



**isber**  
**europa**

**Symposium**  
**BERLIN, GERMANY**  
**February 5-6, 2019**



## **2<sup>ND</sup> Biospecimen Research Symposium**

**FOCUS ON QUALITY AND STANDARDS**

# **PROGRAMME**



INTERNATIONAL SOCIETY FOR BIOLOGICAL  
AND ENVIRONMENTAL REPOSITORIES

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INTERNATIONAL SOCIETY FOR BIOLOGICAL  
AND ENVIRONMENTAL REPOSITORIES

# ISBER 2019

## 2<sup>ND</sup> Biospecimen Research Symposium

FEBRUARY 5-6, 2019  BERLIN, GERMANY

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FOCUS ON QUALITY AND STANDARDS

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ISBER is a global biobanking organization which creates opportunities for networking, education, and innovations and harmonizes approaches to evolving challenges in biological and environmental repositories.



### ISBER VISION

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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## TABLE OF CONTENTS

|                                                                            |    |
|----------------------------------------------------------------------------|----|
| Message from the Scientific Programme Committee Chairs and President ..... | 6  |
| ISBER 2018-2019 Board of Directors .....                                   | 7  |
| ISBER Committee Chairs .....                                               | 7  |
| ISBER Committee, Working Group, and Special Interest Group Listing .....   | 8  |
| General Information .....                                                  | 9  |
| Programme-at-a-Glance .....                                                | 10 |
| Presentation Summaries .....                                               | 12 |
| Venue Map .....                                                            | 17 |
| Exhibitor Listing .....                                                    | 18 |
| Oral Abstract Presentation Schedule .....                                  | 20 |
| Oral Abstracts .....                                                       | 20 |
| Poster Abstracts Presentation Schedule .....                               | 23 |
| Poster Abstracts .....                                                     | 25 |



## MESSAGE FROM THE SCIENTIFIC PROGRAMME COMMITTEE CHAIRS AND PRESIDENT

Dear Colleagues,

It is a matter of fact that many scientific data are produced on the basis of insufficiently characterized biomaterials or from biomaterials of inadequate quality. The rapid and fascinating technological development leads to constantly growing possibilities for the analysis of a broad range of biomaterials with advanced high throughput methods.

This expansion of possibilities but also the related challenges are reflected in the scientific programme of ISBER's 2<sup>ND</sup> Biospecimen Research Symposium in Berlin, Germany. After the great success of the first symposium, the second symposium focuses on three main sessions; (i) in-vivo pre-analytics factors, (ii) ex-vivo pre-analytics factors and (iii) microbiome, covering the most innovative topics in the field today.

The topics of this meeting are presented by experts in their respective domains. The presentations will be driven by the respective scientific topics but a main emphasis will be put on the quality of the biomaterials and their requirements for certain types of analyses. The topics include cancer research, which is also the subject of the key note lecture, employing DNA to RNA sequencing and exosome research. Special attention will be paid to applications of metabolome and proteome research as well as to specific requirements needed to produce reliable data for the interpretation of our circadian rhythms.

Of course, biobanks need the right framework to carry out well defined procedures. This area will be helped by the new ISO norm. This framework is not to be replaced by the specific considerations for biomaterials as used in the research topics presented during the symposium.

The symposium is co-organized by the German Biobank Node (GBN), a member of the pan-European biobank infrastructure BBMRI-ERIC. Together with a number of biobanks that have joined forces within the German Biobank Alliance (GBA) we are currently establishing a national biobank infrastructure. The biobanks of this alliance are operating in an IT network to enable cross-biobank queries while complying with common quality standards to allow cross-biobank compilation of biomaterial collections. Thus we are convinced that the German biobank community is well prepared for future biobank requirements.

Welcome to Germany, welcome to Berlin!

Enjoy the 2<sup>ND</sup> Biospecimen Research Symposium!



**Michael Hummel**

*ISBER 2<sup>ND</sup> Biospecimen Research Symposium  
Programme Committee Co-Chair*



**Cristina Villena**

*ISBER 2<sup>ND</sup> Biospecimen Research Symposium  
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- Pharma
- Rare Diseases
- Regulatory and Ethics

### ISBER SPECIAL INTEREST GROUPS

- Automated Repositories
- Hospital-Integrated Biorepositories
- Pediatric





## GENERAL INFORMATION

### Venue

Mercure Hotel MOA Berlin  
Stephanstr. 41, 10559  
Berlin, Germany

### Meeting Dates: February 5-6, 2019

*Main sessions are located in MOA 4-5 (first floor)*

### Conference Registration

*Mercure Hotel MOA Berlin Atrium (second floor)*

Tuesday, February 5 | 8:00 AM – 5:00 PM  
Wednesday, February 6 | 8:30 AM – 3:30 PM

### Exhibits

*Mercure Hotel MOA Berlin Atrium (second floor)*

#### EXHIBIT INSTALLATION:

Tuesday, February 5 | 8:00 AM – 11:00 AM

#### EXHIBIT HOURS:

Tuesday, February 5 | 11:00 AM – 5:30 PM  
Wednesday, February 6 | 9:30 AM – 1:30 PM

#### EXHIBIT TAKEDOWN:

Wednesday, February 6 | 1:30 PM – 6:00 PM

### 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 19% VAT*

#### FULL CONFERENCE 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 conference meals served in the Exhibit Hall.

### Networking Dinner

Date: Tuesday, February 5, 2019  
Time: 6:00 PM – 8:00 PM  
Venue: Mercure Hotel MOA Berlin  
Ticket Price: \$75 USD

Please note that the networking dinner venue is located on-site at the convention center. For a map, please see page 17 of the programme.

Tickets are available at the registration desk while quantities last.

### Certificates 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.

### Wi-Fi

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

#### Network: Mercure

*No password is required. Simply confirm the Terms and Conditions.*

### Poster Presentations

*MOA 4-5 (first floor)*

#### POSTER SET-UP:

Tuesday, February 5 | 11:30 AM – 12:00 PM

#### PRESENTATION TIME:

Tuesday, February 5 | 4:10 PM – 5:30 PM

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

#### POSTER TAKEDOWN:

Wednesday, February 6 | 12:30 PM – 1:30 PM



## PROGRAMME-AT-A-GLANCE

Please note that all scientific sessions will take place in MOA 4-5 (first floor).

Registration Desk and Exhibit Hall are located in the Atrium (second floor).

| TUESDAY, FEBRUARY 5, 2019 |                                                                                                                                   |            |
|---------------------------|-----------------------------------------------------------------------------------------------------------------------------------|------------|
| 8:00 AM – 5:00 PM         | Registration Open                                                                                                                 | Atrium     |
| 11:00 AM – 5:30 PM        | Exhibit Hall Open                                                                                                                 | Atrium     |
| 8:30 AM – 11:30 AM        | <b>Central Biomaterial Bank Charité Site Visit</b><br><i>Pre-registration required.</i>                                           | Offsite    |
| 11:30 AM – 12:30 PM       | Lunch                                                                                                                             | Atrium     |
| 12:30 PM – 3:20 PM        | <b>Session 1: In Vivo Preanalytics</b><br><i>Session Chair: Michael Hummel (Germany)</i>                                          |            |
| 12:30 PM – 12:40 PM       | <b>Welcome and Introduction</b><br><i>Michael Hummel (Germany) and Cristina Villena (Spain)</i>                                   | MOA 4-5    |
| 12:40 PM – 1:10 PM        | <b>Keynote: Putting Biospecimen Best Practices in Action for the Cancer Moonshot</b><br><i>Helen Moore (USA)</i>                  |            |
| 1:10 PM – 1:35 PM         | <b>Circadian Rhythms and Biospecimens</b><br><i>Edyta Reszka (Poland)</i>                                                         |            |
| 1:35 PM – 2:00 PM         | <b>High-accuracy Determination of Internal Circadian Time from a Single Blood Sample</b><br><i>Achim Kramer (Germany)</i>         |            |
| 2:00 PM – 2:30 PM         | Networking Break with Exhibits                                                                                                    | Atrium     |
| 2:30 PM – 2:55 PM         | <b>The Effects of Death and Post-mortem Cold Ischemia on Human Tissue Transcriptomes</b><br><i>Manuel Muñoz Aguirre (Italy)</i>   | MOA 4-5    |
| 2:55 PM – 3:20 PM         | <b>Biological Variability and Plant Transcriptomics</b><br><i>Marcos Castellanos (United Kingdom)</i>                             |            |
| 3:20 PM – 4:10 PM         | <b>Session 2A: Ex Vivo Preanalytics</b><br><i>Session Chair: Cristina Villena (Spain)</i>                                         |            |
| 3:20 PM – 3:45 PM         | <b>Impact of Ex Vivo RNA Degradation on RNAseq</b><br><i>Irene Gallego Romero (Australia)</i>                                     | MOA 4-5    |
| 3:45 PM – 4:10 PM         | <b>Standardization of Preanalytical Variables for Exosome-based Diagnostic Approaches in Blood</b><br><i>Davide Zocco (Italy)</i> |            |
| 4:10 PM – 5:30 PM         | Poster Reception and Exhibition Tour<br><i>Refreshments provided.</i>                                                             | Atrium     |
| 6:00 PM – 8:00 PM         | Networking Dinner<br><i>Separate registration required. Additional tickets available until quantities last.</i>                   | Restaurant |



