isber europe Symposium LUXEMBOURG
Februrary 27-28, 2018

Biospecimen Research Symposium

QUALITY MATTERS

PROGRAMME

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ISBER 2018
Biospecimen Research Symposium

FEBRUARY 27-28, 2018 LUXEMBOURG

QUALITY MATTERS

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ISBER will be the leading global biobanking forum for promoting harmonized high-quality standards, education, ethical principles, and innovation in the science and management of biorepositories.

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MESSAGE FROM THE SCIENTIFIC PROGRAM COMMITTEE CHAIR AND THE ISBER PRESIDENT

Dear colleagues,

Have you ever tried to compare analytical results from biologically identical samples, processed in different ways or stored for different periods of time?

If yes, you ARE a biospecimen researcher!

This ISBER 2018 Symposium co-organised with the IBBL is all about biospecimen research.

Biospecimen research is not considered the most "attractive" type of research and journal editors often refuse even to consider biospecimen research manuscripts for review, stating the subject is not considered a priority or quoting low readership interest.

However, biospecimen research underpins the accuracy and robustness of ALL research done with biospecimens. This symposium will highlight why. Biobank professionals are especially concerned by biospecimen research since it provides the scientific evidence base that they need in order to develop robust technical SOPs for specimen processing, and be able to provide information about the shelf-life or the fitness-for-purpose of the biospecimens they supply.

The ISBER Best Practices (4th ed.) has just been published and the ISO biobank standards which will allow biobanks to be accredited are expected to be published in 2018. Accreditation is generally linked to method validation. Method validation includes as one of its main components the assessment of the robustness of the samples. This is why biospecimen research is also linked to quality assurance and quality control. During this symposium, we will highlight the above developments and debate whether biospecimen research as a research activity and biospecimen research as part of a quality management system are compatible.

Welcome to Luxembourg!

Enjoy the biospecimen research symposium!

Fay Betsou
ISBER 2018 Biospecimen Research Symposium Program Committee Chair

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GENERAL INFORMATION

Venue

European Convention Center Luxembourg (ECCL)
4 Place de l'Europe
1499 Luxembourg

Conference Registration

Convention Center Foyer

Tuesday, February 27, 2018	12:00pm – 5:25pm
Wednesday, February 28, 2018	8:00am – 5:15pm

Exhibits

Conference Room C Foyer

Exhibit Installation:

Tuesday, February 27, 2018	8:00am – 12:00pm

Exhibit Hours:

Tuesday, February 27, 2018	12:00pm – 6:30pm
Wednesday, February 28, 2018	8:30am – 3:30pm

Exhibit Takedown:

Wednesday, February 28, 2018	3:30pm – 7:00pm

Symposium Registration *(Prices in USD)*

	Regular Rate	On-Site Rate
Member	$350	$400
Non-Member	$450	$500
Technician/Student	$275	$325

**Please note, all rates are subject to 17% VAT*

Full Symposium Registration:

Full conference registration includes participation in all scientific sessions and food and beverage during the symposium.

Exhibit Hall Pass:

Exhibit hall pass includes access to the exhibit hall and food and beverage during the symposium.

Networking Dinner

Date: Tuesday, February 27, 2018
Time: 7:00pm onwards
Venue: La Table du Belvedere, ECCL
Ticket Price: $75 USD + tax

Please note that the networking dinner venue is located on-site at the convention center.

Tickets are available at the registration desk while quantities last.

Certificate of Attendance:

All attendees will receive a certificate of attendance after completing the symposium evaluation. A link to the evaluation will be sent out via email following the symposium.

WIFI

Symposium Delegates can access WiFi in the meeting areas with the following information:

Network: ISBER
Password: ISBER2018

Poster Presentations

Conference Room C Foyer

Poster Set-Up:

Tuesday, February 27, 2018	12:00pm – 1:00pm

Presentation Time:

Tuesday, February 27, 2018	5:25pm – 6:30pm

**Please note that symposium delegates are also encouraged to peruse the posters during session breaks.*

Poster Takedown:

Wednesday, February 28, 2018	3:00pm – 6:00pm

BiO.Li.X!

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The STC series of automated sample stores address the widest range of sample storage applications at temperatures from +25°C to -80°C

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The STC series storage systems are ideally suited for a wide range of storage applications ranging in size from approximatley 100k to millions of samples, and for temperatures ranging from +25°C to -80°C. The STC-ULT series provides all the hallmark LiCONiC advantages such as best in class temperature stability, energy consumption, structural integrity, sample density and simple, effective, software control.

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STT-series

The STT series is the most compact of LiCONiC's fully automated sample storage systems. The STT fits in virtually any lab and is quickly installed. It is ideal for a wide variety of sample types and applications, including integrated workcells. The STT is ideal for sample collections in the 50,000 to 150,000 range and can be configured for various temperatures including -80°C ULT.

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The SAB series is an ideal solution for large sample collections that have high tube and rack variability. It is especially suited for non-automation friendly labware, such as cryovial boxes. The SAB provides a straightforward pathway for converting manual freezer processes to an automated environment.

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PROGRAMME-AT-A-GLANCE

Please note that all scientific sessions will take place in Conference Room C.

TUESDAY, FEBRUARY 27, 2018

9:30am – 12:00pm	**Integrated BioBank of Luxembourg Site Visit** *Pre-registration required.* *Pick-up from Convention Center lobby: 9:30am* *Drop-off to Convention Center lobby: 12:00pm*
12:00pm – 5:25pm	Registration Open
12:00pm – 6:30pm	Exhibit Hall Open
1:00pm – 5:25pm	**SESSION 1: HUMAN FLUID BIOSPECIMENS** *Session Chairs: Fiorella Guadagni and Pierre Lescuyer*
1:00pm	Welcome and Introduction
1:10pm	**FNR Funding Opportunities** *Frank Glod (Luxembourg)*
1:20pm	**Specimens, Standards, and Signatures: Keys to the Vision of Precision Medicine** *Carolyn Compton (USA)*
2:00pm	**Extracellular Vesicle Detection by Flow Cytometry** *Andreas Spittler (Austria)*
2:25pm	**Peptidic and Metabolomic Quality Control Markers for Serum and Plasma Specimens** *Michael Kiehntopf (Germany) and Peter Findeisen (Germany)*
2:55pm – 3:25pm	Networking Break with Exhibits
3:25pm	**Parameters Affecting Cryopreserved Microparticles and PBMCs in Functional Assays** *Philip Norris (USA)*
3:50pm	**Standardising Liquid Biopsy at the European Level - IMI's CANCER-ID and the Importance of Controlling Pre-Analytical and Analytical Variables** *Thomas Schlange (Germany)*
4:15pm	**Oral Abstract Presentations** *See details on page 21*
4:45pm	**Debate: Moral Tribes, Biospecimen Research, and ISO Standards** ***Chair:*** *Katheryn Shea (USA)* ***Participants:*** *Glenn Begley (Australia), Sabine Lehmann (Luxembourg), William Mathieson (Luxembourg), Helen Moore (USA) , Uwe Oelmueller (Germany), Geraldine Thomas (UK)* **10% of the Time It Works Every Time** *Glenn Begley (Australia)*
5:25pm – 6:30pm	Poster Reception and Exhibition Tour *Drinks and hors d'oeuvres provided*
7:00pm	Networking Dinner *Separate ticket required (available for purchase at registration desk)*

WEDNESDAY, FEBRUARY 28, 2018

8:00am – 5:15pm	Registration Open
8:30pm – 3:30pm	Exhibit Hall Open
9:00am – 12:25pm	**SESSION 2: ENVIRONMENTAL BIOSPECIMENS** *Session Chairs: Jacqueline MacKenzie-Dodds and Marcos Castellanos*
9:00am	Opening Remarks
9:10am	**Plants and Transcriptomics** *Sean May (UK)*
9:35am	**The Potential of Anoxia Storage to Delay Ageing of Plant Seeds** *Steven Groot (Netherlands)*
10:00am	**Ancient DNA Preservation - Cutting to the Bone** *Morten Allentoft (Denmark)*
10:25am – 11:05am	Networking Break with Exhibits
11:05am	**Animal Samples at Museum Biobanks: Legacy Collections, DNA Barcoding Campaigns, and Genome-Grade Sampling** *Jonas Astrin (Germany)*
11:30am	**Ensuring High Quality Seed Collections: The Millennium Seed Bank Partnership** *Eva Martens (UK)*
11:55am	**Oral Abstract Presentations** *See details on page 21*
12:25pm – 1:30pm	Networking Lunch with Exhibits
1:30pm – 4:55pm	**SESSION 3: HUMAN TISSUE BIOSPECIMENS** *Session Chairs: Helen Moore and Jens Habermann*
1:30pm	Opening Remarks
1:40pm	**Factors Affecting the Utility of FFPE Preserved Tissue Samples for Proteome and Phosphoproteome Analysis** *Daniel Chelsky (Canada)*
2:05pm	**Defining RNA Quality from Paraffin Embedded Tissue** *Stephen Hewitt (USA)*
2:30pm	**NGS Applications for FFPE Samples: Challenges and Possibilities** *Andreas Leimbach (Germany)*
2:55pm – 3:30pm	Networking Break with Exhibits
3:30pm	**Fitness for Purpose of FFPE DNA for NGS** *Geraldine Thomas (UK) and William Mathieson (Luxembourg)*
4:00pm	**Differentiated Human Adipocytes: Potential Impact and Challenges from an Industry Perspective** *Johan Paulsson (Denmark)*
4:25pm	**Oral Abstract Presentations** *See details on page 21*
4:55pm – 5:00pm	Poster Award Ceremony
5:00pm – 5:15pm	Closing Remarks

PRESENTATION SUMMARIES

INTEGRATED BIOBANK OF LUXEMBOURG (IBBL) SITE VISIT

TUESDAY, FEBRUARY 27, 2018 | 9:30AM – 12:00PM

The Integrated BioBank of Luxembourg (IBBL) will host a site visit for all symposium delegates who wish to attend. This will take place in advance of the Biospecimen Research Symposium on Tuesday, February 27. ***Please note that pre-registration is required.***

Pick up from Convention Center lobby: **9:30am**
Drop-off at Convention Center lobby: **12:00pm**

SESSION 1: HUMAN FLUID BIOSPECIMENS

TUESDAY, FEBRUARY 27, 2018 | 1:00PM – 5:25PM

KEYNOTE PRESENTATION:
Specimens, Standards, and Signatures: Keys to the Vision of Precision Medicine

Carolyn Compton (USA)

The future of medicine depends on the development of molecular biomarkers that provide more precise diagnosis and patient stratification, detect early disease, elucidate risk of disease predict disease outcome, response to therapy, and therapeutic toxicities, and permit monitoring of therapeutic management. Rigorous adherence to standards that are consistent and consistently applied across the development process is required to achieve the reproducibility that is currently lacking in the process. Of primary importance is the quality of the starting materials – the biospecimens used for analysis. Development of complex biomarkers approaches cannot be achieved without the assurance of the provenance of the specimens being analyzed as well as their associated data and consents. The pre-analytical variation to which biospecimens are subjected can dramatically alter their molecular quality and composition artefactually. Pre-analytical artefact may abrogate any ability to define biological effects of interest or distinguish biological signatures of importance in patient samples. This is especially consequential when the biomarker assay is a companion diagnostic and the gateway to access to a therapy. Neither false positive nor false negative tests are tolerable in that circumstance. Biospecimens for biomarker analysis must be systematically collected, processed, stabilized, transported and stored according to standards that render the samples fit for the analytic approach and platform. Regulatory approval of new biomarker assays also is focused on specimen quality as it relates to the quality of the data on which regulatory approvals are based. The biomarker qualification program of the US FDA and the EMA emphasize the need to document the biospecimen quality of diagnostic biomarkers used for either drug or device (assay) development. It is imperative that the entire biomedical community address the need for standardized processes and fit-for-purpose biospecimens to accelerate the delivery of accurate, reproducible, clinically relevant molecular diagnostics for precision medicine.

Extracellular Vesicle Detection by Flow Cytometry

Andreas Spittler (Austria)

Extracellular vesicles (EV) are small particles released by cells during proliferation, activation and during apoptotic processes. EVs can be found in all body fluids and facilitate intercellular communication between adjacent cells and distant cells. In the last decade EVs have received exponential increasing interest as biomarkers of inflammation, coagulation, cancer. There are several techniques for detecting extracellular vesicles, of which flow cytometry is one of the strongest. One of the great advantages of flow cytometry is that it combines the technical and scientific requirements for clinical monitoring. Flow cytometry protocols allow rapid determination within 2 hours. In addition, EVs can be easily quantified and determined for their cellular origin by multicolor staining. However, the technique of flow cytometry also has clear limitations. In general, it is difficult to define EVs based on their size, and small particles below 300 nm may not be visible due to overlapping noise from the flow cytometer. In addition, when determining EVs for specific fluorescence properties, a certain number of bound fluorescence labelled antibodies are required to detect them above the detection limit. Various technical advances in recent years and the establishment of new staining protocols, however, have significantly reduced the detection limit for the visualization of extracellular vesicles. This might be of great importance since the fraction of very small particles, smaller than 300nm, are mainly abundant in the conglomerate of EVs and therefore are an important portion for biomarker detection. In this lecture the possibilities and the latest developments in the measurement of extracellular vesicles by flow cytometry are discussed. In addition, the limitations of this method are demonstrated, and both the pre-analytical and technical pitfalls are explained, which lead to artifacts in the determination of these small particles.

