable analysis.

Results: From 2008-2011, 3,637 patients were approached. 2,717 pediatric patients consented (90% consent rate). Mean age was 8.5 ± 5.8 yrs (57% male; 76% White). 560 adult patients consented (92% consent rate, $p = 0.071$ vs pediatric). Factors associated with lower pediatric consent rates included younger age, non-White race, absence of complex defects and location of consent; these were not associated with adult consent rates. Leading causes for refusal of consent were lack of interest in research (43%), overwhelmed clinically (14%) and discomfort with genetics (11%). Concerns related to privacy, insurability, indefinite storage and ongoing access to medical records were not the leading causes for refusal.

Conclusion: There was a high (90%) pediatric consent rate that was comparable to adults. Ethical, social or legal issues were not cited as leading reasons for refusal of consent. It is important to standardize consent processes and to encourage pediatric participation in population based biorepositories to facilitate the study of the genomics of childhood diseases.

ELSI 02. Comprehensive Genomic Studies: Emerging Strategic and Quality Assurance Challenges for Biorepositories

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Background: Comprehensive genomic studies, including whole genome and whole exome sequencing, are adding vast new dimensions to medical research. However, their enormous power brings strategic and quality assurance challenges for biorepositories. Unlike other common techniques (e.g. Western blotting or immunohistochemistry), genomic procedures may be comprehensive enough to yield data that could inherently identify a patient. This evolving paradigm alters the traditional notion of anonymity for banked biosamples. Quality assurance procedures, such as tumor cellularity and nucleic acid quality assessments, needed by genomic research also pose challenges and opportunities for biorepositories.

Methods: The biorepository at Washington University Medical School (WUMS) works in close association with the Institutional Review Board (IRB), and the NIH-funded Genome Institute on campus, regarding genomic research issues. To address the above challenges, and to provide high-quality science, the WUMS biorepository and/or IRB have developed procedures which are consistent with published best practice biobanking documents (NCI, ISBER) and with the standards for the NIH-supported Database of Genotypes and Phenotypes (dbGaP).

Results: Based on our experiences, we summarize here our best practices for informed consent, use of legacy specimens, quality assessments, documentation, and data sharing as they relate to genomic studies. Our approach to these is continuing to evolve along with the science. We also share our perceptions of emerging trends, and our recommendations.

Conclusions: Given current trends and the rapid advance of technology, biorepositories should consider genomic research issues now, even if they are not currently experiencing sample requests for comprehensive genomic analysis.

ELSI 03. Human Tissue Biobanks: Time for Research Ethics Committees to Re-Appraise the Dichotomy Between 'Personal Sovereignty' and 'The Common Good?'

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Biobanks are currently archiving human materials for medical research at a hitherto unprecedented rate. These valuable resources will be essential for developing personalized medicines and for a better understanding of disease susceptibilities. However, for such advances to benefit all, it is crucial that biobanks recruit donations from all sections of the community. Unfortunately, from our experience of other initiatives within the UK, such as transplant programs, there is a clear demonstration that ethnic minorities are under-represented. Here we suggest that this issue deserves serious consideration to avoid biobanks evolve into ethnically-biased archives which unwittingly promote race-specific research. Specifically, this necessitates Research Ethics Committees engaging in a re-assessment of the relative merits of individual personal sovereignty and the 'common good'.

ELSI 04. Permission to Contact (PTC) for Future Biobanking Research- A Strategy for Sustainable Biobanking

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Background: Historically less than 10% of BC patients are approached about any kind of research participation (including biobanking). We hypothesized that integrating PTC (permission to be contacted) processes into routine outpatient clinic practice would enhance enrollment of patients into biobanks.

Methods: To test this hypothesis PTC projects have been initiated in four types of outpatient clinics (cancer, cardiac, general surgery, womens health) in different BC health centers. Clinic personnel were engaged, clinic flow processes mapped, and a design for each PTC derived by consensus. All patients at these clinics were asked for 'Permission to be contacted for future biobanking research purposes'. Response rates and impact on associated biobank accrual were assessed.

Results: Performance data over 1 year was available for analysis from the first two PTC projects in 'cancer' and 'cardiac' clinics. Overall patient response rates are very high, but are different between the projects (93% of 'cancer' vs 80% of 'cardiac'

patients who were approached provided permission to be contacted, $p < 0.05$). Referrals for consenting to a biobank linked to the 'cancer' PTC project increased by 1. 4 fold (758 vs 410 referrals) while patient consent rates remained the same (~96%) in comparison with the previous year period.

Conclusions: PTC projects are well supported by clinic staff and can significantly enhance biobank accrual. Response rates are very high but may vary in different clinics, likely due to both patient and PTC process factors, but this strategy provides an efficient means of enhancing enrollment into biobanks.

ELSI 05. Optimizing Patient Consent Rate: Perspectives from the UHN Biobank

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Informed patient consent is an essential part of using human biospecimens for medical research. At the University Health Network, a large Canadian clinical, teaching and research hospital system, the UHN Biobank has been storing excess tissue from surgical pathology specimens, as well as blood and body fluids, since 2001. A general biobank consent and information brochure was introduced in 2003 as part of the surgical patient preadmission package, so that consent could be obtained prior to the preadmission visit by the surgeon or their designate. In support of major institutional projects, the Biobank has further optimized consent rates by a reviewing patient charts during the patients' preadmission clinic visits. A biobank clinical coordinator approached selected non-consented patients in an attempt to increase participation. Of 2416 patient charts reviewed, a signed biobank consent was found prior to the preadmission visit in 1529 (63.3%) charts. By comparison, 141 of 148 (95.3%) patients with possible or confirmed thyroid, pancreatic and gynecological malignancies signed the biobank consent after being approached by a biobank coordinator. 2 (1.3%) patients were undecided, 4 (2.7%) refused and 1 (0.7%) withdrew consent. Reasons for nonparticipation included religion, cultural and language barriers, concerns regarding privacy and confidentiality, stress associated with their disease and unwillingness to provide extra blood. The results of our review suggest that when patients are specifically approached, it is possible to obtain consent on almost all surgical patients from whom excess tissue is banked.

ELSI 06. Consent from Pediatric Biospecimen Donors at the Age of Majority: A Framework for Decision-Making

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Background: Research involving pediatric samples is currently challenged by lack of guidance concerning the rights and interests of grown pediatric donors. Individuals who donated biospecimens as children may find the opportunity to give or refuse consent empowering, particularly for controversial research, or may consider re-contact invasive depending upon their donation age, current medical condition, and views about privacy and autonomy.

Methods: We propose a framework for addressing whether to re-contact former pediatric biospecimen donors who have reached the age of majority. The framework is intended for use by IRBs, ethics committees and biospecimen access committees whenever consent is not mandated by DHHS regulations.

Results: Our framework utilizes a "stoplight" (green = proceed, yellow = be cautious, red = stop) rating system to assess across 3 key categories the risks and benefits of re-contacting former pediatric biospecimen donors. The categories are:

- Harm to donor or family
- Research purpose/degree of data sharing
- Feasibility (reliability of contact information and impact on scientific validity)

While the framework may yield a mix of color classifications to guide deliberation, as an ethical matter, greatest weight should be attributed to the protection of donor interests and welfare.

Conclusions: All research projects and biorepositories collecting pediatric biospecimens should establish plans for maintaining donor contact information, attempting communication with donor families, and the appropriate disposition of samples and data if donors cannot be reached or refuse consent for continued storage or future use of samples. Having policies in place will reduce confusion and avoid interruptions in research when donors reach the age of majority.

ELSI 07. The Power of Community Involvement in the Enrollment of Minorities into Clinical Trials

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Background: The 2012 Indianapolis Super Bowl Host Committee has partnered with the Susan G. Komen for the Cure® Tissue Bank at the Indiana University Simon Cancer Center (KTB) in an effort to put an international spotlight upon the KTB. Recognizing that rather than being just a game, the Super Bowl is an opportunity to establish a meaningful legacy, the 2012 Indianapolis Super Bowl Host Committee launched Indy's Super Cure. The goals of this initiative are:

- To increase the number of healthy breast tissue donors, especially from diverse backgrounds,
- To raise awareness of this vital tool among cancer researchers, and
- To generate philanthropic funds to ensure the bank will flourish for years to come.

Methods: Leaders from the local African American, Hispanic, and Asian communities were asked to use their expertise and connections to educate and inform the members of these minority groups about the prevalence and severity of breast cancer within their races. These leaders were tasked with spreading awareness of the KTB and encouraging participation in research by donating healthy breast tissue. Forums included religious services, health fairs, local media, and sporting events.

Results: The number of minority donors on the KTB Interested Donor List has significantly increased since the Super Cure initiative began. These numbers translate into actual donors at collection events.

Conclusions: The involvement of minority community leaders is tremendously important to education about clinical trials and the subsequent enrollment of minority donors.

ELSI 08. Barriers to Sharing in Biobanking: A Qualitative Analysis of Obstacles to Sample and Data Sharing Amongst Biobank Stakeholders in Switzerland

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Background: Calls for collaboration amongst biobanks, at both the national and international levels, have appeared in numerous articles in recent years. A great deal of research, and financial investment, has been dedicated to this matter, resulting in a growing number of biobanks, and increased efforts towards making sample collections widely and easily accessible. However, much of this work is still in the early stages, and there are important steps to be made in facilitating the sharing of samples and data. Our aim is to determine the barriers to sharing currently experienced and perceived by those involved in biobanking.

Methods: We carried out semi-structured interviews with thirty biobank stakeholders in Switzerland, in order to discover their experiences and attitudes towards obstacles to sharing samples and data. The individuals we spoke to included biobank and laboratory managers, technicians, clinicians and lawyers.

Results: We present a discussion of our findings, based on a content analysis of the transcribed interviews.

Conclusions: We focus on three predominant themes concerning barriers to sharing: i) the effects of ethical review boards; ii) the practical aspects of sample management and quality; and iii) stakeholders' views on biobank networks. Our results present a valuable insight into the actual barriers to sharing samples and data currently faced by biobanks.

ELSI 09. But What Does it Cost? A Practical Tool for Modeling Biospecimen User Fees

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Background: Operating and maintaining a biobank is costly, and the question of how to best attribute the unit costs of the annotated biospecimen product provided to a research user is common to many biobanks. Factors influencing user costs include the internal biobank capital and operating activities, increasing demand creating a competitive market, and moral standards that dictate that costs should have an ethical basis. It is therefore important to establish a transparent, reliable and accurate costing model that can be utilized by biobanks.

Methods: We have built a cost modeling tool in both distributable spreadsheet and accessible online formats (http://www.pathology.ubc.ca/pathology/OBER.html) that incorporates the concepts of biobank activities, classification and development phase to aid biobanks in modeling the costs of their biospecimens and appropriate user fees.

The tool was built to allow input of: 1) annual operating and capital costs; 2) costs categorized by the major core biobanking operations (accrual, processing, storage, release); 3) specimen products requested by a biobank user and 4) services provided by the biobank beyond core operations (e.g. histology, tissue micro-array).

The tool was also built to be multi-dimensional in terms of different categories of biobanks including 1) primary biospecimen formats; 2) user models (mono, poly, oligo-user); 3) phases of development.

Conclusions: It is imperative that biobanks understand their internal cost structures and external factors involved in operating a biobank to sustain the supply of quality biospecimens for translational research. The online tool will help biobanks model their costs and calculate user fees.

ELSI 10. Challenges in the Consenting Process in a Multidisciplinary BioBank

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Background: Beaumont Health Systems BioBank was developed to establish a multidisciplinary research structure that facilitates projects that bridge specialties and build a platform for translational research using a broad consent document. Having 45 investigators from 14 diverse clinical departments covered by one ICD has sparked concern with Beaumont's IRB as to whether patients are receiving the proper information when consenting. OBBR and ISBER have presented varied consent guidelines. In particular, caHUB utilized a small group of 14 cancer patients as a "focus group" to assess patient opinion concerning a broad or focused ICD.