## WEDNESDAY, FEBRUARY 6, 2019

|                     |                                                                                                                                                                                                                                          |         |
|---------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------|
| 8:30 AM – 3:30 PM   | Registration Open                                                                                                                                                                                                                        | Atrium  |
| 9:30 AM – 1:30 PM   | Exhibit Hall Open                                                                                                                                                                                                                        | Atrium  |
| 9:00 AM – 10:15 AM  | <b>Session 2B: Ex Vivo Preanalytics</b><br><i>Session Chair: Cristina Villena (Spain)</i>                                                                                                                                                |         |
| 9:00 AM – 9:25 AM   | <b>Long Term Storage of FFPE and IHC</b><br><i>Giorgio Stanta (Italy)</i>                                                                                                                                                                | MOA 4-5 |
| 9:25 AM – 9:50 AM   | <b>Defining RNA Quality from Paraffin Embedded Tissue</b><br><i>Stephen Hewitt (USA)</i>                                                                                                                                                 |         |
| 9:50 AM – 10:15 AM  | <b>DNA Preservation in Degraded Insect Specimens</b><br><i>Ian Barnes (United Kingdom)</i>                                                                                                                                               |         |
| 10:15 AM – 10:45 AM | Networking Break with Exhibits                                                                                                                                                                                                           | Atrium  |
| 10:45 AM – 12:00 PM | <b>Session 3: Microbiome</b><br><i>Session Chair: Marcos Castellanos (United Kingdom) and Lorie Castillo (Luxembourg)</i>                                                                                                                |         |
| 10:45 AM – 11:10 AM | <b>Temporal and Technical Variability of Human Gut Metagenomes</b><br><i>To Be Announced</i>                                                                                                                                             | MOA 4-5 |
| 11:10 AM – 11:35 PM | <b>Mechanisms of Microbiome-led Mucosal Barrier Dysfunction in Intestinal Diseases</b><br><i>Mahesh Desai (Luxembourg)</i>                                                                                                               |         |
| 11:35 PM – 12:00 PM | <b>Quantitative, Population-level Microbiome Monitoring – the Flemish Gut Flora Project</b><br><i>Jeroen Raes (Belgium)</i>                                                                                                              |         |
| 12:00 PM – 1:30 PM  | Networking Lunch with Exhibits                                                                                                                                                                                                           | Atrium  |
| 1:30 PM – 3:30 PM   | <b>Debate / Workshop: SPIDIA4P – CEN &amp; ISO Standards on Liquid Biopsy: Do We All Agree?</b><br><i>Session Chair: Fay Betsou (Luxembourg)</i><br><i>Carole Foy (United Kingdom), Uwe Oelmüller (Germany), and Rui Neves (Germany)</i> | MOA 4-5 |
| 3:00 PM – 3:45 PM   | <b>Grab and Go Break</b>                                                                                                                                                                                                                 | MOA 4-5 |
| 3:30 PM – 4:30 PM   | <b>Oral Abstract Presentations</b>                                                                                                                                                                                                       | MOA 4-5 |
| 4:30 PM – 4:40 PM   | <b>Poster Awards Ceremony</b>                                                                                                                                                                                                            | MOA 4-5 |
| 4:40 PM – 5:00 PM   | <b>Closing Remarks</b>                                                                                                                                                                                                                   | MOA 4-5 |



## PRESENTATION SUMMARIES

### CENTRAL BIOMATERIAL BANK CHARITÉ SITE VISIT

TUESDAY, FEBRUARY 5, 2019 | 8:30 AM – 11:30 AM

The Central Biomaterial Bank Charité will host a site visit. The site visit will take place in advance of the 2<sup>ND</sup> Biospecimen Research Symposium on Tuesday, February 5, 2019. Please note that pre-registration is required.

Pick up from Mercure MOA lobby: 9:00 AM

Pick up from Biobank: 10:45 AM

### SESSION 1: IN VIVO PREANALYTICS

TUESDAY, FEBRUARY 5, 2019 | 12:30 PM – 3:20 PM

#### KEYNOTE PRESENTATION: Putting Biospecimen Best Practices in Action for the Cancer Moonshoot

*Helen Moore (USA)*

Recognizing the key role that biospecimens play in cancer research and research reproducibility, the U.S. National Cancer Institute has been a leader in developing biospecimen best practices and sponsoring research to support best practices. This presentation will describe ongoing work in developing the evidence base for best practices, from ethical and social issues to scientific and operational issues around biobanking. New projects to develop biospecimen evidence-based practices through literature analysis and expert review will be described. A new biobanking program in development, the Cancer Moonshot Biobank, will utilize biospecimen best practices to support team science initiatives in cancer research. The development of this new program will be described along with particular challenges that include: longitudinal engagement of a diverse set of research participants; working with community hospitals across the U.S. and understanding the limits of best practices in different settings; and making the “best” research use of small biopsy samples.

#### Circadian Rhythms and Biospecimens

*Edyta Reszka (Poland)*

Circadian rhythms are ubiquitous at every level of living organism. The 24-hour cyclic changes have been observed at behavioral, physiological and molecular level. This mechanism is important in the regulating of human health and pathological conditions. Evidences from human studies show that chronodisruption (light at night, shift work, erratic lifestyle etc.) and/or genetic disruption of circadian rhythm can lead to sleep, metabolic, psychiatric disorders and cancer disease.

Circadian rhythm seems to be an important but overlooked factor in various types of epidemiological studies and human biospecimens collection. The circadian clock is organized in hierarchy with master clock localized in the suprachiasmatic nucleus and peripheral clocks localized in tissues and cells. Based on transcriptional-translational feedback loops, circadian regulation can generate circadian oscillation of gene expression of clock-controlled genes. Unfortunately, the information on tissue-specific molecular clocks in the humans is scarce. Recently, significant contributions have been made to understanding the 24-hour oscillation of RNAs, coding RNAs, proteins, and metabolites.

Modulation of gene expression by circadian clocks in humans can provide an important confounder for epidemiological study results. However, biospecimen collection time is rarely given consideration using various human target tissue surrogates. In the absence of time-of-day and season information and also single but not multiple biospecimens collection, several algorithms have been applied for identifying of rhythms in gene expression in samples collected in temporal order. The intrinsic and synchronizing to environment biological clock should be considered when designing of good quality epidemiological studies.

#### High-accuracy Determination of Internal Circadian Time from a Single Blood Sample

*Achim Kramer (Germany)*

The circadian clock is a fundamental and pervasive biological program that coordinates 24-hour rhythms in physiology, metabolism and behaviour, and it is essential to health. Whereas time-of-day adapted therapy is increasingly reported to be highly successful, it needs to be personalized since internal circadian time is different for each individual. In addition, internal time is not a stable trait, but is influenced by many factors including genetic predisposition, age, gender, environmental light levels and season. An easy and convenient diagnostic tool is missing. Here, we report the development of a highly accurate and simple



assay (BodyTime) to estimate the internal circadian time in humans from a single blood sample. First, using circadian transcriptomics of blood monocytes from multiple individuals combined with machine learning approaches, we identified biomarkers for internal time. Next, biomarkers were migrated to a clinically relevant gene expression profiling platform, and externally validated using an independent study. Our BodyTime assay needs only a small set of blood-based transcript biomarkers and is as accurate as the current gold standard melatonin onset method at smaller monetary, time and sample number cost. The BodyTime assay provides a new diagnostic tool for personalization of healthcare according to the patient's circadian clock.

### The Effects of Death and Post-mortem Cold Ischemia on Human Tissue Transcriptomes

*Manuel Muñoz Aguirre (Italy)*

Post-mortem tissues samples are a key resource for investigating patterns of gene expression. However, the processes triggered by death and the post-mortem interval (PMI) can significantly alter physiologically normal RNA levels. We investigate the impact of PMI on gene expression using data from multiple tissues of post-mortem donors obtained from the GTEx project. We find that many genes change expression over relatively short PMIs in a tissue-specific manner, but this potentially confounding effect in a biological analysis can be minimized by taking into account appropriate covariates. By comparing ante- and post-mortem blood samples, we identify the cascade of transcriptional events triggered by death of the organism. These events do not appear to simply reflect stochastic variation resulting from mRNA degradation, but active and ongoing regulation of transcription. Finally, we develop a model to predict the time since death from the analysis of the transcriptome of a few readily accessible tissues.

### Biological Variability and Plant Transcriptomics

*Marcos Castellanos (United Kingdom)*

The Nottingham Arabidopsis Stock Centre (NASC), based at the University of Nottingham, collects, preserves, reproduces and distributes diverse seed and other stocks of the model plant *Arabidopsis thaliana* and related species for research and education. In addition to its function as a seed biobank, NASC was one of the first units in the United Kingdom to adopt and promote the use of microarray technology.

Microarrays are a powerful technology capable of measuring expression levels of thousands of genes simultaneously. A typical microarray experiment has many sources of variation which can be attributed to biological (between subjects/samples) and technical (every step involved from the moment the RNA sample is obtained) causes. The latest developments in microarray

technology have reduced to a minimum the risk of technical variability. This means that identifying sources of biological variation and assessing their magnitude, among other factors, are important for optimal experimental design and statistical valid results.

NASC's experience in processing microarrays has given us the opportunity to help and advice hundreds of students and professionals all over the world about the importance of measuring biological variability at the time of preparing a microarray study.

## SESSION 2A: EX VIVO PREANALYTICS

TUESDAY, FEBRUARY 5, 2019 | 3:20 PM – 4:10 PM

### Impact of Ex Vivo RNA Degradation on RNAseq

*Irene Gallego Romero (Australia)*

It is unclear if transcript degradation in low quality RNA samples occurs uniformly, or whether different transcripts are degraded at different rates, potentially biasing measurements of expression levels. This concern has rendered the use of low-quality RNA samples in whole-genome expression profiling controversial. But low-quality samples can sometimes be the only tool available to address a specific question – eg, samples collected in the course of fieldwork. To quantify the impact of variation in RNA quality measurements, as determined by RIN, we collected expression data from samples allowed to decay for varying amounts of time prior to RNA extraction. RNA quality and time to extraction had significant, widespread effects on measurements of gene expression levels, as well as a slight but significant impact on library complexity in more degraded samples. While standard normalizations failed to account for the effects of degradation, we found that a simple linear model that controls for the effects of RIN can correct for the majority of these effects. In instances where RIN and the effect of interest are not associated, this approach can help recover biologically meaningful signals in data from degraded RNA samples, making careful study design essential to success.