Peptidic and Metabolomic Quality Control Markers for Serum and Plasma Specimens

Michael Kiehntopf (Germany) and Peter Findeisen (Germany)

Part 1: Peptides

Preanalytical variations have major impact on most biological assays. Specifically MS-based multiparametric proteomic and metabolomic analyses of blood specimens are seriously affected by limited stability of analytes. However, there are only limited solutions for measuring the preanalytical quality of a given sample.

Proteomics and metabolomics are major tools to identify biomarkers that reflect time dependent changes associated with pre-analytical errors. The aim of our study was the identification of new quality control (QC) markers that indicate the time course from sample centrifugation to freezing (TTF) of human liquid samples by combining results from both analytical methods. Serum and plasma specimens that were aged under controlled conditions (TTF; 1h, 4h, 8h, 24h) were analyzed by mass spectrometry. Endogenous and exogenous peptides that showed time dependent changes of their concentrations were selected as QC-markers. Multiparametric analyses were performed with a set of training data and the algorithm was validated with independently generated test-data. An overall classification accuracy of ~80% was achieved and most errors were observed by the differentiation of specimens aged 4h and 8h respectively. However, a project cooperation with the University of Jena revealed additional metabolomics QC-markers from the same set of blood specimens and classification accuracy could further be improved, when peptidomic and metabolomics QC-markers were combined. These results demonstrate that the time dependent degradation of peptides can be used for quality monitoring of serum and plasma specimen and thus might facilitate a critical validation and verification of existing standard operation procedures for pre-analytical, clinical and biobanking processes.

Part 2: Metabolites

The scientific impact of translational biomedical research largely depends on the availability of high qualitative biomaterials that might be provided by biobanks having well-established QA and QC procedures. Accordingly, strategies have to be established to ensure a high degree of consistency in the pre-analytical phase, and appropriate tools have to be developed suitable for QA of pre-analytical procedures and most important, QC of resulting biomaterials. However, widely-used evidence-based and comprehensive validated quality markers, addressing the majority of relevant pre-analytical variations, are still lacking. In the last years we tried to identify and validate new quality control markers indicating critical pre-analytical process steps e.g. time to centrifugation (TTC) and time to freeze (TTF), for QC of human liquid samples. By using LC-MS/MS we observed TTC dependent changes for several metabolites, e.g. amino acids as well as some lysophosphatidylcholines. Based on taurine as well as the ornithine/arginine ratio discrimination of samples from healthy volunteers with different TTCs was achieved with high sensitivity and specificity. However, further studies revealed the influence of physiological conditions as well as clinical phenotypes on QC-biomarkers. Moreover, analysis of 752/714 metabolites in serum/EDTA-plasma lead to identification of additional TTC dependent QC-marker candidates that can be assigned to several metabolic pathways. In collaboration with the University Hospital Mannheim identification of TTF-QC-biomarkers is underway by combining selected metabolites with endogenous peptides. Based on a comprehensive literature review within the frame work of the German Biobank Alliance (GBA) a QC-biomarker panel will be concerted and further validated in a proficiency testing program for development of a quality control concept among GBA biobanks.

Parameters Affecting Cryopreserved Microparticles and PBMCs in Functional Assays

Philip Norris (USA)

Peripheral blood mononuclear cells (PBMCs) are frequently cryopreserved in liquid nitrogen to allow future analysis of their phenotypic and functional characteristics, such as in longitudinal cohort studies and vaccine efficacy trials. It is known that cell surface markers can be differentially affected by cryopreservation, and some cell types are more tolerant of cryopreservation than others. In addition to PBMC cryopreservation, interest in the signaling properties of extracellular vesicles (EVs) is increasing. These small, membrane-bound vesicles are typically not stored with cryoprotectant like PBMCs are; rather they are recovered from frozen plasma, serum, or other fluid samples. This talk will address the functional activity of PBMCs after cryopreservation, how the activity changes with storage time, and whether distinct cell populations differentially retain functional activity. In addition, data regarding the ability of EVs to deliver an immune signal after cryopreservation and storage will be discussed.

Standardising Liquid Biopsy at the European Level - IMI's CANCER-ID and the Importance of Controlling Pre-Analytical and Analytical Variables

Thomas Schlange (Germany)

Liquid biopsy technologies receive growing interest for the management of malignant diseases due to the possibility to non-invasively monitor disease progression and to identify potentially actionable therapeutic targets. Currently, there is a lack of quality criteria, standards and benchmarking data for technologies trying to enter the market with diagnostic tests. The Innovative Medicines Initiative (IMI) project CANCER-ID connects stakeholders like academic and clinical scientists, technology, diagnostic and pharmaceutical companies to work on best practice documents and SOPs for circulating tumor cells, circulating free-tumor DNA and miRNAs in lung and breast cancer. The consortium aims at making standards available for proficiency testing by technology providers and to establish a network with regulators and patient organisations to address issues in the clinical use of liquid biopsies.

Debate: Moral Tribes, Biospecimen Research, and ISO Standards

Chair: Katheryn Shea (USA)

Participants: Glenn Begley (Australia), Sabine Lehmann (Luxembourg), William Mathieson (Luxembourg), Helen Moore (USA), Uwe Oelmueller (Germany), Geraldine Thomas (UK)

This session will debate the perceived benefits and drawbacks of implementing quality standards in biobanks. The debate will open with a talk on different factors impacting irreproducibility

of research, with particular focus on the factors related to biospecimen quality. The rest of the debate will explore the potential impact, conflicts and synergies between current practices and implementation of ISO accreditation standards on biospecimen research.

10% of the Time It Works Every Time

Glenn Begley (Australia)

As researchers we all want our work to have a long-term impact on human disease. Unfortunately, however, the incentives that drive our research can have undesirable consequences: the majority of publications in "top-tier" journals are unable to be reproduced. Over the course of a decade, Amgen scientists were unable to reproduce 90% of the papers in "top-tier" journals. Worse, on many occasions the original investigators were themselves unable to reproduce their own findings. This is a systemic problem that is inherent to our scientific system. Instead of focusing on the methods that were used to generate a result, we focus on, and reward, the 'flashy' or exciting result, even if it is without foundation. This presentation will briefly highlight the problem and provide some examples of sloppy science that is present throughout the scientific literature.

SESSION 2: ENVIRONMENTAL BIOSPECIMENS

WEDNESDAY, FEBRUARY 28, 2018 | 9:00AM – 12:25PM

Plants and Transcriptomics

Sean May (UK)

At NASC, we have been processing transcriptomic samples since the last millennium. Through many iterations the technologies became vastly more repeatable and reproducible, but the underlying experimental concerns have changed very little. First-past-the-post publication has clearly been driven by machinery progression, and early adoption of experimental tools has rewarded novel discovery, but biological verification, statistical significance and data consistency (let alone longevity or recyclability), have proven more problematic in this fast moving field. Our resource centre has been generating, analyzing, and serving transcriptomic data for nearly 20 years with evangelical attention to replication strategies, controlled vocabularies, and public release. These issues are now beyond question in the field of genomics, but have perceptions really changed with regard to good experimental design and widespread reuse of data for transcriptomics?

The Potential of Anoxia Storage to Delay Ageing of Plant Seeds

Steven Groot (Netherlands)

Plant biodiversity is conserved by genebanks mainly in the form of seeds. Worldwide there are more than 1700 genebanks and it is estimated that about 7.4 million accessions are currently maintained globally. In most of the cases, the dried seeds can be stored for a considerable period of time, but eventually seed deterioration results in the inability to generate healthy seedlings. Regeneration, needed before quality drops too much, is rather expensive and has the risk of reducing genetic diversity. The reason for deterioration is oxidation of cell and organelle membranes, DNA, RNA and proteins. To reduce the rate of ageing the seeds are stored dry (at 30% RH or less) and cool (-20 or 5 °C). Especially storage at sub-zero conditions is costly and frequently not feasible for large collections in tropical countries. From food science it is known that oxygen in the storage environment stimulates oxidation. However, the potential of seed storage under anoxic conditions has received little attention from the genebank community. Moreover, anoxia seed storage experiments that have been performed in the past 50 have given both positive and negative results. We performed experiments with primed celery seeds, reputed for their short shelf life. These showed that anoxia seed storage can improve seed longevity considerably, but only if the seeds are dry. At higher seed moisture levels the seeds experience respiration and will suffocate under anoxia. In subsequent experiments the advantage of anoxia storage has also been shown for seeds from other species. As genebanks store seeds under dry conditions anyhow, we recommend that they should store the seeds also under anoxic conditions to prolong their longevity during ex situ conservation. This recommendation will likely also hold for other desiccation tolerant specimens such as pollen, spores, tardigrades and nematodes.

Ancient DNA Preservation - Cutting to the Bone

Morten Allentoft (Denmark)

Next Generation Sequencing (NGS) data offers detailed insights into the molecular preservation of a given specimen. As a convenient 'by-product' of genomic sequencing, it is possible to estimate the endogenous DNA content, the average fragment length, the DNA decay rate and half-life, and the deamination damage fraction. Based on NGS data from hundreds of ancient skeletons, I compare these signatures of molecular decay in different skeletal elements that differ in respect to age and preservation state. Moreover, I will demonstrate how carefully optimized extraction protocols, normally applied to ancient DNA research, can be used to extract DNA from formalin-exposed museum material that has previously been considered unsuitable for molecular research.

Animal Samples at Museum Biobanks: Legacy Collections, DNA Barcoding Campaigns, and Genome-Grade Sampling

Jonas Astrin (Germany)

Natural history collections (NHCs) constitute highly suitable hosts for environmental and biodiversity biobanks, as molecular samples processed in NHC labs (for e.g. phylogenetics, evolutionary biology, ecology, taxonomy, population genetics) can be conveniently stored on-site. Even more importantly, the necessary morphological specimen vouchers, the pivotal pieces of evidence in biodiversity studies, are deposited in the NHC's associated classical collections. These vouchers are usually whole organisms, e.g. in the form of dry mounted specimens, or formalin-fixed, in 70% ethanol, etc. Biobanks at NHCs store samples of widely varying quality. Usually, a large proportion consists of legacy samples from projects prior to establishment of the biobank or from projects carried out without involvement of biobank staff. But increasingly, NHC biobanks try to collect samples in a form that guarantees the samples' suitability for (gen)ome-level analyses with high-throughput sequencing. Furthermore, DNA barcoding campaigns are frequently coordinated by NHCs, establishing reference databases and reference collections that are used to molecularly identify unknown samples to species. These projects usually produce biobanked samples of high DNA integrity. While data standards for biodiversity samples are in place, physical handling of the samples often remains heterogeneous among biodiversity repositories, especially with regard to protocols, preservation/conservation agents and temperatures. This is partly based in the fact that thousands of different organism groups (with different sizes, metabolisms, etc.) have to be adapted to. On the other hand, sample preservation in the biodiversity context is still often based on tradition. Recently, a group of biodiversity, environmental and veterinary biobanks formed among GGBN, ISBER and ESBB with the intention to comparatively evaluate sample preservation techniques.

Ensuring High Quality Seed Collections: The Millennium Seed Bank Partnership

Eva Martens (UK)

The Millennium Seed Bank (MSB) Partnership, developed and managed by the Royal Botanic Gardens, Kew, conserves propagules primarily from desiccation-tolerant (orthodox) seed-bearing wild vascular plants. It is the largest ex situ conservation programme in the world, currently involving 96 countries and territories.

The conservation value of the germplasm stored at the MSB has been assessed using quantitative and qualitative methods. The MSB holdings represent a high quality, rich biological resource. Substantial and unique taxonomic diversity exists amongst the collections, which represent 365 families, 5813 genera, 36,975 species and 39,669 taxa, and originate from 189 countries and territories. The collections possess significant natural capital and population value - 49% of collections have at least one identified use to humans while 78% of collections, are either endemic, endangered (nationally or globally) and/or have an economic, ecological, social, cultural or scientific value.

The MSB developed Seed Conservation Standards (Standards) for use across the MSB Partnership to ensure seed collections made and held at partner facilities are of an equally high quality to those duplicated to the MSB. They comprise a set of 20 Standards across seven key areas of seed banking and help assure the utility of collections. The Standards were developed for the conservation of wild plant species from a variety of existing protocols for seed banking of predominantly agricultural taxa, and represent current global best-practice for banking orthodox wild species seeds. The long-term conservation of seeds enables their use in a variety of ways: research into seed biology and ecology; habitat restoration and rehabilitation; and for breeding programmes for crop wild relatives and other economic species. Since 2000, 11,182 seed samples have been distributed globally for conservation, research, education and display.