Methods: In this study, we have developed project specific information sheets for three different biospecimen collections and presented them to alternate patients in a cohort of 12 from each project. These collections were concerned with pancreatic, cancer, carotid artery disease and women's urology. A questionnaire was developed to assess the comments of the patients to the consenting process. All patients with or without the information sheet were asked to respond to the mailed questionnaire post-procedure to evaluate the need for in-depth information versus general.

Results: This research project is ongoing through January in order to have a sufficient number of responses. We have yet to come to a conclusion as to whether we adapt the broad or project specific consent process.

Conclusion: We expect our results to help provide clearer guidelines as to the amount of information that patients desire to know.

ELSI 11. Biobank Best Practices: One Size Does Not Fit All

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Background: While much attention has been paid to biobank best practices, consensus is hampered by lack of an agreed-upon definition of biobanks. Some focus on population-based or federally-funded collections and exclude specimens stored by individual researchers, hospital biorepositories, or disease advocacy registries. There is also a dearth of empirical data that characterize biobank organizations and the policies and practices they employ. To address this gap, we report on data from a recent national survey of US biobanks (R01 HG005227).

Methods: A comprehensive list of US biobanks was assembled using a systematic, multi-method search strategy that defined biobanks broadly, as collections of human specimens, original or processed, with/without associated data, stored long-term for future research use. A 30 minute web survey was developed

based on a pilot with 100 biobanks (79% response rate), recruiting more than 800 biobank managers.

Results: Presenting data from academic, government, nonprofit, and commercial biobanks, we demonstrate significant diversity in organizational characteristics (date established; network membership; number, origin, and type of specimens stored) and policies and practices (type of consent; access to specimens; return of specimens/data to biobank; return of individual results to contributors; specimen ownership; and community engagement).

Conclusions: Best practices for biobanks should promote effective and efficient research use of specimens/data for the broadest scientific goals, while protecting the autonomy and privacy of specimen/data contributors and their communities. Our data challenge simple categories presumed associated with biobank policies and practices, and demonstrate that, when it comes to best practices, one size does not fit all.

ELSI 12. Legal and Ethical Hurdles Associated with Exchange/Sharing Biospecimens for Global Integration

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Background: The ultimate goal of collecting biospecimens is to maximize their use and stimulate collaboration and exchange of samples between biobanks worldwide. For this purpose, there is need for global harmonization of the code of conduct applied for legal and ethical procurement of specimens. At present, there is total lack of awareness and consensus with regard to consenting, annotation and the proper preservation, storage and transport of specimens between banks, on the national and international level.

Methods: We tested factors influencing the good will of the public and the success/failure of donor programs in European and Asian biobanks. We also tested the consenting procedures in donors with neurological and mental disorders, and the value of genetic testing and need for clinical consultation.

Results: Comparative studies revealed significant differences in consenting procedures, safety procedures, disposal, custodianship and IP issues. We are in the process of publishing recommendations for the global best practice of the medico-legal and ethical framework conform local legislation; it reflects the daily practice of recruiting, procurement, management, dissemination, confidentiality, cost recovery and genetic testing.

Conclusions: Research uses large numbers of specimens and DNA; the rapid linkage between genes and diseases will have future implications on the international legal and ethical systems. As the legislative and ethical framework is so variable between countries, our recommendations may help in reaching the desired global consensus; ISBER can play a major facilitating role in reaching this goal and minimizing the hurdles on the way to global collaboration/exchange of specimens.

ELSI 13. Re-Thinking the ELSI of Biobanking

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Background: Much of the literature on the ethical, legal, and social implications (ELSI) of biobanking has focused on protecting the interests of specimen contributors (e.g., obtaining informed consent, ensuring confidentiality, and returning individual research results). However, broader ethical implications of biobanking that emerge during the course of everyday work practices are less readily apparent, and have been neglected in the literature.

Methods: We conducted qualitative interviews with 24 personnel from six US biobanks selected to highlight their organizational diversity. Interviews included in-depth examinations of the biobanks' organizational features, such as how they are structured, and how they relate to the researchers who use the specimens and the people who contribute them. Interviews also examined how the biobanks' policies and procedures develop and change over time.

Results: Analysis reveals unexpected ethical issues embedded in the everyday work practices of biobanking. For example, two issues that were especially salient are the underutilization of specimens and data by researchers; and the influence of the larger organizations that biobanks are housed within on the development of policies and procedures.

Conclusion: While these additional ethical issues surrounding the everyday work practices of biobanks may be of little surprise to those who operate them, they are nonetheless not reflected in the current literature on the ELSI of biobanking or in the calls for the development of best practices that would govern policies. This presentation will argue that discussion of the ELSI of biobanking is not complete without understanding their everyday work practices.

ELSI 14. Enhancing the Phenotypic Value of Patient-Derived Induced Pluripotent Stem Cells for Disease Modeling

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Background: Human induced pluripotent stem cells (hiPSCs) can be differentiated into many organ cell types to model human disease in a dish. Samples available through commercial repositories often lack detailed phenotypic information. We assessed cardiac and extra-cardiac phenotypes in patients with childhood onset heart disease (CHD) undergoing skin biopsy for reprogramming.

Methods: Skin biopsies were obtained for reprogramming from patients undergoing cardiac surgery enrolled in a hospital-based biorepository. Demographic and phenotypic data was captured from electronic medical records on an ongoing basis and from intake questionnaires.

Results: 3820 patients were enrolled from 2008-11. Of the 474 patients approached prior to surgery, 368 consented for skin biopsy (78% consent rate). Genetic etiology was identified in 20% skin samples ($n=50$). 86% had additional extra-cardiac malformations and/or non-cardiac medical conditions. These included neuro-behavioral disorders (5.9%), respiratory diseases (5.6%), endocrine (3.6%), neurologic (2.7%), hematologic (1.8%), GI (1.8%), skeletal (1.3%), genitourinary (1%), and others. Cells from several patients with neuro-cardiac disorders have been reprogrammed and are being differentiated into cardiac and neuronal lineages to study cellular phenotypes.

Conclusion: Detailed phenotyping can significantly enhance the value and utility of hiPSCs for human disease modeling. Using genetically characterized hiPSCs can help in deciphering molecular pathways that cause human disease. Knowledge of co-existing medical conditions permits the use of hiPSCs to model multiple organ systems from the same patient in a dish.

ELSI 15. Global Strategies for Improving Future Use Sample Collection: Next Steps

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On 20-21Sep11, DIA (Drug Information Association) held an international symposium discussing the importance and difficulty of collecting human DNA samples consented for future research. Ethicists, health authorities (HAs), academic and pharmaceutical researchers came together from each of the three ICH regions. Sessions reviewed challenges in Japan, Europe, North America and other regions globally. Common themes were identified across all regions and action items were given for follow up.

Common themes identified across regions: International guidance for collection/storage/use is needed; What is allowed for scope of future research is highly variable; Transparency for how samples are used builds trust. Finally, education is needed in several areas: How HAs use these samples to answer important scientific questions; Minimizing biased subsets of samples; Coding practices; Return of results.

Actions: *Industry:* Improve transparency, Create educational tools; I-PWG: Publish best practices, Foster global harmonization, Create educational tools; *Academia:* Review local policies, Determine institution's position; Consider creating greater understanding between institutions and industry on how specimens will be ethically used; *Regulators:* Review policies' impact on industry vs. academia; Improve public awareness of value to drug development; ICH: Consider standardization of future use sample collection.

A White paper summarizing key issues is in progress; PRIM&R hosted a related session; Action Items above are underway.

This DIA meeting fostered global understanding of the challenges of future biomedical research. For personalized medicine to be fully realized, harmonization will take substantial education and will require global standards.

QUALITY ASSURANCE AND CONTROL (QAC)

QAC 01. An Online Tool for Improving Biospecimen Reporting

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Background: Human biospecimens are increasingly utilized in cancer research. In addition to the experimental methods and reagents, better information about the biospecimens used is needed. We hypothesized that previously reported biospecimen data is inadequate for accurate replication and/or validation of studies.

Methods: We set out to analyze biospecimen reporting in a representative cross section of publications over the past 12 years in the journal, Cancer Research (1998, 2004, 2010, $n=46$). We assessed the accuracy and reporting frequency of the first tier recommended data elements from the Biospecimen Reporting for Improved Study Quality (BRISQ) list. The data elements encompass features of biospecimens influenced by the patient, medical procedure, and biospecimen acquisition, handling and storage processes.

Results: Analysis found that while there was a significant increase in frequency of reporting IRB approval status, there was no change across this period in reporting biospecimen criteria. Of the 18 criteria assessed in 46 papers: biospecimen type (96.5%), disease status (94.7%) and clinical diagnosis (85.5%) were most frequently reported, clinical characteristics (41.9%) was infrequently reported, and stabilization type at collection (8.0%) and shipping temperature (0%) were rarely/never reported.

Conclusions: Reporting of biospecimen-related data elements has been incomplete. A new mechanism for reporting is necessary to aid biobanks to promote accurate biospecimen reporting by users and to improve the quality of future research studies. One solution is the development of an online tool (www.ober.pathology.ubc.ca) that can serve as a checklist and data entry form for biobanks to provide reporting criteria for their biospecimen samples on release.

QAC 02. Suisse Biobanks Provide Biospecimens with Good RNA Integrity While Facing Administrative Challenges

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Background: The PRO_10 score is a prognostic profile based on RNA levels of genes expressed in tumor tissue from breast cancer patients. In a further validation of the PRO_10 score we determined: (i) The integrity of RNA in biospecimens of four biobanks in Switzerland. (ii) We estimated to what extent the network of biobank-suisse (BBS) can facilitate such projects.

Methods: Four Suisse biobanks followed a protocol to identify fresh-frozen (FF) and formalin-fixed, paraffin-embedded (FFPE) tumor tissue from postmenopausal women diagnosed with estrogen receptor-positive breast cancer. To each patient with a relapse within 5 years one patient with similar characteristics but no relapse during this time was paired. The RNA was extracted from FF and FFPE biospecimens and analyzed by measuring the RNA integrity number (RIN) and by comparing the efficiency of qRT-PCR.

Results: It was difficult for the four biobanks to identify suitable pairs of patients, due to missing or poorly documented follow-up data in the databases related to biospecimen. With the exception of one biobank, the extracted RNA from FF biospecimens had RINs between 6 and 9. Fresh frozen samples stored in RNAlater® had similar RINs. The integrity of RNA extracted from FFPE biospecimens from three biobanks was sufficient to perform qRT-PCR experiments.

The RNA integrity of biospecimens was satisfactory. However, the work with four different cantonal ethical review boards was cumbersome. The biobanks suffer in general from limited resources and access to patient data. The network of BBS facilitated and improved the interaction between biobanks.

QAC 03. Lean Six Sigma Implementation for the Advancement and Innovation of Biorepository Operations

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Background: The Cooperative Human Tissue Network Western Division at Vanderbilt University Medical Center (CHTN-

VUMC) has implemented Lean Six Sigma (LSS) as a new model of operations that promotes efficiency and innovation. LSS is a management system driven by the need to continuously improve and eliminate complexities and sustain improvements in every part of an organization.