### Standardization of Blood Collection And Processing for the Diagnostic Use of Extracellular Vesicles

*Davide Zocco (Italy)*

Extracellular vesicles (EVs) are lipid membrane vesicles released by many types of cells in both health and disease. EVs can be found in most body fluids, carrying a plethora of biomolecules, including proteins, RNA and DNA that reflect the biomolecular composition of the tissue of origin. Parenchymal and stromal cells actively release EVs in the extracellular milieu



and in circulation, providing valuable information that may be exploited for diagnostic applications. However, isolation of these EV subpopulations in circulation is extremely challenging as they are diluted within more abundant EV subpopulations derived from blood cells (red blood cells, platelets and white blood cells). A number of pre-analytical variables during blood collection and processing greatly impact the levels of blood-derived EVs, thus affecting sample quality. So far, lack of standard protocols for blood collection and processing as well as quality control metrics have limited the clinical validation and adoption of EV-based diagnostic assays.

This presentation describes pre-analytical variables that affect sample quality and suitability for EV-based diagnostic approaches. Biochemical and molecular quality control (QC) metrics are proposed to minimize intra- and inter-study variability and improve data robustness and reproducibility.

## SESSION 2B: EX VIVO PREANALYTICS

WEDNESDAY, FEBRUARY 6, 2019 | 9:00 AM – 10:15 AM

### Long Term Storage of FFPE and IHC

*Giorgio Stanta (Italy)*

Archive tissues can be a very important source for retrospective clinical studies and also in the follow-up of new treatments. Proteins and immuno-histochemistry can be very useful tools. In IHC, the major problem is the same as in extractive type of analysis to obtain high level of reproducibility. There are many contradictory information in literature about the effects of storage of FFPE tissues for protein and immuno-histochemistry. There are factors that have a true long-term storage impact, such as quality of tissue treatment, storage conditions, level of expression of the proteins and different lesions and tissues. Also the specific antigens studied present different research conditions. Other conditions not related directly to the storage type, but to the different treatment of tissues techniques in the past, such as intra-tumour heterogeneity, standardization of preclinical conditions and especially not standardized fixation procedures, can affect historical material. To ameliorate quality in this kind of tissues the improvement of retrieval techniques and the possibility to look for potential protein degradation normalization indexes can be suggested.

### Defining RNA Quality from Paraffin Embedded Tissue

*Stephen Hewitt (USA)*

Quality metrics for biomolecules obtained from paraffin embedded tissue 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 an useful tool 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.

### The State of DNA Preservation in Museum Insect Remains

*Ian Barnes (United Kingdom)*

Museum collections have long provided an important tool through which to investigate evolutionary and ecological questions. Not only can collections contain specimens collected over long time periods, they also contain material from geographical regions which are difficult to routinely access, and individuals which have been identified by a taxonomic authority.

Insects constitute the majority of many natural history collections, and yet remain poorly studied for genomic analyses. Recent developments in DNA sequencing technology have provided an opportunity that significantly increases the potential of these collections, as sources of genome-wide sequence data. However, the recovery and analysis of DNA from museum specimens is not straightforward, and benefits from an understanding of recent technical developments made by ancient DNA workers, particularly in the study of archaeological human bone.

Here, I review some of the recent work conducted at the NHM on palaeontological and museum insect specimens, with a comparison to other sources of degraded DNA such as mammalian archaeological specimens. Many of the same problems that we can identify in these millennia-old samples are present in much more recent (less than 150 year-old) museum insects. These include the very short read lengths, the presence of non-endogenous sequences, and a reduction in sequence complexity.



**SESSION 3: MICROBIOME****WEDNESDAY, FEBRUARY 6, 2019 | 11:15 AM – 12:30 PM****Mechanisms of Microbiome-led Mucosal Barrier Dysfunction in Intestinal Diseases***Mahesh Desai (Luxembourg)*

The human gut microbiome plays key roles in health and disease. Although diet is a major driver of the microbiota physiology, the gut microbiota-mediated mechanisms that link diet to intestinal disorders, enteric infections and allergy sensitization are poorly understood. The research work in Desai lab is focused on discerning these mechanisms and underlying eco-immunological processes via interactions of the gut microbiome with the colonic mucus barrier. Since the modern diet of developed nations includes significantly reduced dietary fiber, the lab seeks to understand how a fiber-deprived gut microbiota impacts our health and contributes to disorders such as inflammatory bowel disease and colon cancer, and how dietary therapeutics targeting the gut microbiome could be employed to improve health.

**Quantitative, Population-level Microbiome Monitoring – the Flemish Gut Flora Project***Jeroen Raes (Belgium)*

Alterations in the gut microbiota have been linked to various pathologies, ranging from inflammatory bowel disease and diabetes to cancer. Although large numbers of clinical studies aiming at microbiome-based disease markers are currently being performed, our basic knowledge about the normal variability of the human intestinal microbiota and the factors that determine this still remain limited. Here, I will present a large-scale study of the gut microbiome variation in a geographically confined region (Flanders, Belgium). A cohort of >5000 individuals from the normal population is sampled for microbiome analysis and extensive metadata covering demographic, health- and lifestyle-related parameters is collected. Based on this cohort, a large-scale cross-sectional study of microbiome variability in relation to health as well as parameters associated to microbiome composition is being performed. In this presentation, I will discuss our experiences in large-scale microbiome monitoring, show how the development of dedicated computational approaches can assist in microbiome analysis and interpretation, and which confounders are essential for inclusion in microbiome disease research. In addition I will show how Quantitative Microbiome Profiling (QMP; Vandeputte et al. Nature 2017), which combines microbiomics with flow cytometry-based cell counts, is profoundly changing our view on gut microbiota variation, disease markers and species interaction network prediction.

**DEBATE: SPIDIA4P – CEN & ISO STANDARDS ON LIQUID BIOPSY: DO WE ALL AGREE?****WEDNESDAY, FEBRUARY 6, 2019 | 1:30 PM – 3:30 PM***Participants: Carole Foy (United Kingdom), Uwe Oelmüller (Germany), and Rui Neves (Germany)***Measurement Procedures and Materials to Support Standardisation of Liquid Biopsy Based Tests***Carole Foy (United Kingdom)*

Liquid biopsies are enabling earlier diagnosis, targeted treatments and improved disease monitoring in a non-invasive and cost-effective way. However, measurements are challenging due to low analyte levels and assays currently suffer from a lack of comparability in terms of analytical performance. This presentation will discuss reference methods and materials under development to improve comparability and support standardisation.

**New Standards for Liquid Biopsies Pre-analytical Workflows: A Key for Reliable Diagnostics, Research and Biobanking***Uwe Oelmüller (Germany)*

Molecular in vitro diagnostics and biomedical research have allowed great progress in medicine. Further progress is expected by new biomarker tests analyzing cellular and extra-cellular biomolecule profiles, including those in liquid biopsies samples. However, profiles of these molecules can change significantly during specimen collection, transport, storage, and processing, caused by post collection cellular changes such as gene inductions, gene down regulations, biomolecules modifications or degradation or post collection release of genomic DNA and other molecules into liquid biopsy specimen. This can make the outcome from diagnostics or research unreliable or even impossible because the analytical test will not determine the situation in the patient body but an artificial specimen analyte profile generated during the pre-analytical workflow. High quality clinical specimens with preserved analyte profiles are therefore crucial to research and diagnostics.

Within pan-European ring trials, the EU FP7 research consortium SPIDIA ([www.spidia.eu](http://www.spidia.eu)) could generate evidence that guidance to laboratories on pre-analytical workflow parameters improves molecular test results. Based on this and other evidence, 9 new Technical Specifications addressing pre-analytical workflows for different blood, other body fluids and tissue based molecular applications were developed at the CEN/Technical Committee 140 "In vitro Diagnostic Medical Devices". The ISO/Technical Committee 212 "Clinical



Laboratory Testing and In Vitro Diagnostic Test Systems” has recently progressed 5 of these to ISO International Standards, 4 more are mostly at a final development stage.

The new EU Horizon2020 SPIDA4P consortium project (2017-2020) aims to broaden this portfolio by generating and implementing finally a portfolio of 22 pan-European CEN/Technical Specifications and ISO/International Standards, addressing pre-analytical workflows applied to personalized medicine, including liquid biopsies specimen.

The SPIDIA project has received funding from the EU’s Seventh Research Framework Program, grant agreement no. 222916. The SPIDIA4P project receives funding from the EU’s Horizon 2020 research and innovation program, grant agreement no. 733112.