SESSION 3: HUMAN TISSUE BIOSPECIMENS

WEDNESDAY, FEBRUARY 28, 2018 – 1:30PM – 5:00PM

Factors Affecting the Utility of FFPE Preserved Tissue Samples for Proteome and Phosphoproteome Analysis

Daniel Chelsky (Canada)

FFPE preserved tissue was evaluated to determine its suitability for proteomics research, using unbiased label-free mass spectrometry. Colorectal cancer and ovarian cancer samples (n=20 each) were divided into adjacent strips and either flash-frozen or preserved by FFPE, approximately one hour after initiation of cold ischemia. Both peptides and phosphopeptides were isolated and analyzed by LC-MS/MS. Similar numbers of peptides, proteins and phosphopeptides were detected in the FFPE and frozen samples. Comparison of the proteins detected and their relative abundance revealed that while the overall results were similar, secreted and extracellular proteins were relatively depleted and protein degradation enzymes enriched in both the colorectal and ovarian cancer FFPE samples. Additional tissue strips from each sample were allowed to sit in a humidified chamber at RT for 2, 3, and 12 hours and compared to the 1h time point. While the protein profile changed very little over 12h, the phosphoproteome showed more significant changes, with phosphorylation increases and decreases being evident at the earliest time points. Although the preparation of FFPE samples is more challenging than frozen samples, these samples appear to be well suited to proteomic research, particularly for comparative studies.

Defining RNA Quality from Paraffin Embedded Tissue

Stephen Hewitt (USA)

Quality metrics for biomolecules obtained from paraffin embedded tissues are critical. The preparation of paraffin embedded tissue is only nominally standardized with multiple variables. RNA is a more labile biomolecule, compared to DNA or protein, obtained from paraffin embedded tissue. Previous measures of RNA quality have been limited to end-assay performance, with no pre-screening mechanism, risking false-negative results and wasting time and resources of investigators, when inadequate material is used. Evaluation of the distribution of RNA fragment size obtained from quantitative analysis of the electrophoretogram provides a useful look for quantifying RNA quality. This RNA quality measure, PERM (Paraffin Embedded RNA Metric), can be applied to evaluation and quantification of variables impacting biospecimen quality as well as a tool to qualify RNA quality in a "fit-for-purpose" approach in RNA-based assays.

NGS Applications for FFPE Samples: Challenges and Possibilities

Andreas Leimbach (Germany)

Next-generation sequencing (NGS) is revolutionizing life sciences, e.g. by enabling personalized medicine. As such, NGS techniques are universally applicable for sequencing both DNA and RNA in a myriad of library preparation techniques. Although NGS is de facto standardized, nucleic acid extraction and library preparation can still be a challenge for some sample types. As a sequencing service provider it is essential to utilize different NGS platforms and be able to handle a large variety of input samples like FFPE tissues. Extraction of nucleic acids from FFPE samples yields only a low amount of degraded material that is difficult to process for NGS libraries and sequencing. Therefore, great care has to be taken to accurately check the quality of the purified DNA and adequately adapt NGS library preparation protocols to acquire high quality data. Different enrichment and amplification techniques can then be used to achieve the high specificity and sensitivity that is required for (high-throughput) diagnostics and other applications.

Fitness for Purpose of FFPE DNA for NGS

Geraldine Thomas (UK) and William Mathieson (Luxembourg)

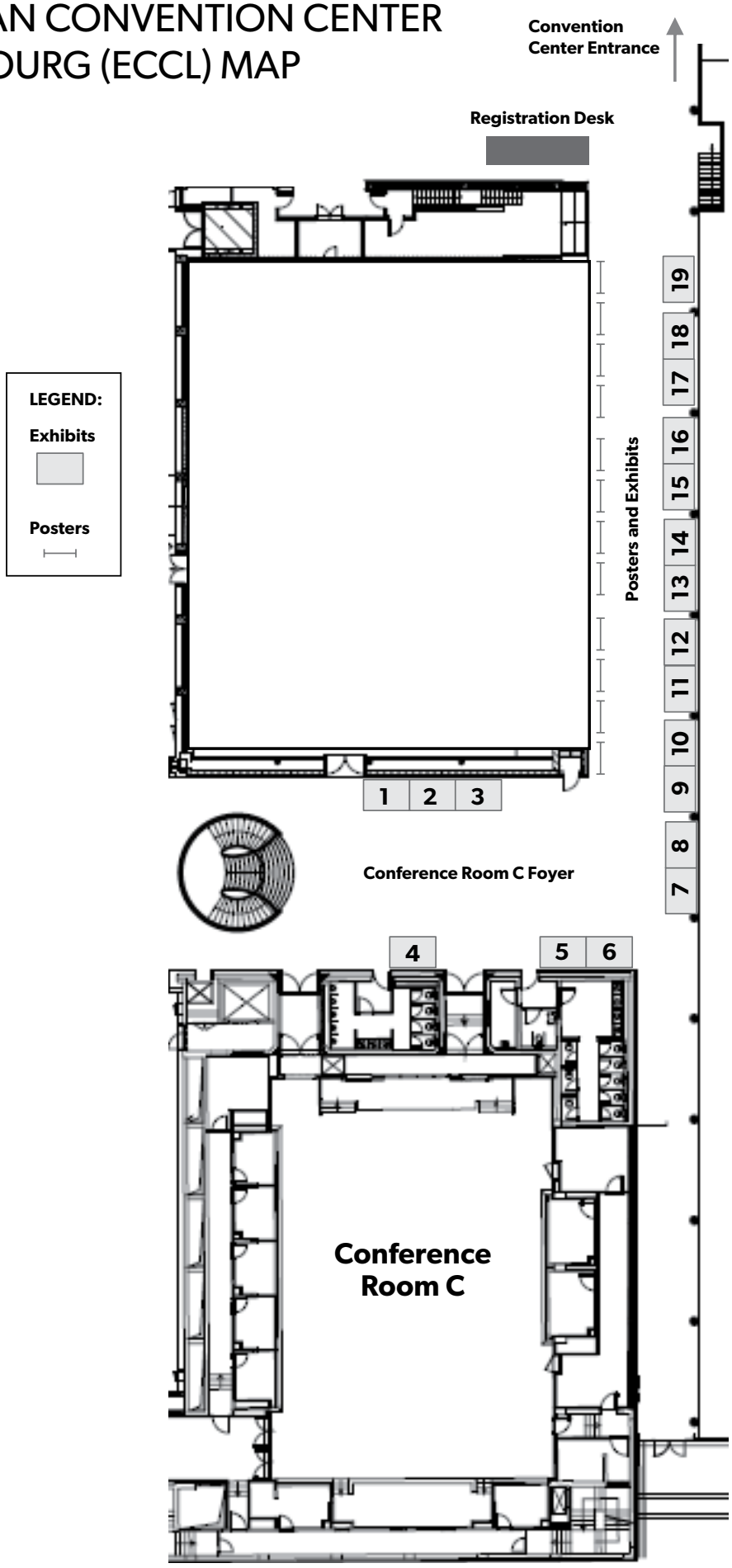
Histopathology departments have spent years validating diagnostic tests on FFPE samples, so FFPE will likely remain the primary diagnostic specimen type. Meanwhile, cancer biospecimens are becoming smaller at diagnosis and diagnosis is becoming more centralised. So, biospecimens will increasingly be transported from theatre to laboratory in formalin because this is practical, prevents ongoing cold ischemia and is amenable to the principal diagnostic procedures – morphology and immunocytochemistry. Molecular technologies such as NGS must therefore be amenable to FFPE or they will not translate into the clinic. Consequently, preanalytical variables occurring after paraffin-embedding and during nucleic acid purification e.g. different extraction kits, laboratories, operators, amplification techniques and NGS chemistry are important. Cancer Research UK has been running the Stratified Medicine Programme (SMPs) for 8 years. In SMP1, 7850 routine diagnostic breast, ovarian, colorectal, lung, melanoma and prostate FFPE samples were analysed using conventional sequencing techniques – this resulted in a failure rate of between 0.9% for colorectal and 5.3% for breast cases. SMP2 focuses on lung cancer using leftover diagnostic biopsy material analysed on a 28-gene Illumina NGS panel. The challenging combination of limited starting material and greater sequencing coverage is reflected in the QC failure rate of 21% (averaged over the lifetime of the project), compared to 2.8% for lung in SMP1, which relied primarily on resection material. It is of note that the annual QC failure rate in SMP2 is decreasing year on year and is now approaching 10%. We have focused our attention on some post paraffin-embedding variables and show how these can influence DNA extracted from clinical FFPE biospecimens.

Differentiated Human Adipocytes: Potential Impact and Challenges from an Industry Perspective

Johan Paulsson (Denmark)

In the pharmaceutical industry, characterization of receptor ligands is commonly performed in transfected over-expressing immortal cell lines. Here we present a case where differentiated human adipocytes were pivotal for progression of a project. Biologics generated as agonists toward a receptor complex did not give rise to receptor activation with corresponding intracellular response in an established screening cell line, while the natural protein ligand did. Subcutaneous pre-adipocytes can be differentiated into adipocytes using medium supplemented with adipogenic and lipogenic hormones. Since differentiated human adipocytes are known to express the receptor complex of interest, the generated biologics were tested on these cells. The biologics as well as the natural ligand gave rise to the anticipated intracellular response leading to the conclusion that the expression ratio of the two receptor subunits in the screening cell line is critical for activation for the biologics but not for the native protein ligand. Therefore, differentiated human adipocytes were used as a screening tool with the limitation of a 2.5 week differentiation protocol, a large donor to donor variation and associated with significantly higher cost. Differentiated human adipocytes inspired the generation of new optimized screening cell lines which responded adequately to both the natural ligand and the synthesized biologics. The pros and cons of using differentiated human adipocytes for screening purposes will be further discussed.

EUROPEAN CONVENTION CENTER LUXEMBOURG (ECCL) MAP



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One year after the launch of SLIMS, in May 2011, Genohm opened its new HQ at the Innovation Park of the EPFL in Lausanne, Switzerland and in January 2016 a US branch in Durham, NC, while keeping its European branch offices in Ghent where the most R&D is performed. Today Genohm proudly serves a growing set of customers in Europe, the Middle East and the US.

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ORAL ABSTRACT PRESENTATIONS SCHEDULE

SESSION 1: HUMAN FLUID BIOSPECIMENS

TUESDAY, FEBRUARY 27, 2018 | 4:15PM – 4:45PM

Abstract #	Title	Topic	Presenting Author
1	Assessing Exosome Derivatives from Archived Sera or Plasma from the AIDS Cancer Specimen Resource: Advances in Deriving Extracellular Vesicle (EVs) for Biobankers	Validation of Processing Methods/Method Comparison	Jeffery Bethony
2	Enabling Detailed and Operator-Independent Plasma QC by an Innovative Spectrophotometric Approach	Quality Control Methods	Andrew Brooks
3	Cystatin C as a Quality Control for Optimal Storage Condition of Human Cerebrospinal Fluid (CSF)	Quality Control Methods	Kathleen Mommaerts

SESSION 2: ENVIRONMENTAL BIOSPECIMENS

WEDNESDAY, FEBRUARY 28, 2018 | 11:55AM – 12:25PM

Abstract #	Title	Topic	Presenting Author
4	Long-Term Stability of Tumor Markers in Human Sera	Stability Studies	Marie Karlikova
5	OPTIMARK Project: Preliminary Results on Antigenicity and Integrity in Non-Tumor Tissue Samples	Quality Control Methods	Cristina Villena
6	Improving Pre-analytical Data Quality with an Automatized Healthcare-Integrated Biobanking Approach	Quality Control Methods	Tanja Froehlich

SESSION 3: HUMAN TISSUE BIOSPECIMENS

WEDNESDAY, FEBRUARY 28, 2018 | 4:25PM – 4:55PM

Abstract #	Title	Topic	Presenting Author
7	Evaluating the Utility of Necropsied Marine Animal Tissues in Genomics	Validation of Processing Methods/Method Comparison	Jennifer Ness
8	Quality Control of Vitally Frozen Bone Marrow Mononuclear Cells	Quality Control Methods	Tiina Vesterinen
9	Development of ISO/AWI 21709, the International Standard for Biobanks Handling Mammalian Cell Lines	Other	Paul Jung

ORAL ABSTRACTS

1. Assessing Exosome Derivatives from Archived Sera or Plasma from the AIDS Cancer Specimen Resource: Advances in Deriving Extracellular Vesicle (EVs) for Biobankers

J L Plieskatt [1,2], S Silver [1,2], J M Bethony [1,2]

[1]AIDS and Cancer Specimen Resource (ACSR), The George Washington University, Washington DC, USA; [2]Department of Microbiology, Immunology and Tropical Medicine, The George Washington University, Washington DC, USA

Background: Extracellular vesicle, especially exosomes, can be derived from a variety of fluids commonly archived in biorepositories such as sera and plasma. As with most banked materials, the requirements for extracting exosomes from sera and plasma were not known when these materials were archived. As the method for extracting exosomes from fluids is well established (ultracentrifugation), we sought to examine methods for assessing the fitness of exosomes isolated from archived serum or plasma.