Methods: CHTN-VUMC is a federally funded resource that provides high quality human specimens to researchers to accelerate the advancement of discoveries in cancer diagnosis and treatment. Borrowing the LSS business philosophies and methodologies, CHTN-VUMC has succeeded in the LSS approach by identifying and prioritizing quality improvement initiatives. Dedicated staff at each level of the operation that were committed to the LSS implementation, proved successful. Phase one implementation consisted of staff members defining a key job function, which would be considered "critical to quality" and completing all five LSS steps (define measure, evaluate/analyze, improve and control). We have completed a reorganization of our ordering, inventory and SOPs, creating a more streamlined and efficient biobanking environment.

Conclusion: The LSS as a process improvement methodology can be leveraged to enhance any organization by creating an infrastructure supporting a culture of assessment and change through eliminating waste, minimizing downtime, reducing errors, and improving productivity. CHTN-VUMC has adopted the LSS system to foster an atmosphere of continuous improvements to achieve the highest quality customer and employee satisfaction and quality control in biobanking.

QAC 04. Is There Anything in There? Histological Evaluation of Prostate Cancer Tissue in Biobanks in Switzerland

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Background: Cryopreservation of prostate cancer is challenging due to a variety of intrinsic factors: it is usually multifocal and located in the periphery of the organ; hence meticulous attention has to be paid to the resection margins. Second, neoplastic tissue is difficult to distinguish from surrounding non-neoplastic tissue at macroscopic examination. These limitations explain the "poor harvest" of prostate cancer cryopreservation in tissue banks compared to other solid organ tumors, where the tumor mass is easily and safely accessible.

Methods: Four different methods of harvesting fresh prostatic cancer tissue, i.e. whole slice, punches, inner triangles of resection specimens and tissue obtained from palliative TURP from four different university institutions were compared for (i) total amount of harvested tissue and (ii) amount of prostatic cancer tissue expressed as total surface in mm^2 and purity (amount of cancer in percent) of harvested tissue. Fresh frozen section H&E slides were digitally scanned and total surface of cancer and non-neoplastic tissue was calculated using imaging software.

Results: The percentage of positive sample recovery, the total amount of cancer tissue and purity of the sample is strongly dependent on the method used. Whereas the percentage of positive sample recovery is low in punches, the purity of the positive samples is high.

Conclusion: The advantages and disadvantages - including time and technical investment - of each method as well as the purpose and requirements of the research project should be taken into account when harvesting prostate cancer tissue. The project is sponsored by Biobanque Suisse.

QAC 05. Validation of Protein Integrity in Serum and Plasma

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Background: The Susan G. Komen for the Cure® Tissue Bank at the IU Simon Cancer Center (KTB) collects breast tissue and blood from healthy female donors. Whole blood is processed to separate serum, plasma and to extract DNA. These specimens are then stored until requested. Quality control of biorepository specimens is vital in order to ensure that research results reflect the biology of the specimens and not storage artifact. By proteomic analysis, protein integrity of stored serum and plasma was evaluated.

Methods: Representative samples from three different donors were tested. Freshly prepared (Day 0) serum and plasma as well as the samples stored at $-80°C$ for 6 months and 3 years were subjected to the test. Two-dimensional gel electrophoresis and image analysis were employed. Two abundant proteins, albumin and IgG were removed from the samples. Proteins in the depleted sample were then separated in immobilized pH gradient strips and, in the second dimension, according to their charge/molecular weight. Initially, silver staining was utilized for protein detection. Alternatively, proteins were labeled with the CyDye™ DIGE Fluor minimal dyes from the Ettan Difference Gel Electrophoresis (DIGE) System (GE Healthcare) and separated on the gel. Laser fluorescent images were recorded and analyzed using ImageMaster™.

Results: Preliminary results of image analysis suggest that the proteome in the tested sample has not been significantly changed over the time period studied.

Conclusions: Current storage conditions at the KTB appear adequate to protect protein integrity. Proteomic analysis can be applied as a standard protocol for quality control.

QAC 06. ISO 15189:2007 Accreditation of a Clinical Pathology Department: Beneficial for an Integrated Tissue Biobank

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Background: To date there is no ISO Accreditation Program specifically designed for (hospital integrated) biobanks. However, biobanks can opt for ISO accreditation of specific procedures such as quality and/or security management systems. The Erasmus MC Tissue Bank is an integral part of the Clinical Pathology department of the Erasmus MC, Rotterdam, The Netherlands. This department was recently awarded with an ISO 15189:2007 accreditation, which specifies requirements for quality and competence particular to medical laboratories. Therefore all Tissue Bank procedures that touch base or share facilities with the diagnostic pathway must also apply to the accreditation requirements. Here we describe our experiences.

Methods: The Tissue Bank standard operating procedures, personnel competence registration, work instructions and equipment manuals and logs were checked and revised if needed to comply with the requirements. An inventory was made of

equipment and its maintenance records that is shared with Clinical Pathology. All documents were implemented in the Clinical Pathology quality informatics system to allow access to the most recent and approved versions at all times. The ISBER 2008 Best Practices for Repositories were studied for comparison. Two subsequent department-wide external audits were performed (Lab Academy, on authority of the Dutch Board for Accreditation (RvA)) with inclusion of the Tissue Bank.

Conclusions: The ISO 15189:2007 Accreditation is beneficial for (hospital integrated) biobanks as the applicable requirements also comply with procedures for proper biobanking such as the ISBER Best Practices and ensures good quality samples and data for researchers and for sharing in biobank network platforms.

QAC 07. The Tomorrow Project: Creation of Mobile Laboratories to Support Collection and Storage of High Quality Biological Samples for Epidemiologic Research

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Background: The Tomorrow Project (Alberta, Canada) is creating a 'population laboratory' to support transdisciplinary research into roles played by genetics, environment and lifestyle in the etiology of cancer and other diseases. It aims to enroll 50,000 Albertans aged 35-69y. Upon enrollment, participants complete a questionnaire and agree to active/passive follow-up for up to 50 years. Samples of blood and urine (spot sample) are also requested. One major challenge is to process and store high quality biological samples donated by participants recruited from communities all over Alberta (661,848 square km).

Methods: Following a detailed review of existing infrastructure, it was deemed that a *de novo* solution was required.

Results: Two portable laboratories, suitable for transportation by cube van, were created. The laboratories may be set up anywhere with sufficient electrical power and sanitary facilities (e.g. Community hall). Blood samples (50ml, non-fasting) are collected into EDTA, serum and SST tubes and on one Whatman FTA card. Thirty two aliquots of serum, plasma, buffy coat, red cells and urine are frozen within two hours of donation ($-80°C$ portable freezers; 2-D barcode tubes). Meta-data include technician identity, duration of all processing steps, time since last food/drink, use of supplements/medications/alcohol/tobacco before donation, and other factors that may impact sample quality. Freezers are battery powered and monitored during transport from remote collection site to the central biorepository.

Conclusion: This solution ensures the storage of high quality and well-documented biological samples that will support a wide variety of transdisciplinary research in cancer and other disease etiology.

QAC 08. An Alternative to RIN for Compromised RNA Samples: Fragment Size Distribution as a Metric for Downstream Gene Expression Applications

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Background: Archival tissue samples are a major source of human material readily available for gene expression analysis. However, tissue preservation methodologies associated with archived material complemented with laser capture microdissection (LCM) yields variable expression data. This is because the RNA isolated from samples following these manipulations is more highly degraded than is generally recommended for use in gene expression studies. The current metric for RNA quality, RNA integrity number (RIN), is an algorithm dependent on the characteristics of ribosomal RNA peaks (as determined electrophoretically) but these often are missing in RNA isolated from archived and LCM-derived samples. Lacking to date is a suitable metric to aid in the determination of the usability of such RNA samples.

Methods: Samples were subjected to pre-analytical manipulations and RNA quality and fragment size distribution was determined on an Agilent Bioanalyzer. In select samples, ribosomal RNA was removed. Utilizing primers dependent on RNA fragment size, qPCR was performed and results were scored by the absence or presence of amplicon or variability in the cycle thresholds. In microarray experiments, the perfect match mean values were compared.

Results: In both qPCR and GeneChip differential gene expression platforms, the distribution of RNA fragment size served as a better indicator of the usability of highly degraded RNA as compared to RIN. This metric could be used in our laboratory in predicting the results of downstream applications.

Conclusion: The distribution of RNA fragment size is a more reliable indicator of the utility of highly degraded RNA than RIN.

QAC 09. Practical Tools for Managing the Quality of Biological and Environmental Specimens Collected from a Distance

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Background: Epidemiologic studies that aim to collect high quality biospecimens in the field require customized quality assurance plans. Our field research settings are diverse in geography, scale, and resources—-in urban medical centers across the U.S. and SE Asia, biobanks in Scandinavia, and rural South African health clinics. Successful specimen management plans for field studies require a strategic approach to handle unique challenges in a consistent and standardized manner.

Methods: Our presentation focuses on four main components of specimen management in the field: Site-Appropriate Technology, Tracking of all Specimen Processes and Test Results, Cultural Awareness of the Site and Population, and Field Site Monitoring/Staff Support. Key methods include: adapting and scaling the management system and technologies for the setting; early clarification of roles & responsibilities; assuring quality in each phase of specimen management; screening materials and methods to avoid possible contaminants; and using field staff expertise to identify potential gaps and propose sustainable solutions.

Results: Sophisticated specimen collections are achievable when crafted within the context of the entire study, never formed in a vacuum. Even the most straightforward of situations pose challenging problems that can be overcome by: (1) avoiding assumptions, (2) designing a detailed specimen plan early, and (3) making adjustments throughout the life of the project.

Conclusions: Creating a successful specimen collection is accomplished by applying lessons from past experience, recognizing similarities among projects, adapting to each setting, and integrating disparate components (hospital bureaucracies,

field staff, community leaders, and study staff) to produce viable, well-annotated, and bankable quality specimens for research.

QAC 10. Dynamic Risk Management in a Multi-Site Tissue Bank

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Background: Sound governance and management of any organization should include a risk management strategy to ensure objectives are achieved and ongoing opportunities exist for performance improvement. The largest biobank in Australia, the Victorian Cancer Biobank (VCB) collects tissue and blood from donors at 27 hospitals in metropolitan Melbourne and regional Victoria. Our decentralized multi-site structure presents particular challenges for implementing a risk management strategy.

Methods: Consistent with AS/NZS ISO 31000:2009, a Risk Management SOP has been developed that outlines processes for identification, registration and management of risks. The document provides a framework for determining likelihood and consequences in 5 areas - people, funding, ethics, services and reputation. From this information a risk matrix has been developed, which is included in a risk register. To integrate risk management into operations, a reporting template provides guidance and encourages staff to identify potential risks and report incidents to the Quality Manager.

Results: Implementation has resulted in a dynamic risk management process. Several sites have completed and submitted risk notifications forms to the Quality Manager. Following assessment, the Risk Register is updated for review by the central Consortium Committee every six weeks. Local Consortium site Management Committees, which form an important part of the VCB governance structure, review the exposure and take action to mitigate future risks.

Conclusion: An SOP has been implemented to integrate risk management into our operations. As risk management needs to be dynamic to be effective, ongoing assessment of the adequacy and relevance of the process forms part of our quality program.

QAC 11. Biobanking a Variety of Biospecimens with a Multi-Disciplinary Approach

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Background: Beaumont Health Systems BioBank was initiated to stimulate investigator driven research and to break the limitations of a traditional hospital by assisting for translational research. The goal was to facilitate the identification, consenting, collection, annotating, and storing of biospecimens for multiple different clinical specialties. Challenges arose with the variety of biospecimen types and obtaining the accurate specimen for future downstream applications while maintaining the highest quality.

Methods: Standard operating procedures, (SOPs) were established for multi-disciplinary collection. Sample types: blood (and components), tissue, saliva, urine, bone marrow, DNA, RNA, CSF all have independent SOP's specifically designed for the special integrity conditions behind preserving the specimen for analysis. Quality measures were established to verify specimen assurance. Specifically, accurate specimen data is gathered, sampling conditions are noted, preservation locations are monitored, histological verifications are performed, nucleic acid and protein integrity is verified and documented. Organization of collection information is streamlined through our sample management system, BIGR, and an in-house Beaumont Integration Management System (BIMS).