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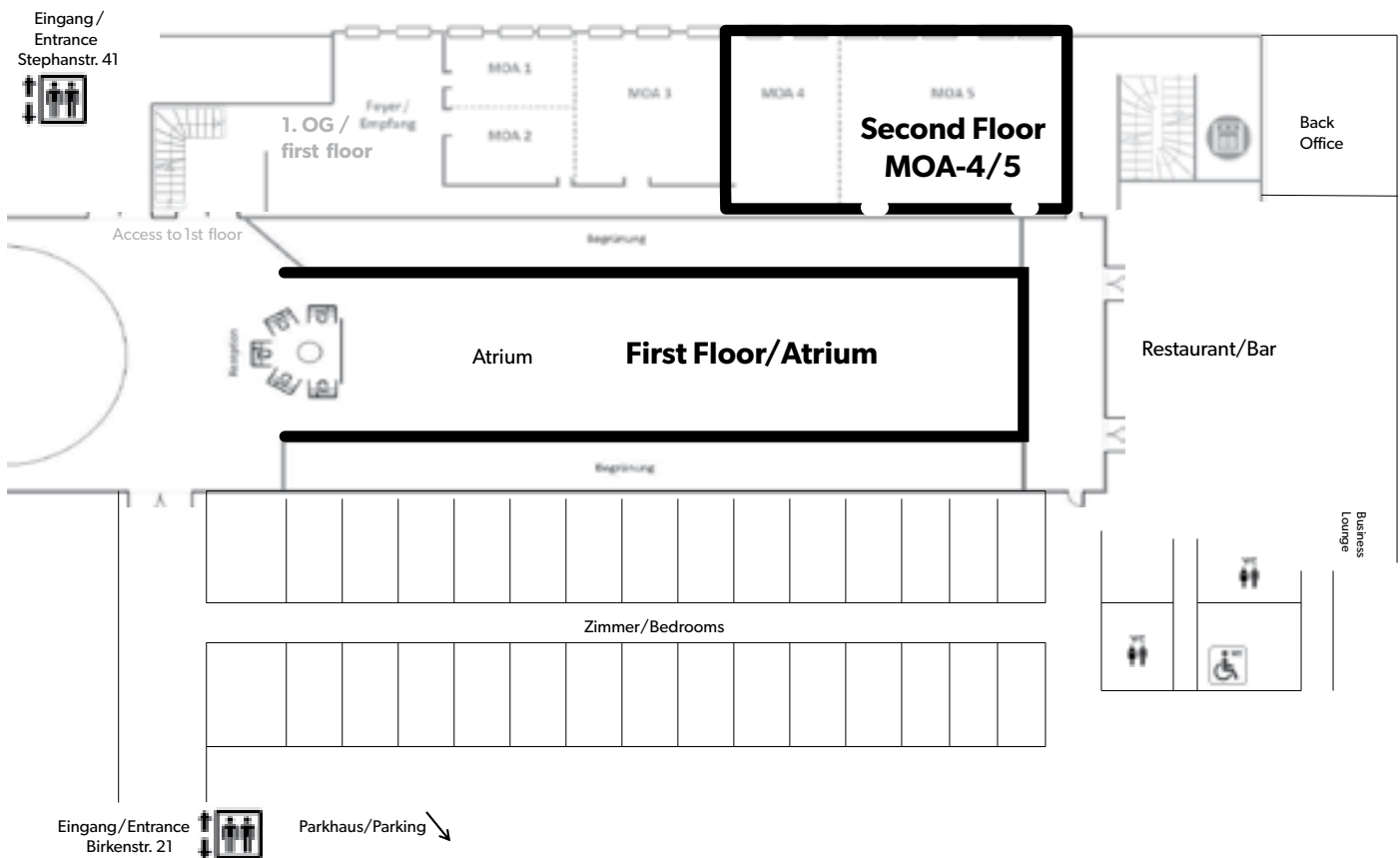
## Standardizing Liquid Biopsy – The CANCER-ID experience

*Rui Neves (Germany)*

The use of circulating tumor material as source of biomarkers is clinically and economically very attractive but technically it is very challenging. Multiple technologies have been developed to deal with this technical challenge but criteria for their evaluation are still lacking. In this context, CANCER-ID was set to evaluate technologies and protocols for blood-based bio-marker analysis such as CTCs, ctDNA and cfmiRNAs for tumor liquid biopsy. CANCER-ID is a European consortium funded by the Innovative Medicines Initiative (IMI) which involves 40 partners from academic and clinical research groups, small-to-medium sized enterprises, diagnostics and pharmaceutical industries. In this presentation, it will be provided an overview of the results obtained so far from ring/proficiency studies highlighting the challenges, the benefits and the infrastructure created for a coordinated multi-lab and multi-national effort for technology verification in the field of liquid biopsy.



## VENUE MAP





## EXHIBITOR LISTING

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**Agilent Technologies****Booth # 7**

Agilent is a leader in life sciences, diagnostics and applied chemical markets. The company provides laboratories worldwide with instruments, services, consumables, applications and expertise.

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**ASKION GmbH****Booth # 1**

ASKION GmbH - your experienced partner for modular biobanking system solutions to handle and store biological material at highest quality standards at temperatures below -185°C. The ASKION C-line® system provides you with a flexible, modularly expandable and fully automatable system approach for all current and future requirements in the field of cryotechnology/biobanking. Our biobank solution guarantees maximum flexibility regarding sample formats and storage configuration and can be upgraded anytime to a fully automated biobank. The system features ice free storage, an uninterrupted cooling chain and the complete and automated recording of sample data.

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**B Medical Systems****Booth # 10**

B Medical Systems is a pioneer in cooling technology. The biomedical world rely on our solutions to safely store, transport and handle biospecimens. All our devices are certified and sustainable.

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**Bluechiip Ltd****Booth # 8**

Bluechiip offers a product ecosystem that provides secure wireless ID sample tracking and temperature readings for use in extreme environments. We aim to be the gold standard for biological sample ID.

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**Brooks Life Sciences****Booth # 5**

Brooks is a leading worldwide provider of automation, lab equipment and service solutions for multiple markets including life sciences and semiconductor manufacturing.

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**Bruker BioSpin GmbH****Booth # 4**

Bruker Corporation is the global market and technology leader in analytical magnetic resonance instruments including NMR, preclinical MRI and EPR.



## German Biobank Node

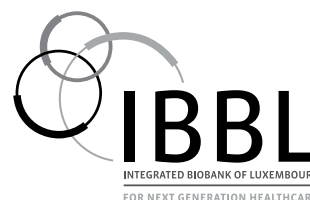
Booth # 2



The German Biobank Node serves as a central cooperation platform for the German biobank community, representing their interests in the European biobank network BBMRI-ERIC.

## IBBL (Integrated BioBank of Luxembourg)

Booth # 6



IBBL (Integrated BioBank of Luxembourg) is an autonomous not-for-profit institute dedicated to supporting biomedical research for the benefit of patients.

## LiCONiC Services Deutschland GmbH

Booth # 14



LiCONiC is driven by its position as the world's leading manufacturer of automated incubators and small size plate storage systems for the life science industry.

## MODUL-BIO

Booth # 18



Modul-Bio is specialised in IT solutions for the management of biospecimen collections, dedicated to biobanking, cohort projects, diagnostic laboratories and cosmetics companies.

## PHC Europe B.V.

Booth # 15



Previously as Panasonic, and now under our new brand name PHCbi, we respond to the needs of our pharmaceutical, biotechnology, hospital/clinical and industrial customers.

## Ziath Ltd. & Biozym Scientific

Booth # 17



Ziath specialises in instrumentation control and information management in both the academic and the pharmaceutical/biotech industry sectors with a focus on the application of laboratory automation.

Biozym are the leading provider for the European Life Science Market. Our product portfolio consists of high performance instrumentation, superior biochemical and specialized plastic ware, used in applications like PCR, Next-Generation Sequencing, identification and purification.



## ORAL ABSTRACT PRESENTATION SCHEDULE

| WEDNESDAY, FEBRUARY 6, 2019   3:30 PM – 4:30 PM |                                                                                                                                                              |                                                    |                          |
|-------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|--------------------------|
| Abstract #                                      | Title                                                                                                                                                        | Topic                                              | Presenting Author        |
| O-1                                             | DNA Quality Assurance Within A Tumour Bank Program; When Identity Matters                                                                                    | Quality Control Methods                            | Daniel Catchpoole        |
| O-2                                             | Method Validation for Extraction of DNA from Human Stool Samples for Downstream Microbiome Analysis                                                          | Validation of Processing Methods/Method Comparison | Lorie Neuberger-Castillo |
| O-3                                             | Quality Control and Assessment of the Pre-Analytical Workflow in Liquid Biobanking: Metabolite Ratios as Quality Control Marker for Pre-Centrifugation Delay | Quality Control Methods                            | Sven Heiling             |
| O-4                                             | Stability of Cerebrospinal Fluid Biomarkers During Processing and Biobank Storage                                                                            | Stability Studies                                  | Eline Willemse           |
| O-5                                             | The Fish Parasite Biobank Tour 2019                                                                                                                          | Other                                              | Ángel F. González        |

## ORAL ABSTRACTS

### O-1. DNA Quality Assurance Within A Tumour Bank Program; When Identity Matters

D Catchpoole and L Zhou<sup>1</sup>

<sup>1</sup>The Tumour Bank CCRU, Kids Research, The Children's Hospital at Westmead, Westmead, NSW, Australia

**Background:** If biobanks are to be the vital resources for translational research as expected, the quality of samples must be assured. The minimal requirement for the quality assurance would be the proper identification of samples. The Fluidigm® SNP Trace™ Panel ('The Panel') is high throughput DNA fingerprinting technology for biospecimen identification and is being marketed to biobanks. The Panel, consisting of 96 single-nucleotide polymorphisms (SNPs) specifically selected for biorepository applications, enables high-throughput QA and detection of sample mislabelling, contamination, and DNA degradation in the biorepository.

**Methods:** The Panel was used to determine the sex of 4 healthy donors for whom their DNA was deliberately compromised using sonication, X-ray radiation, UV radiation, heat, various freeze-thaw cycles, and delayed snap-freeze with different intervals to simulate poor quality situations, providing 80 separate experimental conditions. We have all aspects of performance, including call rate, confidence, concordance within and between plates, fingerprinting and cross contamination. We compared these results to 35 poorly stored bone marrow samples. As a clinically relevant scenario where sample identification may be compromised we explored 30 optimally stored matched samples obtained before and after bone marrow transplant.

**Results:** A total of 26784 SNPs were examined for all the samples with 96.78% showed 'high' confidence. Samples 'identity scores' were 99.74 for known sample replicates with optimum quality, compared to only 47.91 for DNAs from patients following bone marrow transplant, which was expected. Sex determination rate is 100% for known sex donors/patients. In deliberate sample mixing experiments DNA fingerprinting using The Panels gender SNPs detected male-female contamination as low as 1.25%, but only 5% female-female contamination. In bone marrow transplant patients male-female contamination was also detected. We compared The Panel with other techniques currently available in the market by efficiency and cost.

**Conclusions:** In conclusion, we found that Fluidigm SNPtrace Panel has provided a simple, sensitive and accurate solution for sample identification. In light of these data we discuss how we would establish a sample authentication standard protocol for our Tumour Bank quality program to offer better QA solutions for the biobank stakeholders and researchers.