Methods: Three quantitation kits were tested on exosomes isolated by a standard ultracentrifugation technique. The first directly measured isolated exosomes based on their Acetyl-CoA Acetylcholinesterase (AChE) activity, which is known to be enriched in exosomes. The second assay reported on exosome quantity by measuring CD9, a transmembrane protein present on the surface of exosomes. In this assay, exosomes were bound to a microtiter plate, blocked, and an anti-CD9 horseradish peroxidase-conjugated antibody used for the detection of the marker. The third and final assay was a double sandwich ELISA for the direct capture of exosomes directly from serum or plasma, with exosomes quantified by interpolated onto standard curve of exosomes isolated by NanoSight.

Results: While the first assay directly measured the esterase activity known to be within exosomes, the results were not reproducible. The second or CD9 based method exhibited low signal intensity in our hands, and even the standard curve for the CD9 could not be established. The third approach, which eliminated the need for exosome purification by directly measuring exosomes in serum or plasma showed the most promise, as it had the highest signal intensity was both consistent and reproducible over several runs.

Conclusions: The current project involves utilizing the double sandwich enzyme-linked immunoassay to produce both a qualitative and quantitative analysis of exosomes isolated from archived sera or plasma. The double sandwich enzyme-linked immunoassay also does not require previous isolation of exosomes from samples. Additionally, this immunoassay consists of a proprietary pan-exosome anti-exosome antibody, enabling capture of exosomes from different biological fluids. This study further contributes to the ACSRs "fit for purpose" program, providing sampling guidelines and insight on archived materials to investigators for their use of specimens from our biorepository. related research.

2. Enabling Detailed and Operator-Independent Plasma QC by an Innovative Spectrophotometric Approach

T Martens[1], K Plasman[1], T Montoye[1], W Ewart[2,3], E Kwon[2,3], A Brooks[2,3]

[1]Unchained Labs, Gentbrugge, Belgium; [2]RUCDR Infinite Biologics, New Jersey, USA; [3]BioProcessing Solutions Alliance, Indianapolis, USA

Blood plasma and serum, as a biomaterials for both molecular and functional analysis, have become increasingly important as an important analytical resource in both research and diagnostics. As these bio-molecules are present in limited amounts and are sensitive to degradation as a function of collection, processing and storage (i.e. freeze-thaw), it is of utmost importance to qualify and quantify the quality of plasma prior to any analyses. Plasma quality is currently assessed by a rough visual inspection being imprecise, labor-intensive and operator-subjective. Moreover, many current QC tools lack the ability to predict downstream performance of the sample.

This study presents the development of a novel plasma quality control approach utilizing a micro-volume UV/Vis spectrometric approach (Lunatic - Unchained Labs). This technological approach extends the capabilities of standard UV/Vis by dissecting the measured absorbance spectrum into its relevant constituents. As a result, the typical color and clarity grading are decomposed and quantified into its biologically relevant contributors: protein as major component, heme (hemolysis), bilirubin (icteric serum) and turbidity (lipidity). Using this approach, the 4 plasma QC parameters can be objectively quantified in a batch-wise method while consuming only 2 µl of plasma. In this study the correlation between the visual inspection and UV/Vis approach is demonstrated, showing not only good correlation between the two methods but also the more robust, operator independent and in-depth analysis of the UV\Vis method. Lastly, the study demonstrates the correlative value of relating quantitative measurements of plasma, using this new approach, with downstream analyses of both cell free nucleic acid and functional measurement quality. The implementation of this approach is the basis of a global standardization for plasma quality that can help assess the effects of pre-analytical and processing variables.

3. Cystatin C as a Quality Control for Optimal Storage Condition of Human Cerebrospinal Fluid (CSF)

K Mommaerts[1], E Willemse[2], M Marchese[1], F Betsou[1], C Teunissen[2]

[1]Integrated BioBank of Luxembourg, Luxembourg; [2]Department of Clinical Chemistry, VU University Medical Center, Amsterdam, Netherlands

Background: Cystatin C is an endogenous cysteine proteinase inhibitor present in all body fluids, with the highest concentration in cerebrospinal fluid (CSF) and in seminal plasma. The mature active form contains 120 amino acid residues and is a single non-glycosylated polypeptide chain. Carrette et al. demonstrated that upon 3 months of storage of human CSF at -20°C Cystatin C loses its N-terminal octapeptide, whereas this cleavage was not observed at -80°C. Standardization of preanalytical aspects such as storage conditions is required for use of human CSF in protein biomarker research. The observed cleavage of Cystatin C suggests that Cystatin C could be used as a preanalytical quality marker.

Methods: To assess the quantity of cleaved protein, an ELISA assay was developed that allows the quantification of both the full length and the total protein. The monoclonal antibodies developed recognize specifically the full length Cystatin C (aa1-aa120) while those used to quantify the total quantity recognize both the cleaved and the full length proteins. The ratio of these two measurements corresponds to the relative amount of cleaved protein.

First, the developed ELISA was tested on human biobanked CSF. The following variables were tested: storage temperature (RT, 4°C and -20°C) and freeze-thaw cycles (n=1,2,3,5 and 7). Second, to address the long-term storage, samples from an Alzheimer disease cohort (n=116) that were biobanked at -80°C from 2 up to 14 years were tested. Third, a stability study using fresh CSF was designed to further asses the use of cystatin C as a preanalytical quality marker with regards to storage temperature. Three storage conditions (Liquid Nitrogen (LN), -80°C and -20°C) were tested for 4 weeks, 8 weeks and 4 months after baseline measurement.

Results: Upon 1 week of storage at RT or at 4°C, no cleavage of the Cystatin C protein was observed while a linear decrease of the mean ratio was observed when CSF storage time at -20°C increased. The ratio was not impacted up to 7 freeze-thaw cycles. No association was observed between the Cystatin C ratio and long-term storage time in a biobanked Alzheimer disease cohort. Preliminary results from the stability study confirm the cleavage of the protein at -20°C but not at -80°C or in LN storage.

Conclusions: These results confirm the potential use of Cystatin C as a pre-analytical quality control marker for optimal storage conditions of human CSF.

4. Long-Term Stability of Tumor Markers in Human Sera

M Karlikova[1], R Kucera[1], O Topolcan[1], J Kinkorova[1], R Fuchsova[1]

[1]Department of Immunochemistry, University Hospital and Faculty of Medicine in Pilsen, Czech Republic

Background: Serum tumor markers are biomarkers used on a routine basis in clinical decision making in oncology. Retrospective research requires an accurate knowledge of the stability of the biomaker molecules.

Aim of study: To identify the changes in serum tumor markers levels after six to ten years of storage at -80°C. Selected tumor markers were: carcinoembryonic antigen (CEA), cancer antigen 19-9 (CA 19-9), tissue polypeptide specific antigen (TPS), insuline-like growth factor (IGF-1) and thymidine kinase (TK).

Methods: Tumor markers were first assessed in serum samples after sample withdrawal in 2006 and again in 2016, after a storage in -80°C. The same methods were used: chemiluminiscence (CEA, CA 19-9) and immunoradioassay (IGF-1, TPS). Results were compared using Spearman correlation.

Results: IGF-1 levels decreased to 94.7% of original values (mean), the difference was statistically significant. CA 19-9 values increased to 100.8% of original values, the increase was statistically insignificant. TK TPS and CEA values increased to 112, 114 and 125% of original values, respectively; the increase was not statistically significant. There was a strong correlation between results for all markers.

Conclusion: We did not notice any significant level decrease of studied markers which implies that there was no significant molecule degradation. Serum samples stored at - 800C for 10 years can be used for clinical studies.

5. OPTIMARK Project: Preliminary Results on Antigenicity and Integrity in Non-Tumor Tissue Samples

C Villena[1,2], I Almenaral[2,3], MJ Artiga[2,3], O Bahamonde[2,4], R Bermudo[2,5], E Castro[2,6], R De la Puente[2,7], T Escámez[2,8], M Esteva-Socias[1,2], M Fraga[2,9], L Jauregui-Mosquera[2,10], M Martin-Arruti[6], M Morente[2,3], L Peiró-Chova[2,4], DG Pons[1,2], JD Rejón[2,7], M Ruiz-Miró[2,11],P Vieiro[2,9], S Zazo[2,12], V Villar[2,10], A y Rábano[2,13]

[1]Pulmonary Biobank Consortium, CIBER of Respiratory Diseases (CIBERES),ISCIII (Madrid), Instituto de Investigación Sanitaria de Baleares (IdISBA), Hospital Universitario Son Espases, Mallorca, Spain; [2]Spanish Biobank Platform, ISCIII, Spain; [3]CNIO Biobank, Spanish National Cancer Research Center (CNIO), Madrid, Spain; [4]INCLIVA Biobank, Valencia, Spain; [5]HCB-iIDIBAPS Biobank, Instituto de Investigaciones Biomédicas August Pi i Sunyer (IDIBAPS), Barcelona, Spain; [6]Basque Biobank; The Basque Foundation for Health Innovation and Research (BIOEF), Bilbao, Spain; [7]Andalusian Public Health System Biobank, Granada, Spain; [8] IMIB Arrixaca Biobank, Murcia, Spain; [9]Biobank of Research Institute of Santiago de Compostela, Santiago de Compostela, Spain; [10]University of Navarra's Biobank IdiSNA, Pamplona, Spain; [11]IRBLleida Biobank, Instituto de Investigaciones

Biomédica de Lleida-Fundación Dr. Pifarre, Lérida; [12] Fundación Jiménez Díaz Biobank, Madrid; [13]Departamento Neuropatología, Banco de Tejidos Cien, Fundación Centro Investigación Enfermedades Neurológicas (CIEN), Madrid, Spain

Background: The development of many potential disease biomarkers on clinical assistance is limited by the sample quality, affected essentially by procurement, processing and storage conditions. So, many efforts had been made to standardize biological material preservation, although emerging biospecimen science is focusing on study the impact of critical factors over the samples that could affect on the accurate biomarker analysis. In that context, OPTIMARK project, a multi-center initiative carried out by 12 centers with the collaboration of R&D working group of Spanish National Biobank Network, aims to select and validate the essential pre-analytical factors relevant on tissue samples through an algorithm which consider SPREC and BRISQ information and some analytical testing with high predictive value.

Methods: The first phase focused on identifying analytical tools to validate the quality of tissue samples, based on its integrity and antigenicity, in order to evaluate the effect of long term storage. A total of 374 retrospective non-tumor tissue samples (colon, brain, lung, breast, stomach and endometrium) preserved from less than a 1 year old to more than 20 years were tested. In order to evaluate quality of antigenicity, different cellular markers of ubiquitous distribution among tissues were selected, according to Human Protein Atlas database on the formalin-fixed paraffin-embedded (FFPE) non tumor tissue samples. At the same time, RNA integrity number (RIN) was also evaluated for most paired frozen samples using Agilent 2100 Bioanalyzer.

Results: Ki-67 protein was identified as a potential quality biomarker for non-proliferative tissues when long term storage effect was evaluated. However, vimentin and CD31 proteins showed no differences on immunostaining quality between groups. Additional markers recently tested in lung tissue samples that showed a slight correlation between staining intensity and sample age were TTF-1, BCL-2 and beta-catenin. Except on gastric samples, optimal RIN values were obtained, although with high variability, maximum in brain samples. No correlation was observed between the RIN and long term storage. Only in colon, breast and endometrium samples was a slightly reduction of RIN values among time.

Conclusions: Correlations have been found on loss of antigenicity according to sample age depending on the marker used. However, the effect of long term storage on RNA integrity of frozen samples seems to be affected by other factors.

6. Improving Pre-Analytical Data Quality with an Automatized Healthcare-Integrated Biobanking Approach

T Froehlich[1], M Fiedler[1], C Largiadèr[1]

[1]University Institute of Clinical Chemistry, Bern University Hospital, University of Bern: Inselspital, Bern, Switzerland

Despite recent methodological advances in "omics-"technologies, the discovery of new biomarkers has been largely prevented by uncontrolled variability in the quality among and within existing biospecimen collections. In order to meet the quality requirements of liquid samples for high sensitive analytical technologies, such as mass spectrometry, recent efforts have mainly focused on the development of new biobanking infrastructure and on the standardization of pre-analytical protocols. With regard to the reproducibility of research results, not only the physical quality of samples but also the quality of their recorded data is crucial. Currently, pre-analytical information is often recorded manually. This type of recording is not only time consuming but also represents a considerable source of error. Here, we describe the healthcare-integrated biobank sampling process of the Liquid Biobank Bern, Switzerland, which takes advantage of multiple-interfaced IT systems and minimizes manual input of pre-analytical information. In more detail, the collection and processing of biobank samples is integrated in the automated high-throughput processing of hospital routine samples. At every processing step from the blood draw to the storage, the sample and its derivatives are identified, tracked, and directed by their barcodes, and thus, electronically monitored and documented. All essential time points within the pre-analytical pathway are recorded automatically by the processing instruments. With this high-degree of IT integration of hospital routine and biobank processes, we achieve high data quality and rapid sampling processing: > 95% of samples being frozen within two hours after blood-draw and > 75% even within one hour.