Results: Since 2008, the Beaumont BioBank has engaged 45 different investigators from 14 different departments, and standardized the collection of 19 different sample types, resulting in banking of 45,000 specimens. These high quality specimens have stimulated pilot projects amongst investigators, publications, grant applications, and potential IP.

Conclusion: We have fluently provided quality banking of specimens, bridging the research gap to physicians in a community based hospital, offering specimen collection beyond the scope of a pathology department's assistance.

QAC 12. Human Cell Line Authentication Using STR Genotyping

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Background: There have been numerous reports outlining the extent of problems presented by cell line misidentification. Accompanying these reports have been calls for greater diligence in characterizing the cell lines prior to publication. The ATCC Standards Development Organization is in the process of drafting recommendations for human cell line authentication based upon the use of short tandem repeat (STR) loci. We have developed new protocols/systems for generating STR profiles from DNA purified from cell lines, as well as direct amplification methods from cells immobilized on transport matrices (e.g., FTA™ cards).

Methods: Genomic DNA was extracted and purified from human cell lines using the Wizard® SV Genomic DNA Purification System (Promega) and genotyped with several different PowerPlex® STR Systems (Promega), or amplified directly from cells deposited on FTA™ cards (GE Whatman). The amplification products were separated on a variety of Applied Biosystems Genetic Analyzers and allele calls were made using GeneMapper® ID Software.

Results: Methods using purified DNA or direct amplification yielded full, concordant profiles using several different STR systems. The PowerPlex® STR Systems used in this study contain primers for amplifying 8-17 STR loci, yielding matching probabilities of $2\times10\text{^}8$ to $>10\text{^}21$.

Conclusions: Confirmation of cell line authenticity eliminates the wasted time and expense of performing research studies on misidentified cell lines. STR genotyping analysis using the PowerPlex® STR Systems, when accompanied by phenotypic characterization, is a cost-effective tool for confirming the identity of human cell lines.

QAC 13. DNA Quality Control Comparing Frozen and Ambient Storage

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Background: Proper long term storage of biomolecules is an important element in biobanking. The Susan G. Komen for the Cure® Tissue Bank at the IU Simon Cancer Center collects breast

tissue, DNA, serum and plasma from healthy, volunteer female donors. The samples are stored until requested for use in experiments. Storing DNA at ambient temperatures reduces storage space, energy usage and shipping costs. Previous quality control experiments testing DNA stored using Biomatrica® DNAstable showed that the integrity of the DNA was maintained. Further quality control experiments compared the same DNA stored at −80°C and at ambient temperatures to determine the optimal storage method.

Methods: After the DNA was extracted, the sample was aliquoted into 4 tubes on a Biomatrica® DNAstable plate for ambient storage and any excess was then stored at −80°C. PCR was utilized to compare the quality of DNA samples stored at −80°C to samples stored at ambient temperatures, using four primer sets spanning the β-globin gene from previous quality control experiments. DNA samples were rehydrated to a concentration of 0.5μg/μL. PCR was performed using Qiagen Taq PCR Master Mix Kit. The PCR products were run on a DNA gel (1.2% Agarose) using the FlashGel system from Lonza.

Results: PCR showed no difference in the 10 samples tested comparing the frozen sample to the matching sample stored at ambient temperatures.

Conclusions: PCR suggests that ambient storage utilizing Biomatrica® DNAstable technologies maintains DNA integrity as well as frozen storage at −80°C.

QAC 14. Extending Quality Assurance Methodologies to Streamline Data Management in the Biorepository

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Increasingly, biorepositories are becoming storage facilities for escalating amounts of data in addition to physically stored samples. Because of this, biorepository managers have had to embrace novel technologies and software in an effort to optimize efficiencies, reduce errors and streamline data management processes. Therefore, it has become necessary for biorepository facilities to have a fully integrated quality assurance system and comprehensive standard operating procedures that ensure consistently high levels of handling, processing, annotation, storage, audit tracking and transportation during the entire sample lifecycle.

The presenter will provide an illustrated overview of the GxP regulatory requirements and expectations for computerized systems that produce, distribute and archive research samples. The presenter will also underscore the importance of standardized management of electronic data and documents associated with biospecimen collection. Additional quality assurance components that will be highlighted, include:

- how to integrate quality assurance processes as an ongoing component of standard operating procedures for data management; the role of quality assured and validated methods for specimen security and data confidentiality;
- best practices for ensuring business continuity with redundant systems; best practices for establishing a chain of custody for research samples transported globally.

QAC 15. Quality Control for the NW Biobank At Kaiser Permanente Northwest Region

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Background: The NW Biobank collects samples from health plan members who have consented to participate in future genetic research. Residual blood that is marked for disposal is sent to the NW Biobank for processing and long term storage. This repository takes advantage of a stable population of 475,000 members, population-based integrated medical care, and electronic medical records with additional electronic information (e.g. pharmacy records, tumor registry) going back to 1960.

Methods: Specimens are processed using a Ficoll gradient. Buffy coat is deposited on GenPlates for ambient storage in a GenVault (IntegenX, Inc). About 2% of specimens are tested for QC purposes. Manual extraction of DNA is performed according to the manufacturer instructions for GenSolve. For automated extraction, DNA is isolated from GenPlate paper using Promega Low Elution volume cartridges. DNA quantity is assessed by PicoGreen quantitation, genomic agarose gel, and Taqman qPCR. DNA quality is assessed by Nanodrop measurement of 260/280 nm ratios, genomic agarose gel, long-range PCR (1, 5, & 10 kb), and Taqman qPCR.

Results: DNA extracted via automation is up to ten times more concentrated than a comparable manual extraction, and directly usable in downstream applications without a concentration step. On average, we obtain a total yield of about 40 micrograms of DNA per specimen, which is sufficient for use in multiple applications. Purified DNA has shown no inhibition of PicoGreen quantitation or downstream PCR.

Conclusions: The quality control protocol implemented in the NW Biobank demonstrates the high quality material stored in this repository.

QAC 16. ISBER Proficiency Testing Program for Biorepositories

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ISBER has developed a Proficiency Testing (PT) program for biorepositories in partnership with IBBL. The PT program allows biorepositories performing quality control assays/characterization of the biospecimens to assess the accuracy of their testing and to compare their results with those obtained in other laboratories around the world. For biorepositories that want to pursue accreditation, the ISBER PT program will provide a necessary External Quality Assessment tool.

All the Standard Operating Procedures have been written according to the requirements of the ISO17043:2010 norm.

After a successful pilot phase run in April 2011, the first two schemes on "DNA Quantification and Purity" and "RNA Integrity" were launched.

32 participants registered in the DNA scheme and 24 in the RNA scheme. Two different test items were distributed to participants for each scheme. Assigned values were established among expert laboratories.

For the DNA quantification, the assigned values were 183.40 ug/ml (tube A) and 53.00 ug/ml (tube B). For the DNA purity, the assigned values were 1.46 (tube A) and 1.94 (tube B).

For the RNA Integrity scheme, the assigned values were RIN 7.45 (tube A) and RIN 3.68 (tube B).

At the time this abstract is submitted, all results are being analyzed. Reports to each participant will be made available by end of February 2012.

The program for 2012 will open in the 3rd quarter of the year and will include, in addition to the DNA and RNA schemes, the following schemes: "Cell Viability" and "Tissue Antigenicity".

QAC 17. Biospecimen Quality Optimization Through the Refinement of Three Defined Processes

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The Biobank of Lausanne is set up and organized to promote cancer research. The structure is built on three main processes: 1) biospecimen collection 2) data management 3) biospecimen distribution. These processes have to be analyzed carefully to ensure achievements, optimal performances and biospecimen top quality.

Each process involves many different people devoted to specific tasks which have to be coordinated and monitored.

1) Biospecimens are collected according to harmonized procedures. Sample quality is monitored by tracing several timepoints during processing.
2) Each biospecimen is linked with patients' clinical data into a database, which is not only essential to select samples according to researchers' demands, but also to analyze biobank activity. Data management is an important reliable process which should protect patient's privacy: the database is secured, each patient is coded and data quality is monitored.
3) Biospecimens are distributed to research projects approved by both scientific and ethics committees in a timely manner. Biospecimen quality is controlled before shipment and researchers are asked to give their feedback concerning sample quality. Whenever a biospecimen is transferred, patient's privacy is strictly secured and anonymization is waranted.

Each process is independant but closely related to the others. Every step contributes to the Biobank's success, and every failure could have important impacts on the whole organization. It is thus crucial to consider each step to evaluate where improvements could be brought in to optimize the performance of the whole structure.

QAC 18. Statistical Methods for Determining Freezer Maintenance Requirements

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Background: Control of the freezer environment is critical to appropriate quality control for repository samples. Proper ongoing maintenance and monitoring of freezers are necessary to preserve optimal function and thus temperature control. Preventing catastrophic freezer failure must be the primary goal of any integrated maintenance program. This poster presents a method for determining which freezers may require maintenance before failure occurs.

Methods: Freezers were subjected to annual Performance Qualification (PQ) tests using NIST-traceable thermocouples at defined mapping locations. An analysis of the distribution of hundreds of freezer chamber temperature readings, spatially and temporally distributed within and among freezers, was conducted.

Results: Analysis has shown these PQ temperature measurements to be normally distributed around a mean near the freezer setpoint. The temperatures reveal the classic bell curve around that mean.

Conclusions: Statistical analysis of yearly Performance Qualification data can demonstrate which freezers may be prone to failure and should receive maintenance and which fall within the normal range. Selecting units where any temperature reading during the PQ falls two standard deviations above or below the mean value will identify the 5% of freezers that are most likely to require maintenance. Automatically performing maintenance on these freezers in advance of catastrophic failure will maximize sample integrity while minimizing maintenance costs.

QAC 19. Maintaining Data and Sample Quality: Experience with a Hospital-Based Biorepository

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Background: Maintaining data and sample integrity is essential in large-scale biorepositories. We analyzed DNA and data quality in a hospital-based biorepository for childhood onset heart disease (CHD) and mechanisms to reduce error rates.

Methods: 2350 patients < 18 yrs with CHD were enrolled (2008-2011). Data was stored on a secure web-based platform. DNA was stored as master samples at −20°C, and as aliquots at 4°C. 40 participants (2%) were randomly selected for data audit. Data was compared with electronic medical records (EMR) and intake questionnaires for accuracy and completeness, and was assessed for compliance with privacy and international best practices. Sample quality was assessed by gel electrophoresis on 11 randomly selected DNA samples. 10 samples also underwent gender verification using Amelogenin marker.

Results: Data storage was compliant with international best practices. 27% cases had missing EMR data, 47% had missing questionnaire data, 20% had inaccurate EMR data, 17% had inaccurate questionnaire data. Together, these accounted for < 1% of missing or inaccurate data fields for any given patient. Factors contributing to incomplete data were ongoing amendments to data collection forms, technical errors in data upload and use of free-text fields. All DNA samples were of good quality with no cases of misidentification based on gender testing.

Conclusions: Ongoing assessment of data and sample quality is essential. Data completeness can be improved by minimizing amendments in data capture and by minimizing free-text options. DNA integrity can be preserved by minimizing freeze and thaw cycles by storing DNA as aliquots.