**Keywords:** DNA quality SNPs

### O-2. Method Validation for Extraction of DNA from Human Stool Samples for Downstream Microbiome Analysis

L Neuberger-Castillo<sup>1</sup>, G Hamot<sup>1</sup>, M Marchese<sup>1</sup>, I Sanchez<sup>1</sup>, W Ammerlaan<sup>1</sup>, F Betsou<sup>1</sup>

<sup>1</sup>Integrated BioBank of Luxembourg (IBBL), Dudelange, Luxembourg

**Background:** Formal method validation for biospecimen





processing in the context of accreditation in laboratories and biobanks is lacking. A previously optimized stool processing protocol was validated for fitness-for-purpose in terms of downstream microbiome analysis.

**Methods:** DNA extraction from human stool was validated with new collection tubes, stabilizing solutions and storage conditions in terms of fitness-for-purpose for downstream microbiome analysis, robustness and sample stability. Acceptance criteria were based on accurate identification of a reference material, homogeneity of extracted samples and sample stability in a 2-year period.

**Results:** The automated DNA extraction using the chemagic Magnetic Separation Module I (MSMI) extracted 8 out of 8 bacteria in the ZymoBIOMICS® Microbial Community Standard. Seven tested stabilizing solutions (OMNlGene®•GUT, RNeasy, AquaStool™, RNeasy, PerkinElmer SEB Lysis Buffer and DNA Genotek's CP-150) were all compatible with the chemagic MSMI and showed no significant difference in the microbiome alpha diversity and no significant difference in the overall microbiome composition as compared to the baseline snap frozen stool sample. None of the stabilizing solutions showed intensive PCR inhibition in the SPUD assay. However, when we take into account more stringent criteria which include a higher double-stranded DNA yield, higher DNA purity and absence of PCR inhibition, we recommend the use of OMNlGene®•GUT, RNeasy or AquaStool™ as an alternative to rapid freezing of samples. The highest sample homogeneity was achieved with RNeasy- and OMNlGene®•GUT-stabilized samples. Sample stability after a 2-year storage in -80°C was seen with OMNlGene®•GUT-stabilized samples.

**Conclusions:** We validated a stool processing method and various stool stabilizing solutions suitable for downstream 16S rRNA gene sequencing. Collection and storage conditions as well as the type of lysis step prior to DNA purification can influence the microbiome profile results. Laboratories and biobanks should ensure these conditions are systematically recorded in the scope of accreditation.

**Keywords:** method validation, microbiome, 16S rRNA gene sequencing, stool DNA extraction

### O-3. Institute for clinical chemistry and laboratory diagnostics and integrated biobank Jena

S Heiling<sup>1</sup>, N Knutti<sup>1</sup>, N Schwarz<sup>2</sup>, J Geiger<sup>2</sup>, M Kiehntopf<sup>1</sup>

<sup>1</sup> Institute for clinical chemistry and laboratory diagnostics and integrated biobank Jena, Jena, Germany, <sup>2</sup> Interdisciplinary Biomaterial and Databank Würzburg (IBDW), Würzburg, Germany

In medical diagnostics and research, blood samples are one of the most frequently used materials. But exploring the chemical composition of human plasma and serum is challenging due to the highly dynamic influence of pre-analytical conditions. Accordingly for valid diagnostics and reliable, conclusive

research, good-quality samples are of utmost importance. However sample quality and especially the assessment of a good sample are not always easy to achieve. For this reason, substantial efforts are being undertaken to set up biobanks with standard operating procedures and to measure quality biomarkers to ensure high-quality biomaterials. But despite the large scope of research, quality biomarkers that address the majority of relevant pre-analytical variations are still lacking and only a few have been described for critical processing steps such as time-to-centrifugation (TTC), time-to-freeze (TTF) or temperature.

In this study, we performed an unbiased metabolomics approach, in human serum and EDTA-plasma from a healthy cohort (n=10) after 30 min and 120 min of pre-centrifugation delay, to identify novel quality control (QC) markers. We investigated 752/714 metabolites in serum/EDTA-plasma, identified the most significant compounds and plotted them based on their log<sub>10</sub> - fold change between 120 min/30 min according to their metabolic pathways using PathVisio 3.3.0. Applying this approach, we visualized the pathway occupancy and identified the ratio of hypoxanthine/inosine and xanthine/guanosine as possible pre-centrifugation delay QC markers, with high sensitivity and specificity (>80%), in serum. We further validated these ratios in an additional cohort (n=11) with healthy volunteers as well as two cohorts of patients with systemic rheumatologic (n=20) and cardiologic (n=20) diseases showing a high prediction accuracy with AUROC-values of 0.91 for TTC<60 min, respectively.

These results provide a powerful and reliable tool to predict individual pre-centrifugation delays in human serum using metabolite ratios as an essential qualitative feature for clinical and biobanking processes.

**Keywords:** Metabolomics, Biomarkers, Quality Control, Hypoxanthine, Inosine

### O-4. Stability of Cerebrospinal Fluid Biomarkers during Processing and Biobank Storage

E Willemse<sup>1</sup>, Y Vermeiren<sup>2</sup>, M van der Wiel<sup>3</sup>, M Garcia-Ayllon<sup>4</sup>, C Bridel<sup>3</sup>, P De Deyn<sup>2</sup>, S Engelborghs<sup>5</sup>, E Jansen<sup>3</sup>, I Lopez-Font<sup>6</sup>, V Mendes<sup>7</sup>, B Manadas<sup>7</sup>, N De Roock<sup>8</sup>, J Saez-Valero<sup>6</sup>, E Struijs<sup>3</sup>, E Vanmechelen<sup>8</sup>, U Andreasson<sup>9</sup>, W van der Flier<sup>3</sup>, C Teunissen<sup>3</sup>

<sup>1</sup> Amsterdam UMC, Amsterdam Neuroscience, VU University, Amsterdam, The Netherlands, <sup>2</sup> Institute Born-Bunge, University of Antwerp, Wilrijk, Belgium, <sup>3</sup> Amsterdam UMC, VU University, Amsterdam, The Netherlands, <sup>4</sup> FISABIO, Institute of Neurosciences Alicante, and CIBERNED, Elche and Sant Joan d'Alacant, Spain, <sup>5</sup> BIODOM, Institute Born-Bunge, University of Antwerp, Wilrijk, Belgium, <sup>6</sup> Institute of Neurosciences Alicante, and CIBERNED, Elche and Sant Joan d'Alacant, Spain, <sup>7</sup> Centre for Neuroscience and Cell Biology, University of Coimbra, Coimbra, Portugal, <sup>8</sup> ADx Neurosciences, Ghent, Belgium, <sup>9</sup> Institute of Neurosciences and Physiology, Sahlgrenska Academy, University of Gothenburg, Mölndal, Sweden

Background: Biomarkers in cerebrospinal fluid (CSF) can be



useful for diagnostics, prognostics and therapy response monitoring in neurological diseases. Novel CSF biomarker candidates have been identified, but clinical implementation has been hampered due to high variability in biomarker results, especially in multicentre studies. To reduce the variation in biomarker results, we studied the pre-analytical storage and freeze/thaw stability of potential novel biomarkers in CSF.

**Methods:** Three surplus CSF pools, aliquoted into 0.5 ml volumes, were experimentally exposed to pre-analytical storage conditions: 0, 1, 2, 4, 24, 72, or 168 hours at 4°C or room temperature (RT), or 1-4 months at -20°C, or up to 8 freeze/thaw (f/t) cycles before final storage at -80°C. Next, biomarker stability was measured using 11 single biomarker assays, e.g. immunoassays, and two large proteomic discovery screens, SOMAscan and Olink. For the 11 individual biomarker assays, concentrations were normalized to the concentration at time zero per marker and mean relative concentration and 95% confidence intervals per data point were presented. For SOMAscan and Olink, stability was evaluated by whether zero was included in the confidence interval and by the size of the 95% confidence interval of the concentration difference between two extreme conditions, i.e. 168 hours at RT or 8 f/t cycles compared to the reference.

**Results:** For the individual biomarker assays, only 3-methoxy-4-hydroxyphenylglycol (MHPG) linearly decreased with storage time at 4°C and RT or after f/t cycles. The other 10 biomarkers did not show changes in concentrations after common storage conditions. Using SOMAscan and Olink panels 1129 and 831 proteins were screened, respectively, of which 357 overlapped between both panels. For the SOMAscan proteins, storage delay of 168 hours at RT was the most harmful exposure. Still, 67% of the SOMAscan proteins met the stability criteria after 168 hours storage at RT. For the Olink panel, exposure to 8 f/t cycles was the most harmful exposure. Still, 80% of the Olink proteins met the stability criteria after 8 f/t cycles.

**Conclusions:** The large majority of CSF proteins remain stable under extreme pre-analytical storage and freeze/thaw conditions, although samples for MHPG measurement should be processed and stored at -80°C as soon as possible to avoid concentration loss. Our results support multicentre studies and the use of historical samples in CSF biomarker studies.

**Keywords:** cerebrospinal fluid, biomarkers, storage stability, freeze/thaw stability, immunoassays, proteomic platforms

## O-5. The Fish Parasite Biobank Tour 2019

ÁF González<sup>1</sup>, H Rodríguez<sup>1</sup>, A Ramilo<sup>1</sup>, S Pascual<sup>1</sup>

<sup>1</sup> Instituto de Investigaciones Marinas-CSIC, Vigo, Spain

Parasites have been historically considered the Cinderella species of marine communities. Contrary to that impression, parasitism is the most common animal lifestyle dominating the marine food webs. As shown in many examples from different ecosystems, parasites affect host energy budgets, host population dynamics, interspecies competition and ecosystem productivity. Fish parasites may affect the condition, growth and even the decline of an entire fishery. In mariculture a large variety of parasitic pathogens hamper fish production, causing poor growth performance, impaired welfare and cause high mortality rates. Furthermore, fish-borne zoonotic diseases have gained increased consideration. The best-known example is the anisakids which are responsible for a (re)-emergent zoonotic risk associated with a higher exposure level in fish production value chains and trending changes in seafood consumption.