7. Evaluating the Utility of Necropsied Marine Animal Tissues in Genomics

J Ness[1], A Moors[1], R Pugh[1]

[1]Marine Environmental Specimen Bank, Chemical Sciences Division, National Institute of Standards and Technology, Charleston, South Carolina, USA

The NIST Marine Environmental Specimen Bank is a useful tool for long term and retrospective studies relating to environmental health and the health of marine animals with respect to environmental contaminants. Focus on research relating to genetics, metabolomics and proteomics can support measured contaminant data by adding layers to our understanding of the effect contaminants have on animal health, life history, and the environment. The strict protocols established by NIST for the banking of animal tissues and fluid for environmental

contaminants have also preserved sensitive biological molecules for many samples. Research materials banked at the Marine ESB are obtained from live and expired (through necropsy) marine animals. Many of these samples are from federal and state protected marine species and can be difficult for researchers to obtain due to permitting and sampling logistics, especially from live animals, and may be limited in the number and quantity of sample available. Expired animals however can provide larger quantities of tissues from internal organs that cannot be obtained from a live animal, which can also aid in understanding metabolism, genetic expression, and overall health. This research examines how RNA degradation and gene expression is altered in necropsied tissues stored at the Marine ESB for the National Marine Mammal Tissue Bank. It will explore the limitations of these tissues and provide a framework for researchers studying marine animals to determine if more accessible and abundant tissues from expired marine animals can be utilized for their studies.

8. Quality Control of Vitally Frozen Bone Marrow Mononuclear Cells

T Vesterinen[1], M Suvela[1], C Heckman[1]

[1] Institute for Molecular Medicine Finland (FIMM), Helsinki Institute of Life Science, University of Helsinki, Helsinki, Finland

Background: The Finnish Hematology Register and Biobank (FHRB) is a national biobank that provides well-annotated, high quality samples to accelerate hematological research. Based on informed, broad consent, FHRB collects peripheral blood, skin biopsies and bone marrow samples across Finland from patients with a hematological disorder. Serial samples are collected representing different time points in the disease history from the untreated diagnostic stage to remission, relapse and treatment refractory stages.

Methods: FHRB collects approximately 30 bone marrow samples per month. These samples are processed by density gradient separation (Ficoll-Paque) to isolate mononuclear cells (MNC). For storing viable cells, MNCs are prepared in a 10% DMSO - human serum suspension. The cell suspension (106 cells/ml) is aliquoted into cryovials (1 ml per vial) that are slowly cooled at -70°C by using a freezing container, and finally stored in liquid nitrogen vapor phase.

The quality control of the vitally frozen bone marrow cells started in October 2013. One percent of the samples collected during the past six months and one extra sample from each previous quality control time points, are reviewed biannually. During the review, cell viability is evaluated with Trypan Blue and CellTiter Glo. RNA and DNA are prepared from the MNCs and analysis performed to assess nucleic acid quantity and integrity using standard methods with commercially available kits.

Results: By October 2017, altogether 1789 bone marrow samples were collected and 51 samples reviewed. After thawing, the median cell viability per vial was 90% (range 63-98%). 98% of the samples were viable up to five days which is equivalent to experiences gained from fresh bone marrow samples. Biannual measurements (n=7) of the same sample show analogous viability in each vial.

The average RNA yield was 5.8 µg (range 1.3 – 21.0 µg) and RNA integrity numbers (RIN) varied from 3.8 to 10 (median 9.6, SE 0.93). The amount of extracted DNA was on average 8.0 µg, varying from 1.9 µg to 17.0 µg.

Conclusions: Standardized quality assessment of biobanked material is essential to ensure delivery of high-quality samples. Our results confirm that the FHRB's bone marrow sample collection, processing and storing protocols are suitable for long-term storage of mononuclear bone marrow cells. Longitudinal data confirms that storage of vitally frozen cells for five years does not affect their biological quality.

9. Development of ISO/AWI 21709, the International Standard for Biobanks Handling Mammalian Cell Lines

P Jung[1], K H Ryu[1, 2]

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Cell lines have been extensively used in clinical and medical research and development (R&D) and significantly improved our understanding in these areas. Recent reports, however, have shown that numerous cell lines are misidentified or contaminated by microorganisms or other cell lines. Effects of these problems go beyond academic communities as research results generated with questionable cell lines are neither reproducible nor suitable for actual clinical or pharmaceutical applications. More scientists now call for rigorous quality control of cell lines and standardized operation procedures at biobanks handling cell lines. ISO/AWI 21709 is one of the international efforts to address these issues.

ISO/AWI 21709 Process and quality requirements for establishment, maintenance, and characterization of mammalian cell lines is the accepted work item (AWI) for the International Standard developed by ISO/TC 276/WG 2. It is based on the KNRRC (Korea National Research Resource Center) Best Practice Guideline for Animal and Human Cell Lines. In November 2017, the project was discussed at ISO/TC 276/WG 2 meeting in Rome and decided to proceed to a 2-month working draft (WD) ballot. This document is a first sector-specific standard developed by the working group (WG) 2 and excepted to serve as the model standard for upcoming sector standards in WG 2. The content of ISO/AWI 21709 will be further discussed in Beijing at ISO/TC 276 Plenary Meeting in June 2018.

POSTER ABSTRACT PRESENTATIONS SCHEDULE

TUESDAY, FEBRUARY 27, 2018 | 5:25PM – 6:30PM

Posters will be available for viewing throughout the length of the symposium. During the poster reception authors will be available at their posters to answer questions.

Abstract #	Title	Topic	Presenting Author
P1	NMR Based Quality Control and Added Value Generation for Biobanks	Quality Control Methods	Manfred Spraul
P2	Influence of Different Sample Preparation Methods on the Proteome of Serum Extracellular Vesicles	Quality Control Methods	Svitlana Rozanova
P3	Utilising the Chronic Kidney Disease Biobank for the Distinguishing Risk of Progressive Chronic Kidney Disease (DROP CKD) Study	Other	Evan Owens
P4	Develop and Validate PCR and ELISA Methods for Detecting Orthopoxvirus in Georgia	Validation of Processing Methods/Method Comparison	Ana Gulbani
P5	Pathogen Asset Control System (PACS) Integration with Radiofrequency Identification (RFID) Technology at NCDC of Georgia	Quality Control Methods	Svetlana Chubinidze
P7	Stability of Total and Free Prostate Specific Antigen after Ten Years Storage	Stability Studies	Judita Kinkorova
P8	Study of Viability by Using a Previous Defrosting Step for DNA Analyses in Biobanks Stored Collections	Quality Control Methods	Tatiana Díaz Córdoba
P9	Clinical Trials' Samples Management and Creation of Strategic Collections through Bio-banks	Other	Tatiana Díaz Córdoba
P11	Biobanking of Biospecimens for the Epidemiology of Cardiovascular Risk Factors and Diseases in Regions of the Russian Federation Study (ESSE-RF)	Other	Oksana Sivakova
P12	Standardized DNA and RNA Sample Quality Control	Quality Control Methods	Elisa Viering
P13	Developing Standardizes Biobanking Processes for High Quality Samples – Solutions in the Heidelberg Cardiobiobank (HCB)	Validation of Processing Methods/Method Comparison	Steffi Sandke
P14	RNA Quality in Fresh Frozen Prostate Tissue	Quality Control Methods	Toril Rolfseng and Solveig Kvam
P15	The Principle of Cell Hibernation for Conservation in Hypothermia	Cell Preservation and Cryobiology	Zoran Ivanovic
P16	The Human Plasma Metabolome is Sensitive to Delays in Blood and Plasma Processing	Quality Control Methods	Sebastian Neuber
P17	Cross-Border Biobanking: The German-Danish Interreg Project BONEBANK	Other	Martina Oberländer
P18	Developing a Liquid Nitrogen-Based Cooling Chain for a Centralized, Hospital-Integrated Biobank	Other	Martina Oberländer
P19	Factors Involved in DNA and PBMCs Quality in Cancer Research	Quality Control Methods	Fabiana Rodrigues
P20	The Effect of Storage Time and Freeze-Thaw Cycles on the Stability the Mitochondrial Complex of Samples	Quality Control Methods	Svetlana Gramatiuk
P21	Key Factors Affecting the Quality of Human RBCs Cryopreservation	Cell Preservation and Cryobiology	Noha Al-Otaibi
P22	Evaluating Temperature on a Custom Automation Platform to Optimize Chilling Requirements for Sample Protection	Validation of Processing Methods/Method Comparison	Jesse Gore
P23	IL8 and IL16 Levels Indicate Serum and Plasma Quality	Quality Control Methods	Olga Kofanova
P24	PBMC Score: Gene Expression Ratio Indicates Peripheral Blood Mononuclear Cell (PBMC) Quality	Quality Control Methods	Olga Kofanova
P25	German Biobank Alliance – Ring Trial Concept as Part of the Quality Management System for Biobanks	Quality Control Methods	Christiane Hartfeldt
P26	Successful Immune Monitoring with Cryopreserved PBMC – Quality In, Quality Out	Cell Preservation and Cryobiology	Paul von Hoegen

POSTER ABSTRACTS

P1. NMR Based Quality Control and Added Value Generation for Biobanks

M Spraul[1]

[1]Bruker BioSpin, Rheinstetten, Germany

NMR for long time was considered a method for structure elucidation of unknown compounds. With the appearance of Metabolomics, NMR has proven as one of the 2 main technologies in the analysis of bio-specimens and entered the field of complex mixture analysis. Due to its reproducibility and transferability, NMR is especially suited to enable integrated studies on large specimen cohorts by multiple research groups. Standardization of the technology enabled efficient use of NMR e.g. in the International Phenome Center Network (IPCN) inaugurated December 2016. Biobanks with their large specimen cohorts can benefit in multiple ways from this technology:

- Quality Control of incoming specimens with regard to contaminations, impurities, non-reported drugs or food supplements, differentiate plasma/serum, check type of plasma (EDTA, Citrate, Heparine ..), fasting state, time of specimens at room temperature before freezing, freezing cycles
- Generation of spectral data to store in the Biobank generated as part of QC
- Generation of analysis results to be stored in the biobank along with spectra
    - Quantification of a large number of metabolites and ions in urine
    - Comprehensive Lipoprotein analysis in plasma/serum including Subclasses and particle numbers with a total of 115 parameters
    - Quantification of small molecules in plasma/serum
    - Results of existing NMR assays to be stored in the biobank
    - Retrospective analysis on previously measured spectra with extended analysis routines
- Reducing the need of generating new specimens for clinical trials by using NMR spectra and results stored in different biobanks worldwide and generated under standardized conditions, such reducing cost and time efforts substantially

Examples for all aspects described will be given as well as an outlook to future possibilities generated by NMR technology.

P2. Influence of Different Sample Preparation Methods on the Proteome of Serum Extracellular Vesicles

S Rozanova[1], T Gemoll[1], S Strohkamp[1], C Röder[2], A ElSharawy[3], H Kalthoff[2], J K. Habermann[1, 4]

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Background: Tumor biopsies remain standard for tumor diagnostic and screening. However the procedure is invasive and not always feasible. Herewith, "liquid biopsies" have the potential to overcome many challenges, by allowing non-invasive, accurate and rapid clinical analysis. Serum extracellular vesicles (EVs), secreted by cells, including tumorous, carry specific cell macromolecules and metabolites and represent a potential source of new cancer protein biomarkers. In this context pre-analytical conditions play an important role for successful cancer research. In this work, we compared two different sample preparations of EVs with two-dimensional difference gel electrophoresis.

Methods: Using a sample cohort of healthy controls and colorectal diseases, extracellular vesicles were isolated using both, ultracentrifugation (100000 g, 1h) or a commercially available, polymer-based precipitation kit (ExoQuickTM, System Biosciences). Proteins were extracted using two different lysis buffer (RIPA and DIGE) with & without protease inhibitors and compared by means of multiplex-fluorescence two-dimensional difference gel electrophoresis (2D-DIGE). Protein levels between isolation approaches were analyzed with SameSpots® software followed by Principle Component Analysis (PCA).

Results: Isolated microvesicles, prepared by ultracentrifugation and ExoQuickTM showed complementary protein expression patterns. The pilot experiment regarding the comparison of two different lysis buffers have not shown any difference. Independent of the exosome isolation and protein extraction method approach, PCA-analyses revealed good separation between healthy volunteers and the patient group. The results stress the need for SOPs and strict quality controls in microvesicle research.

P3. Utilising the Chronic Kidney Disease Biobank for the Distinguishing Risk of Progressive Chronic Kidney Disease (DROP CKD) Study

EP Owens[1,2], J Coombes[1,4], ZH Endre[1,5] , WE Hoy[1,3], GC Gobe[1,2]

[1]NHMRC CKD CRE, Brisbane, Australia; [2]Centre for Kidney Disease Research, Faculty of Medicine, The University of Queensland, Brisbane, Australia; [3]Centre for Chronic Disease, Faculty of Medicine, The University of Queensland, Brisbane, Australia; [4]School of Human Movement and Nutrition Sciences, The University of Queensland, Brisbane, Australia; [5]Department of Nephrology, Prince of Wales Hospital and Clinical School, University of New South Wales, Australia.