QAC 20. Facilitated On-line Tissue Quality Assessment for Biological Repositories

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Background: The Human Tissue Resource Network (HTRN) at The Ohio State University Medical Center provides shared services for the AIDS and Cancer Specimen Resource (ACSR) and

Cooperative Human Tissue Network (CHTN). Quality control (QC) is vital but expensive and time-consuming in tissue biobanking. Traditionally, pathologists review QC H&E stained tissues via microscope, confirm the regions of interest (ROI%) and record findings on paper. This delays release of tissues to investigators. An on-line tissue QC pathologist review/release process was designed using digital (20X) slide images (Scanscope, Aperio, Vista, CA), image analysis software (Tissue Studio, Definiens, Munich, Germany) and a web-based pathology management system (Spectrum, Aperio) to facilitate pathologist's review of technical QC results on-line, make corrections/additions and release QC results.

Methods: The manual tissue QC process was detailed for two weeks by monitoring times between tissue arrival and release. Time taken by the various steps was tracked. A facilitated on-line QC process was designed and paralleled (second pathologist) using 120 cases (breast, prostate, kidney, gut, sarcoma, liver and lymphoma).

Results: The facilitated on-line QC process reduced turnaround time (3 vs. 10 days), provided digital image and twelve text data fields, a complete visual analysis map of the image, attached pathology report file, forty-one data drop down elements, data security and a tissue QC data management system that required 30% of traditional effort.

Conclusions: A facilitated pathologist on-line QC process provides for improved turnaround, efficient storage and retrieval of tissue QC records with images/ROI maps to share with investigators.

QAC 21. Documentation of Research Tissue Quality: Application of Definiens Tissue Studio 3.0 to Region of Interest Assessment

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Background: Research tissues must meet quality and investigator specifications before release. All must have confirmed diagnosis, sufficient % region of interest (ROI) to meet investigators needs and limited elements such as necrosis and hemorrhage. The Human Tissue Research Network (HTRN) at the Ohio State University Comprehensive Cancer Center including AIDS and Cancer Specimen Resource (ACSR/NCI) and the Cooperative Human Tissue Network (CHTN/NCI) evaluated Tissue Studio 3.0 software (Definiens, Munich, Germany) to determine if recognition of ROI in digitized H&E tissue quality control (QC) sections could be comparable to similar pathologist assessment.

Methods: H&E stained tissues from 95 QC tissue blocks previously assessed by a pathologist were selected for evaluation. A variety of tissue types (breast, cervix, colon, endometrium, kidney, lymph node, ovary, prostate, thyroid and lymphoma) were included. Algorithms were constructed for each tissue/ROI type using 2-4 representative cases to train up to 8 different morphologies. Results were reviewed by a second pathologist and compared to previous pathologist ROI assessments.

Results: Algorithm results were within 10% of the pathologists' visual assessment of %ROI in over 60% of cases. Over and underestimates of >10% ROI comprised the remainder of cases. Simple tissue morphology comprised the 60% and complex morphologies such as prostate cancer comprised greatest differences.

Conclusions: Definiens algorithm assessment of ROI was similar to pathologist assessments. Complicating factors that reduced agreement included tissue, slide, and digital scan quality and complexity of tumor morphology. Definiens algorithms improve with experience and have technical advantages for use in a biorepository tissue QC process.

QAC 22. Developing a Quality Specimen Collection for the NIEHS GuLF STUDY

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Background: The National Institute of Environmental Health Science's (NIEHS) GuLF STUDY is designed to investigate the potential health effects associated with the clean-up activities following the Deepwater Horizon disaster in the Gulf of Mexico (April 2010). Biological and environmental specimens, and questionnaire data, provide a valuable resource for research questions related to the oil spill workers' health.

Methods: Blood, urine, toenail and hair samples, and household dust are collected from workers in five affected Gulf States. SRA International coordinates field operations while Social & Scientific Systems, Inc. (SSS) serves as the central processing laboratory for receipt, processing, short-term storage, and specimen tracking. SSS developed a laboratory Quality Management System (QMS) for long-term specimen quality focusing on: facilities and security; staff training; detailed "best practice" procedures, quality indicators; tracking; and pilot testing. Pilot testing included EBV immortalization of a subset of lymphocyte and whole blood samples processed at different time points.

Results: This presentation describes the practice and impact of QA activities on: field collection issues; in-house assessments, cell preservation methods, annotated records, and validation by external facilities of cell recovery, cell culture, and absence of contamination.

Conclusions: This QMS for the GuLF Study baseline period provides a foundation for ongoing collection for future analyses of biomarkers of interest. The most important practices to yield a quality specimen collection are: SOPs, training, well-defined and secure labeling; storage facilities with monitoring, security, and backup; material tracking, inventory system, and database integration; operation monitoring; preventive maintenance; records and documentation archive; and interim pilot testing.

REPOSITORY AUTOMATION TECHNOLOGIES (RAT)

RAT 01. High Throughput Solution for MicroRNA (miRNA) Isolation from Stabilized Whole Blood in a GLP Setting: Development and Comparison to Established Procedures

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Many scientific groups in academia and in life science companies investigate the use of miRNAs as biomarkers, as they hold much promise for the development of genetic markers of disease. As these small RNAs become more and more important, effective and reliable isolation procedures are urgently needed. Especially standardization and exclusion of human errors require new automated solutions which are able to replace established manual processes without losing quality and quantity of the needed analytes. In this study we compare a newly developed procedure

on a robotic platform to previously published automated (Kruhøffer, 2007) as well as manual procedures.

Whole blood from consented healthy adults was collected into PAXgene Blood RNA Tubes and subjected to RNA isolation. The RNA quality and quantity were analyzed. miRNA yields were determined by qRT-PCR using probe based assays on a nanofluidic high throughput instrument.

Compared to the published partly automated method the workflow could be streamlined resulting in a fully automated procedure and the time needed for manual steps could be reduced by more than 50%. In parallel, the quality and quantity of the isolated RNA was not affected. With respect to miRNA enrichment, the performance was at least comparable to all tested current methods.

This comparison demonstrates the high efficiency of this optimized, fully automated procedure for miRNA purification which provides the standardization required in a GLP setting.

All miRNA enrichment protocols, the PAXgene Blood miRNA Kit and the PAXgene Blood RNA MDx Kit are for research use only. Not for use in diagnostic procedures.

RAT 02. Evaluation of an Automated High Throughput System for Purification of gDNA from 100-350ul of Human Blood

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There is increasing demand to purify gDNA from blood at a small scale using high throughput liquid handling platforms. The Promega ReliaPrep Small Volume HT gDNA Purification System has been created to recover gDNA from 100-350ul of whole blood. Here we report on the automated performance of this chemistry on the Beckman Coulter Biomek FXp. Experiments comparing automated gDNA extraction to a manual precipitation-based chemistry and the manual QIAamp DNA Mini Kit from Qiagen are shown using replicates of fresh or frozen blood collected in EDTA, heparin and citrate tubes. The gDNA from all methods was assayed for yield and purity on the Nanodrop spectrophotomter and also quantified using fluorescent dsDNA stains. Size was evaluated by agarose gel electrophoresis. Compatibility with downstream assays was confirmed by both endpoint and real-time PCR. Genomic DNA isolated with the automated ReliaPrep showed equivalent or superior yields and purity in comparison with the manual kits. Gel analysis confirmed the purified DNA is of high molecular weight and the PCR assays demonstrated that it is compatible with downstream assays. Additionally, the ReliaPrep kit performed well with both fresh and compromised blood samples unlike either of the manual kits. The ReliaPrep™ 96 gDNA Mini HTS Purification System enables purification of high quality, downstream assay-compatible gDNA from human blood with walk-away automation and processing times of less than 2.5 hours for 96 samples.

RAT 03. Sample Integrity and Risk Management as Central Theme for Establishment of a Fully Automated Storage Facility

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Background: LifeLines is a longitudinal cohort study of 165000 individuals in the general population. For storing 8 million tubes with biomaterial an automated storage facility for long-term storage (>30yrs) at −80°C is needed. To minimize risks and to get the best result for the overall project and specifically, the quality of the stored samples, an innovative tendering method was applied.

Method: The procurement of the automated storage equipment used Best Value Procurement (BVP). Few specifications were given during the tender procedure. Besides storage capacity and the maximum temperature of −80°C, we used a fixed ceiling price based on total cost of ownership, including energy costs and additional cost of the building. During two information days BVP and LifeLine's vision on sample integrity was presented. The suppliers had to convince us of being the expert also during interviews with three key-persons of the supplier who really would be involved with the execution of the project. Risk management was incorporated throughout the whole project.

Results: The tender procedure using Best Value Procurement gave a clear indication of the supplier's proposals about scope, risks, value adds, planning and the company's project organization behind the offer. Risks identified and their mitigation measures were developed before award of the tender.

Conclusions: The applied method of Best Value Procurement provided better possibilities to select the provider on dominant issues and to make the best use of the expertise available on the market. Risks for the sample quality, the organization, and the project were minimized.

RAT 04. Quantitative Comparison of Immunohistochemical Staining Intensity Measurements on Tissue Microarrays by Computer-Aided Digital Imaging Analysis versus Pathologist Visual Scoring

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Background: Repositories that store clinically-annotated formalin-fixed paraffin-embedded (FFPE) tissue blocks are essential for the construction of tissue microarrays (TMAs) for high throughput studies. Immunohistochemical (IHC) staining of FFPE tissues is a reliable technique for validating biomarkers discovered through genomic methods. IHC assays performed on FFPE tissue sections traditionally have been semiquantified by visual pathologist scoring of stain intensities. Due to the ubiquitous availability of IHC techniques in clinical laboratories, validated IHC biomarkers may be translated readily into clinical use. However, the method of pathologist semiquantification is costly, subjective, and produces ordinal rather than continuous variable data. Computer-aided analysis of digitized slide images may overcome these limitations.

Methods: Using TMAs representing duplicate samples from 54 ovarian carcinoma specimens stained for S100A1, we assessed the degree to which data obtained using computer-aided methods correlated with data obtained by visual pathologist scoring. IHC staining intensities within pathologist annotated and software-classified areas of carcinoma were compared for each case.

Results: IHC staining intensities obtained from manual annotations and software-derived annotations were highly correlated ($r = 0.99$, $p < 0.0001$). A comparison of IHC intensity data derived using pixel analysis software versus visual pathologist scoring also demonstrated a high correlation ($r = 0.88$, $p < 0.0001$).

Conclusions: This study demonstrates that computer-automated methods to classify image areas of interest (e.g., within carcinomatous areas of tissue specimens) and quantify IHC staining intensity

within those areas can produce highly similar data to manual and visual evaluation by a pathologist.

REPOSITORY INFORMATICS (RIF)

RIF 01. Building a Successful Network: Providing a Virtual Inventory and Single Point of Access

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Background: Regional, national, and international biobanking networks require a unified workflow process that integrates with heterogeneous inventory management systems; manages data import and standardization; provides biospecimen search capability across networked biobanks; manages review and approval processes for biospecimen requests, including Material Transfer Agreements; and allows for shipping, invoicing, and collecting biospecimen quality metrics.

Method: Collaborate with member biobanks, research community, and regulatory agencies to address challenges within biospecimen-based research. Develop a single customizable tool to accommodate different types of biobank networks. Federate commercial, government and hospital biobank networks by synchronizing data from each participating biobank into a virtual, centralized inventory. Establish an open-source virtual biobank for different types of biobank networks and provide ability to browse available biospecimens and locate/request/ship biospecimens in a uniform manner.

Results: Successfully created an open-source virtual biobanking portal that is re-usable and configurable based on biospecimen type, network organization, and research speciality. Utilized technology such as web services, content management systems, and standardized code-sets. Incorporated regulatory policies and guidelines, security compliance, biospecimen usage rules and participant consent, biospecimen location and request review workflow, and support of multiple biospecimen and disease types.