Despite the above many challenges facing marine parasites, the lack of conceptual awareness on the innovation model established in Marine Sample and Data Collection Frameworks have so far prevented the implementation of a Fish Parasite Biobank (FPB) Platform as a strategic tool for Research. The FPB was constructed (under the EU- PARASITE project) in 2013 as a traceable high-quality sampling platform to host anisakids and target molecules (DNA and proteins) to afford epidemiological, genetic and proteomic analysis. This material fuels the models to perform a risk profile for zoonotic parasites in EU-fish production value chains. In 2015, the “fit-for purpose” specific actions for the EU-PARAFISHCONTROL Project in cultured fish included a quality management system as an internal platform for biobanking samples and data for Research. Since 2016, the FPB is certified with the quality management system standard ISO 9001.

Despite this progress, the FPB activity is yet on an expansion phase. Homework for 2019 concentrates on implementing quality assurance as a crucial part of FPB life: standardization of methods for parasite isolation (ISO 23036), automation platform for DNA extraction and PCR reactions, monitoring remote sensing for ultra-low freezers, management software upgrade and normalization of a cost-benefit model. Overall, FPB is a best-value for money approach to trace epidemiological surveillance plans and control strategies, not only for Research at the Academy but also for food safety management at the seafood industry.

**Keywords:** marine parasites, biobank, zoonotic diseases



## POSTER ABSTRACT PRESENTATION SCHEDULE

TUESDAY, FEBRUARY 5, 2019 | 4:10 PM – 5:30 PM

| Abstract # | Abstract Title                                                                                                                                                                          | Topic:                                             | Presenting Author       |
|------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|-------------------------|
| P-1        | Archival May-Grünwald Giemsa Stained Bone Marrow Smears Can Be Used as a Source for Molecular Research                                                                                  | Stability Studies                                  | Kimberly Vanhees        |
| P-2        | Assessment of Feasibility of Investigation of Non-targeted and Transgenerational Effects among Offspring of Radiation Exposed Individuals                                               | Other                                              | Alix Groom              |
| P-4        | Challenges and solutions adopted for the creation of a complex and multicentre prospective collection of tissue samples to evaluate the usability of biomarkers in Biospecimen Research | Quality Control Methods                            | Margalida Esteva-Socias |
| P-5        | Comparison of Three Common Standardization Programs for Biobanks                                                                                                                        | Other                                              | Tamsin Tarling          |
| P-6        | Cryopreservation of Viable Tissue Specimen                                                                                                                                              | Other                                              | Tanja Macheiner         |
| P-7        | Cryopreservation of Whole Tumor Tissue                                                                                                                                                  | Cell Preservation and Cryobiology                  | Ashley Fletcher         |
| P-8        | Current challenges and future prospects for biobanking marine zooplankton                                                                                                               | Other                                              | Ángel F. González       |
| P-9        | Diet Design and Reporting for Studies of the Intestinal Microbiota                                                                                                                      | Other                                              | David Klurfeld          |
| P-10       | Effect of Delayed Blood Processing on Phenotypic Characterization and Apoptosis of Human Peripheral Blood Mononuclear Cell (PBMC) Subsets                                               | Stability Studies                                  | Sandra Voss             |
| P-11       | Emerging Tools for the Management of Data Results for Reliable Replication, Validation and Metadata Analysis of Published Research in Biomedical Sciences                               | Quality Control Methods                            | James McNally           |
| P-12       | Fibroblast Growth Factor (FGF) 23 – Is There Any Potential To Be a Tumor Marker for a Clinical Practice?                                                                                | Validation of Processing Methods/Method Comparison | Judita Kinkorova        |
| P-13       | Formalin Fixation in the Clinical Setting: to what Extent do Delays to Processing Impact DNA and RNA Quality in Formalin-Fixed, Paraffin-Embedded Biospecimens?                         | Other                                              | William Mathieson       |
| P-14       | Homogenization Methods Have a Direct Impact on the Distribution of the Microbiome in Soil Sample Aliquots                                                                               | Validation of Processing Methods/Method Comparison | Laura Dietrich          |
| P-15       | Impact of specimen age on its DNA quality for Formalin-Fixed Paraffin-Embedded HPV specimens                                                                                            | Cell Preservation and Cryobiology                  | James Park              |
| P-16       | Implementation Of A Software Framework for Data Validation According To CEN/TS – A Proof Of Concept                                                                                     | Other                                              | Ida Schönfeld           |
| P-17       | Is it the Amount of Tissue or the Quality of Tissue that is Important for Genetic Testing?                                                                                              | Quality Control Methods                            | Lisa Spary              |
| P-18       | New and Traditional Biomarkers of Liver Cancer Process                                                                                                                                  | Validation of Processing Methods/Method Comparison | Radek Kucera            |
| P-19       | Nightingale experience - Blood sample quality control alongside NMR metabolomics in large biobanks                                                                                      | Quality Control Methods                            | Sandra Schläfle         |
| P-20       | NMR Based Quality Control in Biobanking                                                                                                                                                 | Quality Control Methods                            | Manfred Spraul          |
| P-21       | OPTIMARK project: search for quality markers for paraffin-embedded tissue samples                                                                                                       | Quality Control Methods                            | Mar Iglesias Coma       |



| Abstract # | Abstract Title                                                                                                                   | Topic:                                             | Presenting Author     |
|------------|----------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------|-----------------------|
| P-22       | Optimization of DNA Extraction for Zoonotic Fish Parasites: Preparing the Barcoding for the Seafood Safety Challenge             | Validation of Processing Methods/Method Comparison | Helena Rodríguez      |
| P-23       | Optimizing Deparaffinization Process From FFPE Tissue : Employ a Commercial Solution or Xylene Protocol ?                        | Validation of Processing Methods/Method Comparison | Márcia Marques        |
| P-24       | Performance Comparison between Micro Electro Mechanical Systems Tracking Tags and Other Labelling Strategies for Cryotubes       | Validation of Processing Methods/Method Comparison | Fernando Gómez-Romano |
| P-25       | Quality Control in Cryopreserved Samples Applied in Exome Analysis                                                               | Quality Control Methods                            | Ana Caroline Neuber   |
| P-26       | Spectral fingerprinting of biobanked fish-borne parasites                                                                        | Other                                              | Helena Rodríguez      |
| P-27       | Strengthening Quality Metrics for Human Biospecimens Through the Use of Data Science: A Case Study                               | Other                                              | Zachery von Mechhofen |
| P-28       | Testing the quality and stability of plasma protein and whole blood RNA in archived loggerhead sea turtle blood, Caretta caretta | Stability Studies                                  | Jennifer Ness         |
| P-29       | The Effect of Pre-analytical Conditions on Blood Metabolomics in Epidemiological Studies                                         | Stability Studies                                  | Alix Groom            |
| P-30       | The influence of long-term cryopreservation on human peripheral blood cells                                                      | Stability Studies                                  | Antje KC Echterhoff   |
| P-31       | Validation of processing methods for an extraordinary specimen type: FFPE bone.                                                  | Validation of Processing Methods/Method Comparison | Olga Kofanova         |
| P-32       | Virus Screening Test of Biosamples (Cell Line, Tissue, and DNA).                                                                 | Quality Control Methods                            | Arihiro Kohara        |
| P-33       | New Developments in Nucleic Acid Sample Quality Control                                                                          | Quality Control Methods                            | Elisa Viering         |



## POSTER ABSTRACTS

### P-1. Archival May-Grünwald Giemsa Stained Bone Marrow Smears Can Be Used as a Source for Molecular Research

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**Background:** For biobanks, it is important to ensure sample quality after long-term storage. The University Biobank Limburg and Clinical Biobank (Jessa Hospital) contain a hematological collection of stained bone marrow (BM) smears, stored at room temperature since 1998. For their use in downstream applications, DNA quality of the samples was investigated.

**Methods:** The effect of long-term biobank storage on DNA quality was assessed in samples stored for 1, 5, 10, 15 and 18 years using gel electrophoresis, qPCR, and targeted Next-Generation Sequencing (NGS) (TruSight® Myeloid Sequencing Panel). The stored BM smears were either May-Grünwald Giemsa (MGG) or Perls' Prussian Blue (PPB) stained.

**Results:** Overall, DNA quality decreased over time. But where DNA extracted from PPB stained samples immediately showed smeared patterns on gel, DNA from MGG stained BM smears exhibited less diffuse and more distinct bands. For qPCR, mean dCt values for HMBS and HBB were remarkably higher in PPB stained samples. Generally, DNA isolated from PPB stained BM smears showed to be degraded independent of storage time, while DNA isolated from MGG stained samples were qualitatively suitable for downstream applications. Using the NGS panel, reliable results were obtained for MGG stained samples with a storage time of no more than 10 years.

**Conclusion:** Conclusively, DNA better preserved in stored MGG than in PPB stained samples. The MGG stained BM smears up to 10 years of storage still yielded DNA suitable for reliable NGS analyses. Therefore, the archival MGG stained BM smears can be used as source for molecular research.

**Keywords:** bone marrow smears, DNA quality, targeted next-generation sequencing (NGS)

### P-2. Assessment of Feasibility of Investigation of Non-targeted and Transgenerational Effects among Offspring of Radiation Exposed Individuals

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**Background.** Findings of animal experiments suggest that

high levels of radiation (>1.0 Gy) may induce genetic and epigenetic alterations in offspring of radiation exposed species (Little M. 2013). However some studies of offspring of radiation exposed parents reported no increased risks of any health outcomes. Additionally, it should be noted that data on health effects in offspring of individuals chronically exposed to ionizing radiation, and specifically internal radiation, at low dose rates remains sparse.

**Methods.** A cohort of Mayak Production Association (PA) workers and their families provides a unique source to perform such studies, and one of the main advantages of the cohort is availability of biological specimens contributed by cohort members.