Background: Chronic Kidney disease (CKD) is a major health and economic burden. Irrespective of aetiology, many patients progress through the stages of CKD to end-stage kidney disease, but many are stable and do not progress, and some improve. Unfortunately, clinicians treat patients from early stage CKD without knowing if the patient will progress. Current clinical biomarkers are incapable of distinguishing progressing and non-progressing patients, and new biomarkers of CKD progression are needed. Recruiting a statistically-relevant sample size of patients and matching controls is problematic. A disease-oriented biobank can address this issue by providing access to a curated archive of biospecimens and clinical data. The NHMRC CKD Centre of Research Excellence (CKD.CRE) has established a CKD Biobank, with one focus of research being identification of CKD biomarkers.

Methods: The biobank and biomarker projects received separate ethics approvals. A patient database of ~7000 CKD patients is available to the CKD.CRE from nephrology outpatient services. Healthy controls are recruited from transplant donors. Annual bloods and urines are banked while clinical data are collected from paper and electronic records or questionnaires. Using estimated glomerular filtration rate at 0, 12, 24 months, participants are stratified into declining, stable or improving CKD, and healthy controls. Proteinuria and albumin-to-creatinine ratio are also recorded. Biomarkers assessed at each time point include circulating and urinary inflammatory, fibrotic, tissue injury and repair, and oxidative stress markers. A combination with the best capacity to discriminate between progressing and non-progressing CKD patients will be selected.

Results: An established disease-oriented biobank archiving biospecimens and clinical data from a heterogeneous CKD population with matched healthy controls is being utilised for biomarker research. A multiparameter biomarker panel will be identified from blood, urine, and clinical data sourced from the CKD.CRE Biobank. This will provide clinicians and researchers with the capacity to allocate health resources efficiently for CKD treatment and research.

Conclusion: The CKD Biobank provides the opportunity to reduce the health and economic impact of CKD by supporting clinical CKD research to test research hypotheses. This resource can be used by national and international researchers to fast track outcomes that will improve CKD patient care.

P4. Develop and Validate PCR and ELISA Methods for Detecting Orthopoxvirus in Georgia

A Gulbani[1], I Guledani[1], M Donduashvili[1], O Parkadze[2]

[1]Laboratory of the Ministry of Agriculture (LMA), Tbilisi, Georgia; [2]National Food Agency (NFA), Tbilisi, Georgia

Background: The recent discovery (2013) of a new Orthopoxvirus (OPXV) in Georgia (country) demonstrates the need for poxvirus detection and diagnosis capacity in country. Human illness caused by this virus has implications for differential diagnosis of cutaneous lesion- producing zoonotic infections, principally anthrax. Simultaneously, animal infection may impact agricultural productivity and food safety. Because of the emergence of new pathogenic poxviruses, there is a great need for the development of PCR and ELISA methods for detecting poxvirus. Laboratory of Ministry of Agriculture (LMA) will develop laboratory capacity, recognition and reporting capacity, and human resources necessary to perform routine poxvirus surveillance in animals.

Methods: An optimized ELISA and PCR assay for the detection of orthopoxviruses are in the process of development by LMA researchers in collaboration with CDC. CDC provides training in assays for the detection and identification of poxviruses, including standard PCR and quantitative PCR, and ELISA for detection of anti-OPXV IgG in serum.

Initial testing at LMA involved screening field collected swabs for the presence of OPXV according to published qPCR protocols (Li et al. 2007). This is a generic assay designed to detect all OPXV species except Variola virus. In this way, will be recovered any additional new isolates or other species of OPXV that may be circulating in the region. Any positive samples will be further characterized to establish species identification and marked for genome sequencing.

Conclusion: New assays will be adopted and validated for detecting new OPXV variants in, rodents, domestic and wild animals found in Georgia.

Training and educational outreach will result in improved capacity for efficient identification and diagnosis of emerging OPXV, and will as well improve bio-surveillance capacity for OPXV in both human and animal populations.

The improved surveillance activities and understanding of OPXV disease burden in the agricultural sector will promote further research collaborations with local and international partners.

P5. Pathogen Asset Control System (PACS) Integration with Radiofrequency Identification (RFID) Technology at NCDC of Georgia

S Chubinidze[1], M Grdzelidze[1], G Mgeladze[1], S Tsanava[1]

[1] Department of Biosafety and Especially Dangerous Pathogens, National Center for Disease Control and Public Health of Georgia

The National Repository of Bacteria and Viruses (NRB&V) is a part

of National Center for Disease Control and Public Health (NCDC) of Georgia. There are kept collection of Especially Dangerous Pathogens - obtained from humans and environment, other pathogenic and potentially pathogenic microorganisms that are of a scientific or practical value and reference strains; The Pathogen Asset Control System (PACS) is implemented and successfully used for biological agent stocks accounting and control, that is a secure, comprehensive information system developed under Cooperative Biological Engagement Program that is implemented by the Defense Thread Reduction Agency (DTRA) to track biological materials. In order to increase Biosafety/ Biosecurity capacity at biological laboratories, a pilot project was made to integrate PACS radiofrequency identification (RFID) technology. The goal of the integration was not only to allow enhanced security of storage but also to simplify tracking and improve effectiveness of laboratory operations. Pilot Project was implemented in the NRB&V located at the Lugar Center. PACS-RFID System included following components: Standalone workstation with PACS database and application; Barcode printer; Barcode scanner; RFID reader and desktop antenna; RFID plate reader; RFID-enabled -80C freezer (manufacturer – Terso Solutions); RFID printer; Plastic vials with embedded RFID tags; Variety of RFID tags to be used with existing vials. Each component was used for specific purposes. Methods included: New material registration, Material transfer, Material subculturing, Material aliquoting, Material destruction, Inventory Audit, Freezer Operations. Pilot Project showed that not all RFID technology enabled equipment provides benefits of the same level, some equipment tested during the project was not deemed reliable (e.g. RFID-enabled non-sterile vials). Project participants identified that RFID technology increased security of biological materials storage and tracking but to a limited level (e.g. box-level tracking by Terso Freezer), generally increased efficiency of operations (e.g. fast inventory), as well as improved accuracy. It was identified that RFID technology increased convenience and speed of operations with PACS, especially inventory audit, as well as enhanced general accuracy. At the same time, it provided limited benefits to the security as the technology still requires further improvement – e.g. vial-level tracking by Terso Freezer.

P7. Stability of Total and Free Prostate Specific Antigen after Ten Years Storage

J Kinkorova[1], V Simanek[1], O Topolcan[1], M Karlikova[1], O Dolejsova[2], R Fuchsova[1], D Slouka[1], R Kucera[1]

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Background: PSA is a serine protease composed of 240 amino acids in a single polypeptide chain and is a routine parameter in prostate cancer diagnostics. Retrospective research requires an accurate knowledge of the stability of the biomarker molecules. The aim of our study was to test the long term stability of tPSA and fPSA after ten years storage at −80°C.

Methods: We analyzed two aliquots from 50 serum samples. Serum was separated within 3 hours of blood collection. Serum samples were immediately aliquoted and processed or frozen at −80°C. The first aliquot was assayed in routine testing in 2006. The second was thawed for further testing after ten years storage at −80°C. We compared 50 results of tPSA, 20 results of tPSA and 20 calculated results of the fPSA/tPSA ratio. Serum tPSA and fPSA levels were assayed using chemiluminescent kits Access Hybritech PSA and free PSA (Beckman Coulter, USA). All statistical analyses were performed by SAS 9.3 software.

Results: The mean decrease in fPSA after 10 years stocking was 4.5%. fPSA increased 9.4% on average and fPSA/tPSA ratio increased 18.1% on average. On clinical evaluation three samples dropped to the lower category of malignancy.

Conclusion: Stability of tPSA levels is sufficient after 10 years stocking at −80°C. fPSA is less stable and its using after ten years is limited. The calculation of the fPSA/tPSA ratio is not recommended due to the alteration towards false negative results.

P8. Study of Viability by Using a Previous Defrosting Step for DNA Analyses in Bio-banks Stored Collections

C Acosta-Andrade[1], P Ferro[1], T Díaz[1], M Fernández[1], J Ortega-Pinazo[2], I Martín[1], A Jiménez[1], B Martínez[1], M L Hortas[3]

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Background: Human samples are commonly collected and long-term stored in bio-banks for current and future analyses. Even though techniques for freezing human blood are well established, DNA stability is sometimes compromised. It has been previously studied that fresh blood samples can be stored at 4ºC for a maximum of 48 hours, or even a month at -20ºC whereas long-term storage requires -80ºC. Nevertheless, hardly any progress has been made about a suitable procedure to defrost frozen samples before DNA analyses, particularly within the scope of returning samples from bio-bank collections to researchers. Normally, protocols for DNA isolation and purification recommends defrost the samples on ice during manipulation. However, it has been previously suggested that an intermediate defrosting step could be key for DNA stability. There still remains controversy over implementation of an optimum protocol. With this premise, the aim is to determine the most suitable method for defrosting blood stored samples in Biobank collections to obtain high quality DNA for later analyses.

Methods: Blood was collected from 5 donors and stored at -80ºC. Next, DNA was extracted from blood samples by using two different defrosting procedures: samples from -80ºC to 4ºC before manipulation, or samples from -80ºC to -20ºC during 24

hours, and further 4◦C before manipulation.

Results: The results showed no significant difference between both defrosting protocols tested here.

Conclusions: As a conclusion, experiments performed here indicate that direct defrosting protocol would be optimum because shorter handling procedures translates directly into time saving.

P9. Clinical Trials' Samples Management and Creation of Strategic Collections Through Biobanks

A Jiménez[1], M Fernández[1], I Martin[1], T Díaz[1], B Martínez[1], P Ferro[1], C Acosta-Andrade[1], M Hortas[2]

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Background: A high proportion of independent clinical trials (ICTs) from public agencies are carried out in Spain with the goal of improving patients' life quality and becoming increasingly personalised medicine. ICTs layout, proceedings and methods should require an special supervision and implementation. The main objective has consisted in designing an efficient collection compliant to obtain sample surplus from ICTs. These strategies are developed in Malaga Hospitals with the aim to create new strategic collections stored at Bio-banks, which could be used in a foresight research manner.

Methods: Blood samples from ICTs corresponding to many pathologies (diabetes, obesity) were collected. Donors were properly informed by means of Bio-bank specific consent, and samples were processed by laboratory technician to obtain different cellular fractions. Thus, these samples were stored and recorded following the established protocol to guarantee simple quality and tracking, as it is indicated in Spanish Law "Real Decreto 1090/2015".

Results: As a result, laboratory technician have recorded and processed samples of many ICTs, obtaining a representative donation number which key interest to future investigations in different biomedical areas.

Conclusions: Strategic collections were created from ICTs samples surplus. These collections would be of great interest for prospective research projects focus on improving medicines related to the pathologies to face with.

P11. Biobanking of Biospecimens for the Epidemiology of Cardiovascular Risk Factors and Diseases in Regions of the Russian Federation Study (ESSE-RF)

MS Pokrovskaya[1], OV Sivakova[1], AN Meshkov[1], VA Metelskaya[1], GA Muromtseva[1], SA Shalnova[1], SV Anisimov[2], SA Boytsov[3], OM Drapkina[1]

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Background: At the present moment the second phase of epidemiologic study ESSE-RF 2 is conducted in four Russian regions (Ryazan, Krasnodar, Omsk regions, republic of Karelia) and is coordinated by the National Medical Research Center for Preventive Medicine (NMRCPM). ESSE-RF2 targets investigation of epidemiology of cardiovascular diseases and their risk factors. Biobank of NMRCPM is able to store large amount of biospecimens. The aim of our study is organization of biospecimens biobanking from Russian regions.

Methods: Special schemes of interaction with local personnel were developed to set up correct and standardized procedures for blood draw, sample proceeding, labeling and shipping of biospecimens from the regions. Detailed instructions for every stage of work were prepared and training of all participating personnel was performed; all sample collection kits were prepared in our Biobank. Special inform consent forms that could be shipped together with biospecimens were designed. Representative sample of population was targeted for each region. Specially designed software for data entering has been developed by our Biobank.

Results: ESSE-RF2 study covered 4 regions, where biospecimens from >6800 subjects have been collected. All samples were shipped to and stored at NMRCPM Biobank. For each participant, 8 aliquots of serum (2 x 1.0 ml + 6 x 0.5 ml), 3 of Na-Citrate plasma (x 0.5 ml), 3 of EDTA plasma (x 0.5 ml), 4 ml EDTA whole blood and 2 ml of EDTA RBC concentrate were stored. Shipping of frozen samples from regions to NMRCPM was conducted with strict temperature monitoring. All biospecimens and sample-associated data were collected within 3 months. Large amount of encoded detailed clinical and socio-demographic information from study participants was collected.

Conclusions: In Russian ESSE-RF2 epidemiological study, a centralized biobank provided key services related to personnel training, preparation means, sample collection, transportation, storage and data handling. To guarantee a quality of biospecimens and accompanying information in large epidemiological studies, effective organizational means are critical, covering work with participants in regions, shipping, temporary and long-term storage. Organizational schemes were tested and troubleshooted, not only supporting this important study but also providing a reliable foundation for the future studies led by NMRCPM.