Conclusion: Benefits of a virtual open-source networked biobanking model include broader reach to the research community, sharing of investment resources and collective domain knowledge, and improved visibility of biospecimen assets across heterogeneous biobanks. Several regional, national, and international networks have adopted the tool for their virtual biobanking network.

RIF 02. Text Mining to Extract and Evaluate Biospecimen Provenance Information

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Background: Biospecimen provenance information is the detailed history of a sample, including its source, collection, processing and storage parameters. Inadequate or inaccessible provenance information for samples used in experiments may confound analysis and reuse of research results. Recently, standards for reporting and recording of biospecimen provenance information (BRISQ and SPREC) have been published. Although developing and disseminating these guidelines and standards is an important step in changing practice, the adoption of these innovations may be delayed by the cost of implementing them across a variety of existing organizations. Systematically extracting and evaluating the adequacy of provenance information in research literature may provide an incentive to implement best practices in recording and reporting these variables.

Methods: Text mining tools may be trained to systematically evaluate provenance information in the literature. The annotations for over 1400 publications in the NCI Biospecimen Research Database (BRD) provide a starting point for development of text mining tools. Using the labels and snippets of information from BRD annotations, we will train a classifier to extract terms, assign labels, and classify documents according to level of provenance information.

Results: The result of this project will be an informatics tool to extract and classify biospecimen provenance information. The tool will be evaluated both in terms of its technical performance, and its value to potential users such as journal publishers, editors, organizations that fund research with biospecimens, and individual scientists or laboratories.

Conclusions: Text mining may be a useful tool to evaluate and improve best practices for reporting biospecimen provenance information.

RIF 03. The Integration of Biobanking and Bioinformatics with Routine Health Services - A Blueprint of the Nottingham Health Science Biobank

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The Nottingham Health Science Biobank (NHSB) has established a centralized resource for the storage and management of high quality biomaterials which has obtained generic ethical approval. Permission to take tissue samples for research is embedded within the routine hospital consent process and allows prospective collections of biosamples from any patient undergoing surgical/endoscopic procedures or attending outpatient departments within Nottingham University Hospitals. Harvesting and transport of samples uses routine hospital services and patient consent for the Biobank is conducted and overseen by trained patient advocates. The NHSB also has approval to use the existing tissue archive. In order to utilize existing skills in tissue processing and management the NHSB is supported by a dedicated research infrastructure and management in the Department of Pathology.

The scientific value of the sample is not only determined by the quality, but also linkage to valuable patient data. Existing hospital information systems which hold patient data are difficult to access or search. We have therefore elected to develop a new coding architecture and informatics capacity (ORCHID) which can order, access and interrogate patient data for research purposes and will replace the existing Trust clinical management tools. ORCHID will permit routine linkage between the accumulating patient information record and the NHSB. In order to maximize the benefits of this resource further real time links between ORCHID and other hospital information systems have been constructed.

Taken together, we anticipate that this novel research platform will offer a powerful resource for translational medicine and enhance productive partnership with industry.

RIF 04. Acquire: A Data Management and Reporting Tool for the Texas Cancer Research Biobank

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Background: Over a three year period, the Texas Cancer Research Biobank (TCRB) is collecting ≥2,000 tumor and matched normal specimens, meeting The Cancer Genome Atlas (TCGA) criteria from study participants enrolled at sampling site institutions across Texas. Specimens then undergo nucleic acid sequencing by the TCRB Nucleic Acids Core (NAC) at the Baylor College of Medicine Human Genome Sequencing Center.

Methods: TCRB Acquire is a secure, web-based, Oracle database-backed, Enterprise Edition Java application that utilizes standard controlled vocabularies, ontologies and objects from the National Cancer Institute, TCGA, Clinical Data Interchange Standards Institute, and other national and international standards bodies.

Results: Acquire is a modular system being developed to manage study participant demographic and consent, tumor specimen and histopathology, and matched normal specimen data in virtual repositories (caTissue Suite 1.2) and clinical annotations (CCA); provides real-time reports of the total number of collected specimens broken down by sampling site and by anatomic sites of origin in study subjects; generates non-identifying data reports for shipping as specimens in Acquire are sent to the TCRB NAC; allows for construction of ad hoc queries and report generation (Query Portal); will provide a mechanism to manage scientists' requests for TCRB resources and for TCRB oversight committee review (TARA). Acquire is continuing to evolve, with the end goal of these modules all being seamlessly accessible through a single Portal page.

Conclusions: Acquire is available at https://tcrb-acquire.research.bcm.edu

RIF 05. Future-Proof Your Biorepository LIMS

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Background: Millennium's Sample Management System has evolved significantly in a twelve year period from a homegrown database to a customized Laboratory Information Management System (LIMS) that tracks over 800,000 biological specimens from Drug Discovery to Development. The highly customized product lacks vendor support and falls short of the lab's requirements and technologies.

Methods: Millennium has evaluated a number of LIMS software to find a replacement solution that not only meets business needs but also have the flexibility for future upgrades, configuration and integration with internal database applications. The software selection process consists of needs assessment, sending Request for proposal (RFP) to qualified vendors, demos/site visits and product evaluations.

Results: Millennium has invested in a commercial-off-the-shelf (COTS) LIMS solution that provides all the features required to manage the dynamic workflow of the biorepository from sample collection to data reporting. The product's technology and business logic are separate components of a multi-tiered architecture that allows modification of one without compromising the other. Implementation of an adaptable LIMS platform will preserve existing business rules while permitting ongoing configuration and system upgrades.

Conclusion: Innovation and change are the norm in research labs and informatics. Future-proofing your LIMS product to keep pace with the rapidly changing landscape will reduce cost of ownership and maintenance throughout the LIMS Lifecycle.

RIF 06. Engaging Campus Biobanks in the Requirements Specification, Software Selection and Implementation of an Enterprise-Wide Biobanking Information Management System (BIMS)

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Background: Biobanking at Duke has developed over time in silos, resulting in numerous collections banked individually by independent researchers and maintenance of partially redundant parallel biobanking facilities. Furthermore, separate and disparate biological specimen tracking systems evolved to meet the changing and distinctive needs of Duke's researchers. Duke researchers and biobank administrators identified a need to harmonize the existing biobanking systems, as well as to have an institutionally supported biobanking informatics system.

Methods: The Duke Biobank, together with key operational and informatics experts from Duke's major biobanking groups, formed a Biobank Informatics Working Group (IWG). The IWG developed a formal Request for Proposal to select a comprehensive Biospecimen Information Management System and issued it to pre-qualified vendors. A dedicated Project Manager kept IWG members focused and drove the project goals and timelines. Members of the IWG as well as subject matter experts evaluated and scored the vendors' proposals, and selected three finalists. The finalists demonstrated their product at Duke and a single BIMS was selected and recommended by the IWG.

Results: Through active involvement in requirements specification and solution selection the IWG members were engaged and their specifications were represented in each phase of the selection process. Together, this group selected a central biospecimen tracking and information management platform to serve all the biobanking informatics needs at Duke.

Conclusion: The significant effort invested by the biobanking experts in this collaborative process built consensus and facilitated buy-in and adoption of the enterprise biobanking informatics platform at Duke.

RIF 07. Extending a Traditional LIMS to Create a Recruitment Management System

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Background: In 2005, the Research Program on Genes, Environment and Health (RPGEH) set a goal of recruiting 500,000 Kaiser members to provide either saliva or blood samples along with a survey on their environment, lifestyle behaviors, health conditions, and their families' health conditions and store those samples in a biorepository. To support the initial growth of the program, RPGEH developed three in-house systems to manage all biorepository activities including recruitment management, sample processing, and storage. However, with the construction of a state-of-the-art biorepository in 2010-11, the RPGEH saw an opportunity to expand the scope of traditional biobanking activities to include recruitment, mail batching and call event management all within a single integrated system.

Methods: To support its growth, the RPGEH partnered with LabVantage Solutions, Inc. to extend their Sapphire Laboratory Information Management System (LIMS) to not only provide a traditional LIMS for lab operations, but also to build a highly configurable Recruitment Management System.

Results: From September 2010 until October 2011 the LIMS was implemented and deployed at the new RPGEH biorepository. The LIMS extends the traditional LIMS beyond the laboratory to track potential participants from the first mailing to collection and storage.

Conclusion: The LIMS went live in the Fall of 2011. The system currently manages more than 1,000,000 Kaiser members, 200,000 of whom have provided consents and specimens.

RIF 08. caTissue Suite 2.0: An Open-Access, Feature-Rich Tool for Biospecimen Annotation and Data Sharing

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Advances in molecular technologies and clinical trial design have mandated new requirements for the operation of biorepostories. caTissue Suite is a caBIG™ application, now in its sixth iterative release, that is designed to manage the complexities of biospecimen annotation data.

New features and architectural redesign of caTissue Suite 2.0 are based on continued requirements gathering and acceptability testing by the biobanking community across multiple institutions worldwide. Its open program interface (API) permits access to the application's features and facilitates data integration with other systems. The application supports role-based access to administrative functions, biospecimen accessioning, and investigator queries. caTissue Suite 2.0 includes several usability enhancements and a new functionality to define and record specimen processing procedures and events in the biospecimen life cycle. In addition, caTissue Suite 2.0 provides interoperability with the NCI's Clinical Trial Reporting Program (CTRP), has improved caGrid operability, and allows for the export of biospecimen data in MAGE-TAB format, suitable for use with other integrative cancer research tools such as caArray.

caTissue Suite is sufficiently scalable and configurable for broad deployment across biorepostories of varying size and function. A caBIG™ supported, web-based "Knowledge Center" (https://cabig-kc.nci.nih.gov/Biospecimen/KC) provides ongoing application support via discussion forums, technical and user guides, training, and webinars.

caTissue Suite is a freely available, fully supported, open-access software application for biospecimen data management. Use of caTissue Suite by several NCI Cancer Centers and other biospecimen resource groups is providing a rapid and facilitated path toward standardizing biospecimen informatics and promoting biospecimen data sharing both nationally and globally.

RIF 09. Patient Data and Research Databases: A Strategy for Balancing What Researchers Want and What a Cancer Biobank Can Deliver

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Background: A great deal of attention is rightly paid to ensuring good laboratory practice in biobanking. However, most cancer biobanks are of limited use without good quality clinical data and follow up. Obtaining this data is often difficult, most biobanks do not have appropriate databases to store it and there is no apparent consensus on what constitutes a minimum dataset or what researchers want. Moreover, any data generated by researchers would ideally be recorded and associated with the patient so that new users do not repeat analyses already done.

Method: Using our colorectal cancer collection we have assessed what data was required from collaborators in France, Singapore, Australia and the United States and the feasibility and cost of obtaining this data.

Results: A minimum core of clinical data was required by all researchers mostly relating to diagnosis including staging. Treatment data was universally requested but the detail required varied from basic yes/no to comprehensive details of all treatments given. There was a poor comprehension of what constitutes 'follow up' by way of treatment, recurrence and survival. We present a cost analysis of collecting the varying levels of data required. Finally we present a strategy for how data generated by researchers may be reintegrated in the biobank database and what resource requirements this imposes.

Conclusion: The feasibility of collecting a data point varies and should be determined depending on what researchers actually need as well as on what is feasible. Early planning can prevent misallocation of resources and management of researcher expectations.

RIF 10. Vision on the Application of an Electronic Laboratory Notebook for Biobanks

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Background: Detailed annotation of each sample's lifecycle, and the fact that the value of a sample depends on quantity and quality of supplementary data, pose a particular challenge to data management. The situation becomes even more demanding in view of data protection-conformity, separation and storage of data. Separate documentation of analytical, phenotypic, and biomaterial data plus keeping the usual laboratory notebook clearly increase the documentation effort.