**Results.** To date the Russian Radiobiology Human Tissue Repository (RRHTR) stores biological specimens for 1415 family triads (119 families with an exposed mother, 650 families with an exposed father, 497 families with both spouses being exposed and 150 control unexposed families). The range of preconception gonadal absorbed doses from external gamma-rays was wide (0 to 5.7 Gy). The mean cumulative preconception gonadal absorbed doses from external gamma-rays were  $0.74 \pm 0.81$  Gy in fathers and  $0.58 \pm 0.62$  Gy in mothers.

**Conclusions.** Available individual medical information, data on parental reproductive health, non-radiation factors and other variables, as well as individual measured annual (in some case, monthly) doses from chronic radiation exposure and sufficient statistical power enable investigations of non-targeted and transgenerational effects among offspring of radiation exposed parents.

**Keywords:** genomic instability, offspring, radiation exposed individuals, Mayak worker cohort





## P-4. Challenges and solutions adopted for the creation of a complex and multicentre prospective collection of tissue samples to evaluate the usability of biomarkers in Biospecimen Research

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Seventeen biobanks of Spanish Biobank Network (SBN) as part of the ISBER Biospecimen Science Working Group are developing a collaborative prospective collection of tissue samples with controlled pre-analytical variables. The main objective of this collaboration is to measure the impact of pre-analytical variables, mainly cold ischemia and fixation time, on tissue samples.

Sixteen tissue blocks of 0,5 cm<sup>3</sup> per organ were collected per patient (8 snap frozen and 8 formalin-fixed paraffin-embedded (FFPE)) with controlled cold ischemia times (30 minutes, and 1, 3, 6, 12, 24, 48 and 72 hours). During cold ischemia, samples are kept at room temperature in a sealed box with a damp tissue to prevent them drying out. Past the scheduled time, the fresh samples are either fast frozen and stored at -80°C or formalin fixed, paraffin-embedded and stored in a dry, dark place at +2-10°C. Currently the SBN are collecting bladder, brain, breast, colon, kidney, liver, lung, stomach, thyroid and tonsil samples.

Challenges identified during the design of the protocol were the overlap of the dehydration process at some ischemia time points, limited by the number of tissue processors available. With a specifically dedicated processor, fixation time was set up between 12 and 24 hours in order to avoid the start of the processor's protocol overlapping for the various samples with different cold ischemic times.

Furthermore, depending on surgical excision day/time, not all biobanks have trained personnel available to handle the

planned tasks. To solve this issue, one of the strategies adopted was to coordinate all time points of ischemia and evaluate staff availability to collect the samples. A timetable was established to work shifts that involved collaborative work between at least two members of the biobank staff to cover all ischemic time-points. Additionally, initial material of large dimensions is required when 16 samples per patient is required. So, organ donors and surgeries where large quantities of tissue or the complete organ is removed from the patient were selected, and not all biobanks have access to such kind of material.

A common procedure for collaborative sample collection has been established, which will make well-characterized tissue samples available, with control of pre-analytical variables for biospecimen research. Additionally, the main challenges for a prospective and multicentre collection process have been identified and addressed as described above.

**Keywords:** Tissue, BioSpecimen research, quality, collection

## P-5. Comparison of Three Common Standardization Programs for Biobanks

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Background: Biospecimen science aims to inform biobanking standards that ensure the optimal quality of biospecimens that will be utilized for downstream applications. As we strive to implement personalized medicine the biobanking process is conducted by many entities across many environments. Biospecimens may be collected for both research and clinical applications and the requirement for standardization, validation or verification is a strategic consideration for biobanks.

Currently, there are three standardization programs for biobanks: College of American Pathologists Biorepository Accreditation Program (CAP BAP), International Organization for Standardization (ISO) 20387 and the Canadian Tissue Repository Network (CTRNet) Certification program which are hosted in the United States, Internationally and Canada respectively. While these standards address the same overall goal, each has a different emphasis. We set out to identify the overlapping and unique qualities of all three programs and their standards and delineate for biobankers how these standards align best with their purpose.

Methods: We closely examined each of three sets of standards; CTRNet ROPs (2017), ISO standard 20387 (2018) and the CAP BAP checklist (2012) in order to map their requirements. While the organization of each standard is different, all describe a set of discrete statements (elements, sub clauses or requirements) that comprise the standards that are contained in sections (CTRNet), clauses (ISO), and checklists (CAP BAP). We also





identified the background scope, principles, qualifying terms and statements that convey the importance of each standard.

Results: The process identified 362 unique elements for CTRNet ROPs, 290 unique sub clauses for ISO 20387 and 189 unique requirements for CAP. Initial analysis and comparison suggests that 13% of CTRNet elements are unique, 16% of ISO sub clauses are unique and 21% of requirements are unique to CAP.

Conclusions: Each program takes a different approach and subdivides its standards into different clusters and categories. The CAP BAP program has a focus on specimen handling, ISO has an emphasis on Quality Management Systems and CTRNet addresses a broader range of operational components in biobanking. As a result of this comparison, biobankers will be able to identify which standard best fits the scope of their biobank.

*Keywords: standard, quality, biospecimens, fit for purpose*

## P-6. Cryopreservation of Viable Tissue Specimen

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Background: State-of-the-art in cryopreservation is snap-freezing in the field of biobanking which leads to damaged and physiological inactive cells and therefore reduced applicability of these samples.

This project aims to develop a new tissue cryopreservation technique for an extended range of applications of cryopreserved biospecimens of biobanks by maintenance of cell-viability due to specific cutting and freezing.

Methods: Based on previous research with ovine esophagus, human skin samples from tightening are punched out to ring-shaped pieces of tissue. The tissue viability after thawing is tested in comparison between conventional snap-freezing method and the newly developed slow-freezing method (-1°C/hour). After thawing the samples are incubated in enzyme-solutions to break the basal membrane for cell growth out of basal-epithelial cells, which were cultivated in a special keratinocyte medium.

Analyses of viability of these cells are performed by inverse microscopy, standard stainings as well as immunohistological stainings. Additionally, RIN values were analysed.

Results: Basal epithelial cell grow out from slowly frozen skin samples after cryopreservation of six weeks in preliminary tests.

In comparison, in snap-frozen samples any physiologically intact cells were not found after thawing.

Furthermore, yielded cells showed a typical morphology, differentiation and immunohistological characteristics of epithelial cells.

Additionally, RIN-values were compared between fresh, snap and slow frozen tissue samples to analyze differences of RNA-integrity. However, the analyses lead to implausible results for human skin samples.

Conclusions: The cryopreservation of viable tissue specimen was performed successfully in preliminary tests, but further investigations are necessary to improve the efficiency of the method. Additionally, RIN-value analyses have to be adapted for human skin samples since the procedure seems to lead to implausible results by a difficult sample homogenization. Nevertheless, the described freezing method suggests a high potential for a broad range of applications with biobank tissue samples in the future biomedical research.

## P-7. Cryopreservation of Whole Tumor Tissue

*A Fletcher<sup>1</sup>, T Ribar<sup>1</sup>, S McCall<sup>1</sup>, and S Jiang<sup>1</sup>*

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For years, researchers have been exploring different methods of cryopreservation. Whether it be for single cells, whole tissues or even whole organs, scientists are still coming up with newer and safer methods of freezing and thawing viable tissue. The most common form of cryopreservation for research labs today is digesting tissue into single cell suspensions and freezing them in media containing 5-10% DMSO. While this may be a good method for a lot of single cell assays, it is both time and resource-intensive for the biobank. Single-cell suspensions may also no longer be 'fit-for-purpose' for PDX or organoid model creation.

As science advances and evolves, biorepository methods must also evolve. Researchers have been requesting viable tissue and cells for downstream assays, ie. single cell RNA seq, organoid, and primary cell culture development. Locally, our biorepository is becoming a "living" Biobank, storing viable human tissue samples in a manner that can be used for many applications requiring live cells.

We sought to develop a general, quick and inexpensive method to cryopreserve tissue. After an extensive literature review, we proposed to test the success rate of our proposed protocol. For the study, we procured samples of sarcoma and prostate tumor tissue. Working in a laminar hood, we finely minced each sample with a sterile razor blade to about 1mm<sup>3</sup> chunks and placed them into 2 different cryovials since the starting material was ~1cm<sup>3</sup>. We added 1.5mL of our freezing media made up solely of 20% DMSO/FBS, then placed them in a slow freezing cooler at -80°C. The following day samples were placed in the liquid nitrogen vapor tank for storage.

For viability testing, we pulled one sarcoma and one prostate sample from the liquid nitrogen tank. Tissues were placed



into sterile petri dishes and further minced with scissors, then incubated at 37°C in a special digestion media (collagenase-hyaluronidase/dispase/F-Media) for 5 hours, vortexing for 30 seconds every 30 minutes. Trypsin was then added to the samples at a concentration of 2.5% and incubation/vortexing continued for another hour. Cells were subsequently plated and left at 37°C ON to recover. The following day cells were counted using Trypan Blue exclusion. Both samples were at 80% viability, making these samples more than suitable for assays and procedures requiring live cells.

*Keywords: tumor, tissue, cryopreservation*

## P-8. Current challenges and future prospects for biobanking marine zooplankton

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**Background:** Knowledge of the structure of the zooplankton allows characterizing marine ecosystems and knowing the interactions (connectance and nestedness) that occur in them. Zooplankton responses to environmental variability bring about fundamental changes in the dynamics of marine ecosystems, causing fluctuation in primary production. Many species of zooplankton within the marine environment has also a key role in the transmission of parasites to higher trophic levels. Since 2004, as a part of a large sampling plan for mesozooplankton in a seasonal upwelling system carried out by the Institute of Marine Research (IIM-CSIC), a large number of samples were collected for further research projects. The matter raised was if the Fish Parasite Biobank (FPB) Service already established at the IIM-CSIC would turn the challenge posed by monitoring these samples over time into an opportunity to preserve traceable zooplankton samples and their associated data.