P12. Standardized DNA and RNA Sample Quality Control

E Viering[1]

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Many factors have an influence on nucleic acid quality, such as sample source, handling, extraction method and storage condition. The responsibility of the Biobanks to collect, store and ship samples makes it essential to determine sample quality at the point of receipt and release. Sample quality includes concentration and integrity which are both important parameters to ensure that nucleic acid samples are fit for purpose. Nucleic acid quality can be assessed using conventional gel or automated electrophoresis systems.

The DNA Integrity Number (DIN) has been established for genomic DNA (gDNA) qualification with automated electrophoresis systems. It provides an assessment of gDNA sample quality by assigning a numerical score from 1 to 10. A high DIN indicates intact gDNA, and a low DIN degraded gDNA. The DIN enables comparison of samples and allows defining a DIN quality threshold for specific types of samples or preparation. This poster shows examples of DNA sample patterns and correlating DIN across a wide quality range for DNA originating from blood, fresh frozen tissue and formalin-fixed paraffin-embedded (FFPE) material.

The RNA integrity number equivalent (RINe) delivers an objective assessment of total RNA degradation for samples from eukaryotic or prokaryotic origin. The RIN is independent of sample concentration and analyst and allows unbiased confirmation of RNA sample quality. RNA samples extracted from FFPE tissue are typically highly degraded. Many tailored FFPE RNA library protocols use an additional quality metric DV200 to define the optimal RNA input amount for successful NGS library preparation. The DV200 represents the percentage of RNA fragments above 200 nucleotides. This poster exhibits sample patterns and corresponding quality scores of intact and degraded RNA including FFPE RNA samples.

P13. Developing Standardized Biobanking Processes for High Quality Samples – Solutions in the Heidelberg Cardiobiobank (HCB)

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Background: In the era of precision and personalized medicine, clinicians and experimental researchers are focusing on analyzing genomics, proteomics and metabolomics of human patients and healthy donors to identify novel and promising targets for the development of new treatment options for various diseases. To facilitate this intention Research Institutions and Hospitals establish biobanks with collections of liquid and tissue biosamples and meaningful clinical data. In the present work we evaluated the entire workflow of the HCB for sample collection, logistics and storage in order to develop specific Standard Operating Procedures, to ensure the highest sample quality and integrity.

Methods: End of 2014 an automated custom-built cryogenic storage with a capacity of up to approximately 1.2 million samples was installed. In addition, the HCB has been able to extend further large-scale equipment for the complete automated processing of biomaterials. We investigated the influence of preanalytical parameters on RNA quantity and quality. For this we varied the incubation time of the PaxGene® tubes as well as different storage procedures.

Results: By evaluating and improving the work processes, the transport time of the biomaterial could be drastically reduced by connecting to a pneumatic tube system. The samples will be processed in between 1-4 hours, including preparation and aliquoting of plasma and serum. Followed by automated DNA and RNA extraction and associated by quality and quantity analyzes. Precise documentation is done with a LIMS which records every single step with exact time of the process. This standardized and harmonized workflow leads to an overall high sample quality. By changing the DNA extraction method, from manual extraction to an automated system, we could significantly increase the amount of extracted DNA. Furthermore, it has also been shown that automated RNA extraction is robust and consistent. The quality analyzes prove that the results obtained are excellent and highly reproducible. Interestingly, our results indicate that the patient or donor profile (stage of disease, treatments) leads to changes in DNA and RNA quantity and quality.

Conclusions: The introduction of standardized and fully automated sample processing systems produces the highest quality and integrity of biomaterials essential for translational research. In addition, it must be pointed out that precise blood collection and handling of the primary tubes is essential.

P14. RNA quality in fresh frozen prostate tissue

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Throughout history, patients and healthy people have given information about their health and disease into the large, common knowledge base called scientific medicine. In this collection of information, analysis of biological samples, such as tissue samples, is a very important part. That way everyone has been able to take advantage of what previous generations have submitted of information and, in return, contributed themselves with information about improving health care for future generations. Today's modern medicine is the result of a huge international empowerment project that has been going on for hundreds of years, many of whom have made a contribution

and everyone has gained a lot. Probably, information hidden in biological samples can answer many of the questions that determine further development of the medicine. To make sure that the biological materials collected is of good quality after many years of storage, it is important to exam parameters that can determine the quality of the material. There is a need to increase the availability to researchers of large numbers of high-quality, well-annotated samples of diseased and control tissue, blood, and other biological materials and, in this way, accelerate cancer research. To do this, samples need to be collected, processed, and stored in standardized ways that give assurance to researchers that they are fit for purpose. Quality assurance is an essential part of good science and this study describes how quality assurance can be applied in cancer biobanking.

The fresh frozen tissue material used in this study is from prostate. The collection of prostate tissue is consent-based and follows a standardized protocol, which is performed in conjunction with planned radical prostatectomy. All samples were collected in collaboration with Biobank1®.

To determine RNA quality the RNA Integrity Number (RIN) is measured in isolated total RNA from tissue collected from 2006-2016. The protocol and kit used for isolation of total RNA is mirVana miRNA Isolation Kit, with phenol (Thermo Fisher Scientific).

In this study we have shown that there are no differences in RNA quality, measured by RNA fragmentation (RIN), in fresh frozen prostate tissue stored for ten years at -80 degrees.

P15. The Principle of Cell Hibernation for Conservation in Hypothermia

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Recently we proposed efficient way to optimize short-term cell conservation without freezing. Exposure to hypoxic/hypercapnic (HH) gas mixture (5% O_2/9%) maintained extensively hematopoietic stem and progenitors cells for 10 days at 4°C. Hypoxia/hypercapnia also doubled the survival of – short-term Scid Repopulating Cells, CD34+ cells, committed progenitors and primitive aldehyde dehydrogenase expressing cells with respect to the ambient air (20% O_2/0.05% CO_2). Cell-protective effects are associated with an improved maintenance of plasma membrane integrity, mitochondrial functionality, the intracellular catalytic iron pool at the physiological level and a conversion to the glycolytic energetic state. Also, we evidenced better preservation of the global cellular protein content containing some protein families known to be implicated in the prolonged survival of hibernating animals in hypothermia.

However, this experimental model consisted in a direct exposition of cells to a severe hypothermia (4°C), a temperature which does not allow the protein synthesis and gene expression in human cells. Hence, this model, although demonstrating a beneficial effect on cell maintenance, did not allow judging if hypoxia/hypercapnia could stimulate a protective specific gene expression and protein synthesis against cold injuries at the cellular level as it is the case in the animals adapted to a long-term survival at temperatures near 0°C (hibernation) during their introduction in hypothermia.

In order to test this hypothesis, before the storage at 4°C, we preconditioned the CD34+ cells with hypoxia/hypercapnia at moderate hypothermia (25-30°C), which is still compatible with the cellular synthetic processes. We demonstrated that this treatment enabled prolonged (up to 20 days) survival of functional CD34+ cells in hypo-metabolic state during their storage at severe hypothermia and during their warming to a physiologic temperature (37°C). In the CD34+ cell population, the highest positive impact concern the Hematopoietic Stem Cells exhibiting in vivo reconstituting potential (NSG immunodeficient mice xenogeneic transplantation model) The same principle was confirmed with the human bone marrow Mesenchymal Stem Cells (MSC) and the FDCP-Mix cell line.

We are using now the proteomic and transcriptomic approaches to reveal specific genes and proteins critical for the establishment of the cellular tolerance to severe hypothermia and induction of the hypo-metabolic, hibernation- like state.

P16. The Human Plasma Metabolome is Sensitive to Delays in Blood and Plasma Processing

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Background: Metabolomics is a powerful technology with broad applications in life science. The discovery of novel biomarkers for diagnosis, prognosis and prediction of diseases, the identification of new drug targets, the characterization of drug-adverse effects, and the monitoring of treatment response are just a few examples where metabolomics could be applied to improve medical care. Blood-based samples are particularly attractive in these research areas due to their minimally invasive accessibility and the comprehensive coverage of the human phenotype, which is directly represented by the metabolome. However, since metabolites may be impacted by improper specimen handling, accurate quality control of the pre-analytical phase is necessary for metabolite profiling.

Methods: Human EDTA blood and EDTA plasma samples were collected from altogether 20 self-reported healthy volunteers and exposed to the following pre-analytical conditions: prolonged blood incubation and extended plasma storage, each for up to 48 hours at room temperature. Semi-quantification of metabolite concentrations was performed using the GC-MS- and LC-MS/MS-based MxP® Broad Profiling approach, and sample quality was assessed by the MxP® Biofluids Quality Control assay.

Results: We observed that prolonged blood incubation affected up to 36% of 292 tested plasma metabolites (20% increased, 16% decreased), and extended plasma storage resulted in a statistically significant increase of up to 10% and reductions of up to 10% of the analyzed metabolites. Nucleobases were greatly affected by both confounders, carbohydrate and amino acid levels were primarily changed by prolonged blood incubation, and lipids were generally more robust to the variations in sample processing. Interestingly, the amounts of 1-methyladenosine and allantoin – which are both discussed as biomarkers for various diseases – were already changed by a 4-hour delay in blood processing. By using the MxP® Biofluids Quality Control system, compromised and control samples were identified with an accuracy of 97%.

Conclusions: The human plasma metabolome is sensitive to prolonged blood incubation and extended plasma storage at room temperature. Thus, in clinical research, and particularly in -omics approaches, it is mandatory to implement quality control measures for sample processing to achieve reliable results and to ensure reproducibility. In this context, metabolomics offers a promising tool to identify low-quality samples before performing big data analysis.

P17. Cross-Border Biobanking: The German-Danish Interreg Project BONEBANK

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Organizations from Germany and Denmark work together in BONEBANK, a German-Danish biobank and innovation platform for stem cells in bone regeneration. Experts from academia and industry are working closely together to i) develop an innovative extraction method of human bone marrow mesenchymal stem cells (BM MSCs) from routine surgeries, ii) to conserve them long-term through nitrogen based cryo-storage in a cross-border biobank, and iii) to supply research facilities and companies with BM-MSCs. At the moment, bones and bone fragments with valuable stem cells are disposed of within the framework of fracture-related routine operations. However, stem cells have a high potential for regenerative therapies (e.g. osteoarthritis, spinal cord injuries, diabetes, stroke, myocardial infarction). Through BONEBANK, BM-MSCs from fracture-related routine operations will be made available for research exploring new therapy options. To establish this cross-border biobank at the locations Odense in Denmark and Lübeck in Germany, harmonization of processes is a necessity, particularly focusing on standardized methods of using the biomaterial for research and treatment purposes. At the moment, vital BM-MSCs from bone fragments could be isolated and successfully cultivated at both locations. The best method for freezing and thawing has yet to be found and determined. Also for the transport over the border quality standards have to be respected. The project also includes quality assessment of BM-MSCs, functional characterization for their therapeutic potential as well harmonization and standardization of data transfer by IT solutions according to legal and ethical regulations in both countries.

P18. Developing a Liquid Nitrogen-Based Cooling Chain for a Centralized, Hospital-Integrated Biobank

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Background: During the collection and processing of biospecimen in a hospital-integrated biobank, samples must be transported between different sites like the operating theatre, pathology department, research labs and biobank facilities and might therefore be exposed to variable temperature changes increasing the risk of becoming ineffective or not fit for purpose.

As a centralized, hospital-integrated biobank, the Interdisciplinary Center for Biobanking-Lübeck (ICB-L) addressed this problem by developing a new workflow for keeping the cold chain of fluid and solid biomaterials collected at all different sites at the University Hospital Schleswig-Holstein on Campus Lübeck.

Methods: Immediately after processing in the biobank lab, all fluid or solid samples to be stored in liquid nitrogen are kept in a CryoPod Carrier™(Brooks) that enables to keep the temperature at -150°C. Integrated temperature logging and alarm control allow to keep and collect further samples during the daily routine until all samples are ready for transportation to ICB-Ls cryostorage, equipped with fully or half-automated liquid-nitrogen tanks. Another possibility of monitored short-term storage below - 120°C is the cryo-workbench WB220™ (Askion), also allowing the temperature-controlled freezing of viable cells or the assembling of sample collectives from various

storage boxes or tanks. Furthermore, ICB-L is equipped with a CryoXtract CXT 351 frozen sample aliquoter that can produce multiple aliquots from a frozen bisospecimen (e.g. serum or tissue) without the need of thawing and therefore diminishing the sample quality. Since 2016, ICB-L has already processed more than 1.000 serum samples using the CXT351 aliquoter.

Results and Conclusion: By developing this cold chain workflow for a centralized, hospital-integrated biobank, special attention was paid to keep the samples below the glass transition (Tg) phase (-135°C). Keeping the cold chain and constantly monitoring the temperature during the collection, processing and storage of fluid and solid biospecimen might have a strong impact on the sample quality and therefore on future research results. This workflow is constantly under development and improvement, as more and more clinical departments and institutes participate in ICB-L's biobank infrastructure.

P19. Factors Involved in DNA and PBMCs Quality in Cancer Research

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Background: Biobanco-iMM JLA - CAML is a structure that includes more than 170000 samples from more than 16000 donors. The appropriate quality controls that ensure the quality of the samples offered and their adequate long-term preservation in repositories are crucial.