Methods: In order to decrease documentation effort and increase quality of annotated data, thus augmenting total sample quality, we propose the use of an electronic laboratory notebook (ELN) for biobanks. The ELN should be viewed as a portal for data entry. Data entered into the ELN will be automatically sorted and forwarded to the databases for administering biomaterials, for phenotypic data, and for genetic analysis data.

Results: Replacement of paper-based documentation by an ELN would potentiate benefits such as single ELN-login providing one data-entry-mask and automatic distribution of items to distinct databases. Simultaneously, data protection laws are being observed and users profit from an effective SOP-based standardized metadata documentation process.

Conclusions: For linking all annotation data of biospecimens within the data generating research unit, ELNs could operate as a real-time internal research database – with defined rights and roles – in which searching for keywords, full text and query-by-example is supported. Existing concepts for generation of pseudonyms and storage of identifying data need to be adapted. In addition, the metadata recorded in the ELN should be used for the required long-term preservation.

RIF 11. Advances in Sharing Biorepository Information Through the Common Biorepository Model (CBM)

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Background: In 2009, we introduced the United States' National Cancer Institute Common Biorepository Model for vendor and biorepository software to expose summary-level data about specimen collections available to researchers. A number of biorepository management system vendors and biorepositories are participating in the CBM Challenge to share specimen data, and thereby populating the NCI Office of Biorepository and Biospecimen Research's (OBBR) Specimen Resource Locator.

Methods & Results: Covering diseases besides cancer, diagnosis lists from the specimen resource community across additional NIH institutes were incorporated. Key vendors have participated in testing, and an associated caBIG® service has been developed to enable repositories to publish queryable summary-level information about their specimen inventories under a common data model and vocabulary set. Direct feeds from repository software pave the way for keeping the shared data up to date. At least two vendor and open-source solutions with partnering biorepositories will be shown publishing data and queryable information via the NCI Specimen Resource Locator.

Conclusions: The CBM initiative has drawn participation from vendors of biospecimen management applications, both homegrown and open source. Biorepository data can now be shared across sites, regardless of biorepository management software used, as long as terms are mapped to a CBM standard vocabulary. Through use of the caGrid, the CBM makes the interoperability envisioned in OBBR's Best Practices for Biospecimen Resources more easily achievable; providing current information to researchers and institutes as they attempt to locate specimens and ascertain their availability.

RIF 12. Development of a Biobank Information Management System: Proof of Concept Study

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Background: Biobanks are defined by the samples and associated (minimal) clinical data. In this regard, information management systems are an indispensable tool in biobank management. The tumour biobank@UZA conducted a comparative study between different Laboratory Information Management Systems (LIMS) and conducted a proof-of-concept (POC) study.

Methods: Different LIMS systems were compared based on efficiency, costs, flexibility, user friendliness and connectivity, advantages and disadvantages. SLims (Genohm, Belgium) was selected and evaluated in the POC over a six month period. The use cases involved the import of historical data, real-time data integration and data export, sample management and processing. A serum biobank was integrated in the same LIMS.

Results: The POC resulted in a custom-made sample management system, enabling efficient data import and transfer. The use of an integrated biobank system identified data inconsistencies and resulted in an overall quality increase of the minimal clinical data associated with the tissue tumor samples. Interconnectivity between data sources and devices enables import of valuable qualitative parameters. The system was validated using virtual and real test cases. Sample management for serum samples was successfully integrated and tested in the existing system.

Conclusions: Product comparison and the POC resulted in a custom-made sample management system for the tumour biobank@UZA. Further optimization is still required to meet existing and future requirements.

Acknowledgements: The tumor biobank at the Department of Pathology (UZA) collaborates with surrounding hospitals for sample collection and as such contributes to the development of a virtual tumor biobank of the Belgian Cancer Registry.

RIF 13. Development of a Repository Database Utilizing the Clinical Electronic Medical Record

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The Spectrum Health Cerner Millenium system integrates all aspects of the electronic medical record (EMR) including its Anatomic Pathology Module (PathNet-Laboratory Information System). We have developed a separate numbering sequence and reporting methodology for research specimens that is linked to the corresponding surgical pathology report and to all clinical information present in the EMR; at our institution this extensive clinical information includes laboratory results, radiology reports, admission notes, operative notes, and more. Specimen parameters, e.g. cold ischemic time, weight, and QC data, are stored in the research specimen report. Discrete data points may be pulled from an associated data warehouse. SNOMED coding is applied automatically and a robust data retrieval application allows for nimble case retrieval. The link between the research number and patient identifiers is secure, available only to those with a defined "honest broker" role.

Utilization of the Laboratory Information System (PathNet) allows for easy research specimen accessioning and labeling using the same familiar practices that are utilized for clinical specimens including bar coding functionality. Similarly, research charges are attached and units of service (UOS) are monitored in a way that parallels the clinical service.

Data are easily exported as spreadsheets or other versatile formats to be utilized in a variety of research databases.

The principles we have developed are applicable to any integrated electronic medical record. We will demonstrate our accessioning process, report format, case retrieval functionality and data warehouse capability and provide examples from our system of exportable search results that will be of use to biorepositories.

RIF 14. The Data Warehouse: Building Access to the Study of Women's Health Across the Nation Resources

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Background: The SWAN Repository, established under the leadership of Dr. MaryFran Sowers, is the biospecimen bank of the Study of Women's Health Across the Nation (SWAN). The

goal of SWAN, a NIH-funded multi-site, longitudinal study of women's health, is to describe the biological and psychosocial changes that occur during midlife and the menopausal transition. Over 17 years, SWAN has collected over 18,000 variables, using over 120 different instruments.

Methods: SWAN Repository developed the Data Warehouse, a data-rich website which makes SWAN resources more accessible to the scientific community and investigators. This system uses a keyword search engine which connects users to SWAN-collected data, Repository-generated data, SWAN publications, and descriptions of available biospecimens.

Results: Each SWAN variable has been individually linked to keywords based on the National Library of Medicine's MeSH (Medical Subject Headings) hierarchy. From each keyword users can see all variables associated with that keyword, along with actual questions, response codes, and methodology. The same keyword list will also link to all previous and current studies and publications of SWAN, by chosen topic. Data generated from Repository-supplied studies is returned to the Repository within three years of the close of study and incorporated into the Data Warehouse. The Data Warehouse will also provide methodology and availability of nearly 2 million collected biospecimens (DNA, serum, plasma, urine) across study years, and information on gaining access to these specimens.

Conclusions: The Data Warehouse is a valuable tool in the management and utilization of SWAN resources.

RIF 15. Implementing New Technologies and Data Migration of Existing Data at a Multi-site Biobank: The AIDS and Cancer Specimen Resource Experience

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Background: The AIDS and Cancer Specimen Resource (ACSR) was established by the National Cancer Institute in 1994 as a multicenter biospecimen repository. In addition to physical specimens from patients with HIV-associated malignancies, the resource houses specimen and patient associated demographic, epidemiological and clinical data. The ACSR has become a unique and valuable resource for research studies of AIDS-related cancers. However, informatics needs have changed over time, necessitating a reengineering of the existing 12-year old database system.

Methods: ACSR protocols, procedures and activities were evaluated in relation to the existing database system via: 1) detailed interviews with Primary Investigators and staff and 2) regional site visits. In-depth assessments of site-specific personnel, expertise and technical resources were made to determine how to best accommodate current and projected biobanking needs.

Results: The overall assessment showed that although the biobanking staff was highly skilled there was extensive variability in informatics expertise and technical resources. Further, the diverse workflow of each regional site complicated the adaptation of a flexible well-integrated system that would meet the needs of all users and the overarching goals of the ACSR.

Conclusions: Formal evaluation confirmed a critical need for a more flexible, dynamic database platform. Results are being applied to develop software tools that allow: 1) migration and clean-up of existing data and 2) modifications to integrate key utilities that foster seamless ACSR functioning. Ongoing system appraisal and built-in system flexibility will facilitate successful incorporation of prospective collections and assure support for evolving needs of the AIDS and Cancer research community.

RIF 16. Biobank Data Management in 2020

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Background: Consumers are increasingly used to being connected to the world around them and being able to access data and information wherever they are. It is a good moment to consider how these changes in technology and connectivity will influence the life in the biorepositories and biobanks in the next 8-10 years when it comes to data management.

Methods: Today there are some challenges to having people be the laboratory interface technology, simply because they are not good at it. Human transcription has an error rate of about 3-6 errors per 1000 transcriptions and under pressure (e.g. when mathematics is involved) that increases to 3 errors per 100. Also outside influences affect their behavior, which may also have an impact on the result you are recording.

Results: As a consequence, a lot of controls in the lab are there to prevent mistakes and errors from getting into your analytical results of the valuable samples to be stored and retrieved. Technology such as tablet PCs, cloud based computing, advanced integration tools, as well as advances in instrumentation capability has the potential to significantly change the way the laboratory operates.

Conclusions: Innovative developments in repository informatics will enable biorepositories' staff to carry out lab workflow in and easy to use, familiar environment completely based on the role they have in the laboratory in the next decade.

RIF 17. Regular Expression Matching Algorithm (REMA) Simplifies Operative Schedule Searchability for Prospective Tissue Procurement

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Background: Streamlining operational procedures for increased efficiency is an ongoing process in the biobanking industry. To ensure sustainability, we have continually reviewed and updated operations with innovative technologies. To increase the efficiency and simplify the process of targeting tissues on daily Operating Room Schedules (ORS), we have developed a multi-tiered application. This application was developed using Regular Expression Matching Algorithm (REMA) which is capable of searching narrative free-form text for key word variants as patterns, without regard to extraneous characterization, to generate discreet data elements.

Methods: A Boyce-Codd compliant referential data structure was developed to store the definitive parameters of cross-referential terms from 1) digitally accesible ORS, 2) biosample request datasources and 3) biobank procurement/inventory databases. Non-repeating descriptors of character patterns (data elements) found in ORS, is stored via a data engine contained in a MYSQL data server. The application tier, written in JAVA, runs

automatically from a Linux-CRON schedule. With the data element definitions in place, REMA application performs automated "scans" of ORS textual procedures and flags applicable procedures for technician review.

Results: On a daily basis, REMA application searchs ORS at multiple institutions within our health system. Over 300 ORS procedures are scanned with an accuracy rate of about 92%. REMA's capacity allows the technician to spend more time in procurement activities than in searches.

Conclusion: Using REMA application, we have shown that automation of targeting processes enhance the accuracy and improves consistency of technician's workflow while maximizing the opportunities in obtaining tissues for the biobank.

RIF 18. Deployment of caTissue Suite After System Optimization and Migration of Legacy Data: Experience at a Large Academic Medical Center

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Background: Biorepositories software tracks biospecimens and additionally participant data including clinical history, visit-level data including consents, and specimen data including diagnoses. Biorepositories often faced dual tasks: migrating legacy data and initiating use of a new system. Few reports describe the process by which biorepositories navigate these tasks.

Methods: We selected caTissue for biospecimen inventory management, as part of an information technology (IT) architecture. An installation process, budget, and timeline were prepared including data security plan, hiring a contractor, designing 2D-barcoded labels, migrating legacy data on ~70,000 specimens from ~30,000 participants, and optimizing software to match workflow. At the conclusion of the project, initial expectations were compared with final results.

Results: The project required 140% more time than anticipated (24 months versus 10 months expected), and 2.1% larger budget (contractor and equipment expenses; negating biorepository personnel time). Unanticipated time was required to map data elements from the legacy database to allowable elements in caTissue. For many cases, appropriate diagnostic coding required review of QC slides and pathology reports. Some data fields required new (Dynamic Extension) fields. Other fields were discarded due to low anticipated use. Software improvements included restriction of label printing to printers available at the site of login. Final methods differed from those anticipated; much data input occurs via uploaded CSV files rather than via the main caTissue UI.

Conclusions: Biorepositories considering migration of legacy data and use of caTissue may benefit from our experience. Notably, the structure of legacy data importantly determines the time required for this process.

RIF 19. Sample Receipt and Management at the Genome Sciences Centre

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Background: Canada's Michael Smith Genome Sciences Centre (GSC) is a leading international center for genomics and bioinformatics research with a mandate to develop and deploy genomics technologies in support of life sciences research, in particular cancer research. We are involved in many collaborative research projects, both nationally and internationally, engaging our high-throughput sequencing, bioinformatics and proteomics platforms. We receive multiple sample types, from a wide variety of organisms. Increased throughput provided by current technologies has placed increased demands on sample management and information tracking.

Methods: The Biospecimen Core group was created to provide dedicated support for sample receipt, information management, upload, and distribution to technical and research platforms within the GSC. Modifications to the in-house Laboratory Information Management System (LIMS) were implemented to facilitate more structured and streamlined pipelines.

Results: The following processes have been established: 1) Collaborators for approved projects submit a Sample Information Form (SIF) which is reviewed and once approved the samples are shipped; 2) Chain of Custody form initiated at shipment; 3) Received samples verified to ensure correspondence with SIF; 4) Sample information uploaded into LIMS, samples are barcoded and exported to destination groups for processing. Further improvements are planned including an online submission process to improve efficiency.

Conclusion: Receipt of wide ranging sample types presents unique challenges and requires a flexible database capable of capturing and tracking a diversity of data relevant to each sample type. Centralizing these activities has resulted in a streamlined process for collaborators submitting specimens, the technical groups processing the samples, and downstream analysis.

RIF 20. The Duke Index of Biospecimens: Leveraging the NCI's Informatics Tool to Enable Translational Research at Duke

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Background: Facilitating translational research by enabling secondary use of collected biospecimens is an objective of the Duke Translational Medical Institute. Duke, like many academic medical centers, has multiple biobanking core facilities operating as separate and distinct silos. Also, many individual researchers have amassed biospecimen collections from their own research projects. The existing biospecimen informatics systems lack the semantic interoperability needed to connect researchers who need biospecimens with those who have them.

Methods: The National Cancer Institute (NCI) funded the development of the Common Biorepository Model (CBM) and the Specimen Resource Locator (SRL) to reduce the time and effort required by researchers to locate a biobank that has the specimens they need. Leveraging work done by the NCI, the Duke Biobank created an Index of Biospecimens containing metadata on collections at Duke. The SRL was customized to meet Duke's security and functional needs. Data from the Cancer Institute, the Center for Human Genetics, and independent researchers were harmonized to the CBM terminology and manually loaded. The governance and policies for participation in the Index were developed in parallel with the technology.

Results: The SRL was modified to meet Duke's specific needs for a tool to advertise the existence of specimen collections at Duke to other Duke researchers and data from select collections have been loaded into the initial release.

Conclusion: An important aspect of translational research is a simple mechanism to connect researchers in need of specimens to

contact other researchers that have collections they are willing to share.

RIF 21. Innovative and Agnostic Digital Pathology Solution Utilizing Cutting-Edge Technology to Increase Production and Overall Advancement of Translational Research

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Background: The Research Informatics Core & the Biomedical Imaging Team at The Research Institute of Nationwide Children's Hospital, with VectorForm LLC, are committed to advancing the field of digital pathology by increasing performance of the technology and supporting an agnostic approach to support the pathology discipline and translational research. The emergence of multiple vendors/solutions and the need for advanced solution integrator to leverage advantages of all solutions was apparent.

Methods: The Image Viewer utilizes Microsoft .NET and Silverlight for display in Microsoft Deep Zoom Image format. The annotations utilize Windows Communication Foundation (WCF) service in relation to Image Viewer and Annotations database (SQL Server). The Image Analysis suite utilizes algorithms written in C# with Image Magic wrappers. Microsoft's Kinect is a motion sensing input device featuring an RGB camera, depth sensor and multi-array microphone. The design is modular in nature, with a service-oriented structure, to enable integration and interoperability.

Results: The Digital Pathology solution will utilize multiple Microsoft products including HealthVault, Azure Cloud, Deep Zoom, Windows Presentation Foundation, and open-source tooling to complete the informatics plumbing. The innovative solution creates an experience for viewing high fidelity imagery and patient models. Pathologists and investigators can utilize various input methods to quickly navigate and create visual and audio. The digital pathology system supports remote collaboration between physicians and real-time annotation.

Conclusion: The innovative solution will facilitate standardization in the field, advancing telemedicine, computer-assisted decision support, pattern recognition, integration of disparate sources and the overall workflow to support the scientific community.

RIF 22. High Dimensional Repository: Informatics Solution Supporting Translational Pediatric Cancer Research

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Background: The Biopathology Center, biorepository for the Children's Oncology Group (COG), collaborated with the Research Informatics Core and COG leadership to design and develop an innovative enterprise informatics solution providing greater transparency into specimen workflow, including: institutional submission, repository accessioning specimen processing, molecular analysis, investigator specimen/data distribution, and the eventual receipt of processed results.

Methods: The team utilized an Agile Scrum methodology providing new functionality every 30 days, allowing stakeholders and subject matter experts (e.g. oncologist, translational scientist, repository manager, and informatics specialist) a voice and the opportunity to define and validate key functionality, workflow, and governance. The solution integrates and harmonizes the operational activities of several participants in the biospecimen lifecycle for pediatric cancer clinical trials, including: participating institutions, clinical data managers (the statistical data center), biorepository management, assay laboratories, and the investigator community.

Results: The team developed a dynamic data warehouse leveraging several innovative design elements, including: split backroom/front room data management, automated extraction/transformation/loading, a messaging-based data submission and cataloging system to ensure end-to-end data integrity and tracking, and a portal featuring extensive interactive querying against vast datasets pertaining to patient enrollment, specimens, assays and clinical variables.

Conclusions: Meeting the aims of the solution should increase the volume of translational projects produced by the pediatric cancer scientific community as well as the number and reach of publications. Further, we expect this highly-integrated platform to decrease the overall time from scientific concept to deliverable.

ISBER WORKING GROUP ABSTRACTS (WG)

WG 01. Activities of the ISBER Biospecimen Science Working Group in 2011

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The ISBER Biospecimen Science Working Group was created in 2007 to advance biospecimen science. In 2011, we compiled a significant update of biospecimen science literature. We implemented the Standard PREanalytical Code (SPREC) to standardize traceability and reporting of the preanalytical steps involved with collection, processing, and storage of human biospecimens. We developed and published a paradigm of SPREC for environmental specimens and an IT SPREC tool (OLOSPREC). Next, we performed a critical review of our literature compilation and identified potential evidence-based quality control tools, critical information about biospecimens often

lacking in research papers. One experimental project was conducted on the room temperature stability of extracted RNA, a second on the impact of logistics on cell viability. Finally, we developed and launched in October 2011 the first international Proficiency Testing schemes for biobanks - DNA quantification and purity and RNA integrity - in collaboration with the Integrated Biobank of Luxembourg (IBBL).

WG 02. ISBER WG on Hospital Integrated Biorepositories (HIBs) – Continuation of the WG on Clinical Biobanking Representation

As this WG is currently undergoing this transition from Clinical Biobanking Representation to Hospital Integrated Biorepositories, the final formation of members, including those who joined this WG at the ESBB meeting, will be provided on the poster.

In 2011 the ISBER WG on Clinical Biobanking Representation (CBRWG) officially started with a kick-off meeting but soon it became apparent that the term 'Clinical Biobanking Representation' allows for different interpretations. Therefore the term, definition and goals were revised.

The term 'Hospital Integrated Biorepositories (HIBs)' can be defined as 'biorepositories integrated within health care systems that collect biospecimens making use of the diagnostic and curative pathways of routine medical care'.

The goals of this WG are to identify the specific problems for HIBs, to notify the biorepository community of these problems and to supply a platform to work on these problems.

In general HIBs are non-project driven and part of or cooperate with a (university) hospital department. HIBs serve a wide community of researchers, providing a big diversity of sample types and conditions, with careful regulation of access to and issuance of samples and in compliance with consent and potential stakeholders.

Hot topics in biobanking such as 'return of results' and 'sharing of samples' but also new and stricter laws are of great concern for HIBs. The organization of a population repository is usually less complicated as compared to a HIB and usually more in favor of such new topics in biobanking, whereas the HIBs need to challenge many more obstacles. The caveat for HIBs in this is that these innovations in biobanking may be seen as (near) future standards for all biorepositories. HIBs are then forced to quickly adapt while they actually need more time and funding for implementation or even just cannot cope with these new 'standards'.

WG 03. ISBER RARE DISEASES WORKING GROUP

D. Carpentieri, E. Gunter, Y.Rubinstein, M. Barnes, B. Gendleman, F. Betsou, D. Lewandowski, J. Kessler, C. Rumpel, M. Watson, R. Ravid, J. Muller, B. Greenberg, A. Sharif, S. Sommer, J. Black, J. Motil, L. Neylon, J. Eliason, C. Portella, K. Goetz, P. Puchois, N. Kayadianian, M. Fernandez, I. Lomba, F. Franchini, M. Ozguc, M. Zink

Background: Orphan or rare diseases (RD) are a clinically heterogeneous group of over 7,000 disorders which are commonly diagnosed during childhood and often have deleterious long term effects. The World Health Organization has suggested a frequency of less than 6.5–10 in 1,000. Based on this definition, approximately 25 million individuals in the United States alone will be diagnosed with a RD at some point in their lives. Unfortunately, only a small percentage (around 300) of these disorders has an effective drug therapy. In this context, several organizations have been advocating for better funding and support. While significant clinical disparity exists among the many RD, these disorders may share key molecular features like hub proteins responsible for multiple protein-to-protein interactions. As expected, many of the problems and difficulties associated with biospecimens for common diseases also apply to RD biospecimens. In the latter, however, these problems are more acute. RD specimens, to the extent that they are available, are widely dispersed across geographical regions and among various government-supported and private biorepositories. In addition, lack of a consensus on human subject issues and ethical and legal regulations (informed consent, ownership, and patient privacy) interferes with global sharing of material, information, and final outcomes data.

Proposal: The working group is currently composed of 28 members from United States, Europe and Australia representing NIH, Biobanks, Private Institutions, Academia and Business. The major goals are to support advocacy groups and researchers by helping to standardize legal, ethical and scientific protocols across borders for future projects on specimens provided by patients with RD.

2012 PROJECTS:

1. Recognition award for initiatives supporting RD groups and research.
2. Pharma and biotech companies survey.
3. The Office of Rare Diseases Research/NIH database-RD-HUB advisory support.
4. Material Transfer Agreement templates.

REFERENCES

1. Institute of Medicine of the National Academies. Rare Diseases and Orphan Products: Accelerating Research and Development. October 04, 2010.
2. Rubinstein Y et al. Creating a Global Rare Disease Patient Registry Linked to a Rare Diseases Biorepository Database: Rare Disease-HUB (RD-HUB). Contemporary Clinical Trials. 2010; 31(5):394-404.

Abstract Author Index*

*Abstract Codes: HT, Hot Topics; NIBN, National & International Biobanking Networks; ROR, Return of Results; ER, Environmental Repositories; HSR, Human Specimen Repositories; PSR, Plant/Seed Repositories; BSS, Biospecimen Science; CCP, Cryogenics and Cell Preservation; ELSI, Ethical, Legal and Social Issues Related to Repositories; QAC, Quality Assurance and Control; RAT, Repository Automation Technologies; RIF, Repository Informatics; WG, ISBER Working Group Abstracts.