By routine, we perform quality control of all DNA samples and once a year of some isolated PBMCs. In this context and considering that oncology is one of the most important areas of our Biobank, we proposed to determine and report the quality control results of DNA samples from Urological Patients extracted from fresh and stored whole blood; and peripheral blood mononuclear cells (PBMCs) from Hematologic Malignancies Patients, regarding the time between blood collection and PBMCs isolation.

Methods: DNA was extracted from fresh and frozen blood samples. Its integrity was confirmed using agarose gels. DNA purity and concentrations were obtained by measuring A260/A280 ratios by Infinite 200 NanoQuant. PBMCs were isolated from fresh blood using Ficoll isolation method and a viability assay was performed using FACSVerse.

Results: For DNA fresh samples were obtained A260/A280 ratios of 1.84 and concentrations of 72,77 ng/µl (n=100) and stored samples (n=100 stored until 2 years) had A260/A280 ratios of 1.82 and concentrations of 80,06 ng/µl. For PBMCs isolation (n=8), the obtained results show that samples isolated immediately after blood collection have significantly higher percentages of living cells (p-value < 0,05) than samples isolated 24 hours later.

Conclusions: Obtained results clearly indicate that our DNA samples meet the required quality standards. However long-term storage of whole blood represents a significant loss of purity of these samples (p-value < 0,05). Regarding PBMCs, it is recommended the immediate execution of the isolation protocol to improve the cell viability.

P20. The Effect of Storage Time and Freeze-Thaw Cycles on the Stability the Mitochondrial Complex of Samples

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Background: Fresh frozen plasma is exposed to numerous factors affecting the quality and stability of RNA factors during blood collection, preparation and storage. They are necessary for accurate reproducibility of experiments in the field of biomarker discovery as well as achieving optimal specificity of laboratory tests for clinical diagnosis. In research at the Ukraine Association of Biobank, we evaluated the impact of pre-analytical conditions on the stability of biobanked blood samples by measuring mitochondrial complex.

The aim of our study was to obtain selected stability data of the mitochondrial complex over a storage period of more than 2 years at –80°C.

Material and Methods: 120 donors plasma – derived from CPD whole blood were processed according to current national and European guidelines. The plasma units were aliquoted and frozen within 12 h after donation at below –75°C. The storage temperature was held between –78 and –82°C during the total storage period of 24 months. In the long-term storage, 4 parameters of the mitochondrial complex NAD, NADH, ATP and ADP were determined in aliquots in laboratories ASK-Health Biobank.

Results: The levels of mitochondrial complex NAD, NADH, ATP and ADP were changed significantly depending on both the the total storage period. Different collection tubes revealed comparable concentrations of miRNA and levels of mitochondrial complex NAD, NADH, ATP and ADP. Storage of samples at -80°C period of 24 months extended the miRNA stability remarkably, however, ATP and ADP levels in long-term stored (12 months) blood samples were significantly changed, which is in contrast to the level NAD and NADH, where levels were found to be stable. Repetitive (n = 6) freeze-thaw cycles resulted in a significant reduction of miRNA concentration and levels of mitochondrial complex NAD, NADH, ATP and ADP in samples.

Conclusions: As a research result, mitochondrial complex NAD and NADH, with considering the variability of unstable analyses, showed adequate stability after 24 months. The mitochondrial complex ATP and ADP the showed adequate stability after 16 months of storage at −80°C. These results suggest that

mitochondrial complex measurements can be used as quality control markers for certain pre-analytical conditions for future research in the biobank.

P21. Key Factors Affecting the Quality of Human RBCs Cryopreservation

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Human red blood cells (hRBCs) are the most transfused blood component involved in patient care worldwide. Blood transfusions are needed to replace lost blood in accidents, surgeries, and to treat health conditions such as anemia. Blood banks have been established to provide hRBCs when needed, but it is a significant challenge to meet the demands of health care services, especially during times of crises. Cryopreservation is the most reliable method to preserve living cells for a prolonged period of time, it assures the accessibility of hRBCs at anytime. However, there are number of factors affecting the quality of cryopreserved cells.

Here, the quality of cryopreserved hRBCs was assessed with consideration to number of factors that may affect the obtained results. These include: the freshness of blood, the collecting procedures and the donors age. The data showed that cryosurvival rate is inversely correlated with the age of hRBCs itself. At day 5 post donation hRBCs were frozen in glycerol then thawed 24 h later, the rate of cryosurival hRBCs was 63.75±1.6%, this was decreased to almost 30±8.72% when freezing hRBCs at day 15 post donation. This suggest that the rate of recovery of hRBCs is greatly affected by the freshness of the blood. Unlike the age of blood itself, blood obtained from healthy donors, which belongs to different aging groups between (20-30) and (50-60) showed almost no effect on cryosurvival rate of hRBCs post-thawing. In addition, examining blood collected in different type of tubes such as; EDTA, CPT or Na-heparin, demonstrated different response to the cryomedia. Most critically, hRBCs collected in EDTA can only cryopreserved in glycerol solution but not trehalose. This is due to EDTA effect which removes the essential solutes for trehalose loading protocol, an important step prior freezing the cells.

This investigation concludes that the freshness of biospecimens and the collecting methods are important factors to successfully cryopreserved hRBCs. hRBCs collected by different methods have a preference toward specific cryo-media.

P22. Evaluating Temperature on a Custom Automation Platform to Optimize Chilling Requirements for Sample Protection

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Statement of the problem: Maintaining samples in a cold state is necessary during processing procedures for certain sample types. This can help to improve their overall stability by preventing analyte degradation. However, these processes are commonly performed after sample thaw using ambient temperature automation protocols, or manual procedures on ice that are labor intensive and can introduce an increased risk of contamination and misidentification. Moreover, processing on ice can subject samples to temperature extremes since tubes are often removed at the time of sample transfer to visualize sample surface height or identifiers.

Proposed solution: To provide a solution for these challenges, we employed a customized automation platform that is designed to control cold temperatures in both source and destination tubes while aliquoting. This liquid handling robot is outfitted with specific protocols and labware that allow for rapid batch processing of samples into as many as 16 aliquots, and is adaptable to multiple tube sizes and rack formats. In this study, we aliquoted plasma and serum samples using this platform, and inserted Type T thermocouples into source and destination tubes to monitor sample temperature. Two protocols were run per sample type that were designed to aliquot from relatively large (10mL) or small (2mL) tubes. Destination tubes were placed into racks on plate chillers or into chill plates that fully encase individual cryovials. Thermocouples were placed into tubes at various heights, and in various positions within each rack to assess the impact of sample volume and tube position on temperature. In addition, we varied the setpoints of the chill plate labware, and repeated the automation protocols and temperature measurements to assess the impact of each setting on sample temperature. Follow on QC studies are being performed to measure the stability of samples aliquoted in this manner to demonstrate improved performance versus larger temperature changes associated with ambient aliquoting.

Conclusions: The results of this study can be used to develop standard aliquoting procedures to ensure samples are maintained at low temperatures based on volumetric requirements, or respective sample and tube types.

P23. IL8 and IL16 Levels Indicate Serum and Plasma Quality

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Background: Longer pre-centrifugation times alter the quality of serum and plasma samples. Markers for such delays in sample processing and hence for the sample quality, have been identified.

Methods: Twenty cytokines in serum, EDTA plasma and citrate plasma samples were screened for changes in concentration induced by extended blood pre-centrifugation delays at room temperature. The two cytokines that showed the largest changes were further validated for their "diagnostic performance" in identifying serum or plasma samples with extended pre-centrifugation times.

Results: In this study, using R&D Systems ELISA kits, EDTA plasma samples and serum samples with a pre-centrifugation delay longer than 24hr had an IL16 concentration higher than 313pg/ml, and an IL8 concentration higher than 125pg/ml, respectively. EDTA plasma samples with a pre-centrifugation delay longer than 48hr had an IL16 concentration higher than 897pg/ml, citrate plasma samples had an IL8 concentration higher than 21.5pg/ml and serum samples had an IL8 concentration higher than 528pg/ml.

Conclusion: These robust and accurate tools, based on simple and commercially available ELISA assays can greatly facilitate qualification of serum and plasma legacy collections with undocumented pre-analytics.

P24. PBMC Score: Gene Expression Ratio Indicates Peripheral Blood Mononuclear Cell (PBMC) Quality

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Background: Uncontrolled preanalytical variables can reduce the accuracy and reproducibility of downstream analytical results from peripheral blood mononuclear cells (PBMCs) and hence the specimen's fitness for purpose for experimental immunology. Blood precentrifugation conditions are important annotations to avoid bias in PBMC-based gene expression or functional studies. In our study we selected two PBMC gene targets sensitive to the precentrifugation delay, examined the performance of their combination in the diagnosis of the pre-centrifugation conditions of the original blood samples, and established a PBMC preanalytical score.

Methods: PBMCs were isolated from several independent populations, including healthy, inflammatory and infected samples collected with EDTA and citrate as anticoagulants. RNA samples from isolated PBMCs were examined for gene expression changes induced by extended blood pre-centrifugation delays at 4°C and room temperature. Using Taqman RTqPCR we analysed the two selected genes that showed their "diagnostic performance" in identifying EDTA and citrate blood samples with extended pre-centrifugation times.

Results: In this study we established PBMC Score - a gene expression assay to asses the PBMC quality related to the pre-centrifugation delay. PBMC preanalytical score measurement can be used to identify:

(1) EDTA PBMC samples or RNA extracted from these PBMCs with RT precentrifugation times of more than 24hr with sensitivity 99% and specificity 98% at the cutoff 28 (healthy donor populations).

(2) EDTA PBMC samples or RNA extracted from these PBMCs with RT precentrifugation times of more than 48hr with sensitivity 98% and specificity 87% at the cutoff 57 (healthy or diseased populations).

(3) citrate PBMC samples or RNA extracted from these PBMCs with RT precentrifugation times of more than 48hr with sensitivity 92% and specificity 84% at the cutoff 348 (healthy or diseased populations).

Conclusion: The precentrifugation conditions are now possible to assess based on the proposed PBMC preanalytical gene expression score. This score will enable objective PBMC sample qualification for downstream applications (such as gene expression, ELISPOT or HLA multimer assays).

P25. German Biobank Alliance – Ring Trial Concept as Part of the Quality Management System for Biobanks

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Background: The German Biobank Alliance (GBA) follows up on the achievements of the German Biobank Node (GBN) project which comprises the development of a quality management system (QMS) for the German biobanking community.

The GBA quality concept consists of three main objectives: i) establishment of a QMS compliant with international standards, ii) development of a quality assurance concept by identification of quality relevant biomarkers and iii) development of a ring-trial and audit program.

Methods: In order to provide consistent quality of individual samples a ring trial concept will be established in 11 biobank sites of the GBA focussing especially on continuous improvement of processes and quality management. In the ring trials, reference samples will be processed, nucleic acids will be isolated and analysed according to the standard operating procedures at the different biobanks. Subsequently these nucleic acid samples will be sent to and analysed by the reference biobank 'Integrated Biobank of Luxembourg' (IBBL). The ring trial for tissue samples has already been conducted using pig liver as reference tissue.

For the ring trial for liquid samples human blood will be used.

For a 'quality assurance concept' serum and plasma samples will be analysed for quality control (QC) markers, which had previously been identified based on an intensive literature research.

Results: A pilot test as well as the first round of the tissue ring trial has already been successfully performed with 11 participating biobanks and data analysis and interpretation is in progress.

The liquid ring trial for the verification of nucleic acid isolation procedures in participating biobanks will be conducted and evaluated in 2018 as well as the collection of samples for the quality assurance trial.

The results will be thoroughly reviewed by the quality management working group in order to assess efficiency of processing and extraction techniques of the participating biobanks.

Conclusions: Interlaboratory comparisons are highly desirable to harmonise, improve, and to refine preanalytical processes, in order to identify factors which may have an impact on sample quality. To provide consistent high quality of individual samples a ring trial concept with the focus on continuous improvement of processes is being established in GBA.

P26. Successful Immune Monitoring with Cryopreserved PBMC – Quality In, Quality Out

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The limits of science are frequently defined by the limits of technology. The limits of immune monitoring are largely set by our ability to cryopreserve PBMC, while successfully recovering the cell numbers, and maintaining their viability and function. Ideally, freshly isolated PBMC are subject to functional tests of T and B cells, or of NK cells. Data obtained with fresh cells serve as the reference standard for the impact of storage, shipping, and cryopreservation. In 2003, our group was among the first to report -- contradicting the then long-standing notion – that CD4 and CD8 cells can be cryopreserved without any loss of function. As protocols for successful shipping and cryopreservation are still debated I will share what we have learned since, in systematic studies on this issue and during implementing it in regulated immune monitoring trials. Limited quality of frozen PBMC should no longer be a limitation to immune monitoring.

Also, the choice of media is critical and we developed highly adapted serum free media to optimize best quality of freezing, recovering and analyzing immune cells of different species. The specifically developed anti-aggregate wash allows an over 95% recovery of viable cells and is not only limited to use with PBMC, like all the serum free media specialties. Even analysis of dormant Th2 responses could be shown by cultivation in a special medium CTL plus. Further are these frozen cells an ideal source for performing ADCC assays under standardized conditions.

NOTES

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