**Methods:** Zooplankton samples were collected by nets equipped with 200 µm mesh size in the Rías baixas (NW Spain). Net filtered approximately 200 m<sup>3</sup> of seawater and zooplankton samples were fixed on board in 96% ethanol or 10% formaldehyde. Water samples were collected with a rossete sampler equipped with Niskin bottles and data of CDT were taken. In the laboratory representative samples (250 ml) were obtained using Folsom splitter. Each subsample was identified by a Bank Code associated with data collection. Zooplankton organisms were identified to the lowest possible taxonomical level and then separated to DNA extraction.

**Results:** Data from 1474 zooplankton subsamples, which included location, depth, volume of filtered seawater, oceanographic data (Temperature, Salinity, O<sub>2</sub>, Upwelling index, Fluorescence) and nutrients (Chla, NO<sub>3</sub>, NO<sub>2</sub>, PO<sub>4</sub>), are being introduced into the database. The FPB service is currently working to adapt the platform to the new sample format.

**Conclusions:** Zooplankton samples are storing smoothly in the

Biobanking platform. Such a preliminary experience can ensure that the requisite level of trust is built in order to provide large number of zooplankton samples for multiple research targets such as analyse the coupling between zooplankton dynamics and environmental variability, detect global change effects on biological systems, study the diversity and abundance of fish and cephalopod larvae species commercially valuable, and detect zoonotic parasites recruited in zooplankton.

*Keywords: Biobank, marine zooplankton, monitoring, data collection*

## P-9. Diet Design and Reporting for Studies of the Intestinal Microbiota

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**Background:** Much research has addressed the intestinal microbiome since development of genetic sequencing methods have provided the ability to identify most bacteria and their functional capacities. Inadequate attention has been paid to diet in many of those studies even though that is recognized as the primary source of nutrients available to the colonic microbiota. To foster increased rigor and reliability of such studies, attention was focused on this issue at a US government-sponsored meeting.

**Methods:** A two-day workshop organized by USDA and NIH program staff to address best practices of diet in studies of the intestinal microbiota was held in June 2017. Sixteen invited speakers spoke to about 200 attendees, either in person or via webinar. Substantial time was built into the schedule to allow vigorous discussion of each section of the agenda's four themes: how the structure of fermentable carbohydrate influences the microbiota, variables in studies using animal models, in vitro systems, and human studies.

**Results:** Dietary fiber is one of the main nutrients for colonic bacterial growth but is presented to the colon in multiple different physical and chemical forms. This indicates the need to accurately describe the foods provided to human subjects or animals. For animal studies, standard commercial rodent feed varies from batch to batch, so researcher may consider using opensource formulas or purified diets depending on the hypothesis being tested. The commonly used purified diets contain no fermentable substrate; therefore, a customized formula may be required. Many animal housing parameters also affect the microbiome include bedding, group housing, and use of acidified drinking water. For in vitro studies, detailed information on the fecal donor's health and diet should be provided. In human studies, controlled feeding from a metabolic kitchen and/or accurate recording of all foods and beverages is needed.

**Conclusions:** There is little definitive information on the factors that modulate both the bacteria in the gut and their metabolic



activities. Greater attention to diet in design and reporting of studies on the intestinal microbiota will lead to resolution of this dilemma. A summary of the workshop is in the American Journal of Physiology, Endocrinology & Metabolism, doi: 10.1152/ajpendo.00058.2018.

*Keywords: diet, nutrition, microbiota, animal models, in vitro models, human interventions*

## P-10. Effect of Delayed Blood Processing on Phenotypic Characterization and Apoptosis of Human Peripheral Blood Mononuclear Cell (PBMC) Subsets

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**Background:** Isolation and analysis of human PBMCs is one of the most commonly performed tests for studying human immune responses. Processing delays prior to PBMC harvesting may compromise the results of immunoassays due to a lower detection of cell populations and impaired cell function. Although several studies have examined the effect of cryopreservation of PBMCs on cell phenotype and function, it is not yet known whether processing delays before isolation of PBMCs affect immunophenotypic studies of leukocytes.

**Methods:** Venous blood from 10 healthy individuals was collected and PBMCs were isolated without any delay (0 h) or after a processing delay at room temperature of 1, 2, 4, 8, and 12 h. PBMCs were then cryopreserved and tested simultaneously. Cellular yield was determined before freezing, and PBMC recovery and viability were assessed after thawing. PBMC subpopulations were characterized by flow cytometry. A fixable aqua dead cell stain and phosphatidylserine were used to distinguish viable, apoptotic, and dead PBMC subpopulations.

**Results:** Processing delays beyond 1 h resulted in a decreased yield of viable cells after PBMC isolation ( $p < 0.001$ ). Delayed processing had no effect on the viability of PBMCs after thawing. Flow cytometry revealed a marked increase in B cell frequencies after processing delays beyond 1 h ( $p < 0.001$ ). In contrast, we observed a selective loss of CD3+ T cells after processing delays of 4 to 12 h in comparison with immediately processed PBMCs. The percentage of CD4+ and CD8+ T cell subsets in the early stage of apoptosis was not altered at all time points investigated. However, we found significantly higher percentages of apoptotic B cells over time after a processing delay beyond 1 h (0 h vs. 12 h:  $9.4 \pm 1.2\%$  vs.  $16 \pm 1.8\%$  of total B cells,  $p < 0.001$ ). Frequencies of early apoptotic CD56++ CD16+ NK cells and early apoptotic CD56++ CD16- NK cells were higher after delays beyond 8 h ( $p < 0.05$ ). Similar results

were found for the classical monocyte subset. A processing delay did not affect the frequencies of late apoptotic/secondary necrotic cell subsets.

**Conclusion:** We demonstrated that specific PBMC subsets are significantly influenced by processing delays prior to PBMC isolation and are sensitive to those delays with respect to apoptosis. The time between sample acquisition and the initiation of processing should be carefully considered in study designs involving PBMC immunoassays.

*Keywords: Processing delay, PBMC*

## P-11. Emerging Tools for the Management of Data Results for Reliable Replication, Validation and Metadata Analysis of Published Research in Biomedical Sciences

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A growing number of publications and review projects have focused on the difficulty of replicating results and validating outcomes emerging from scientific research. This is a particular problem within the clinical sciences where the oft-cited “gold standard” of double-blind control studies routinely presents findings that cannot be replicated by interested scientists. This problem of replicating results was noted specifically at the ISBER 1st Biospecimen Research Symposium in 2017 by Glenn Begley. Several highly regarded organizations such as the Cochrane Collaboration invest considerable research activity into improving the reporting and reproduction of data results emerging from controlled studies. This presentation continues this work and addresses many of the concerns raised by Begley through the use of Block Chain technology within a controlled repository setting. Working with by Biorepositories, clinical researchers, lab technicians and analysts in collaboration with digital repositories such as the NACDA Program on Aging, new technology and approaches allow researchers to safely store and disseminate research findings and source code. The use of Block Chain technology allows us to verify the analysis used in original research generation and ensure foundation researchers get appropriate credit for their work under a reanalysis or metadata framework. Much of the failure in replication and validation studies comes from a lack of detailed information on coding, variable choice and case wise elimination of information. Our presentation will describe a system that overcomes these barriers and makes validation studies a more realistic reflection of success and failure rates within research paradigms.



## P-12. Fibroblast Growth Factor (FGF) 23 – Is There Any Potential To Be a Tumor Marker for a Clinical Practice?

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**Background:** Fibroblast growth factor 23 (FGF 23) is secreted by osteocytes in response to an increased concentration of the active form of vitamin D-calcitriol. The result is a reduction of reabsorption and an increase in excretion of phosphates. FGF23 is also a 1-alpha-hydroxylase inhibitor that catalyzes the conversion of the vitamin D (calcidiol) stock form to the active form of vitamin D (calcitriol). Recently, several studies have been done to investigate the relationship of elevated levels of FGF 23 and the development of colorectal neoplasia. The new research results show the involvement of FGF 23 in the angiogenesis process. The first aim was to measure the levels of FGF 23 in the normal population to obtain reference values and the second aim was to evaluate the possible using of FGF 23 in differential diagnostic between colorectal cancer patients and patients with the colorectal origin liver metastases.

**Methods:** The first group of the patients included 124 patients with colorectal cancer (clinical stage I. and II). The second group of the patients included 95 patients with advanced colorectal cancer (clinical stage IV with liver metastases). Control group consisted of 365 healthy individuals. Blood samples were collected prior surgery and prior any therapy initialization. FGF 23 assessed by CLIA method using automated instrument LIAISON® XL (Diasorin, Saluggia, Italy).

**Results:** According to the results of the FGF 23 assay by the CLIA method, FGF 23 reference values for the healthy population were set up at 30-105 pg/mL. In patients with colorectal cancer, the level of FGF23 vary with the stage of the disease. In early stages is the level higher than in advanced stages with the liver metastases. The levels of FGF 23 in patients with the stage IV of colorectal cancer before surgery were statistically significantly higher than the levels after surgery. FGF 23 levels did not correlate with any other marker. The evaluation included the comparison of the levels in the individual groups and comparison with already established tumor markers CEA, CA 19-9, TPA and TPS whose levels were determined in the same groups.

**Conclusions:** FGF 23 is not yet usable as a tumor marker in clinical practice but it can be used for the study of tumour disease etiopathogenesis.

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**Keywords:** FGF 23, colorectal cancer, diagnostics

## P-13. Formalin Fixation in the Clinical Setting: to what Extent do Delays to Processing Impact DNA and RNA Quality in Formalin-Fixed, Paraffin-Embedded Biospecimens?

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**BACKGROUND:** A typical clinical workflow is for biospecimens to be placed in formalin in Theatre or Pathology, remaining in formalin until the tissue processor starts its run, converting the samples into formalin-fixed, paraffin-embedded (FFPE) blocks. Typically, the tissue processor runs overnight, but not on Friday and Saturday nights. A sample's fixation time will therefore depend on which of the following scenarios apply: (i) sample processed overnight on day of surgery, (ii) sample processed overnight the day after surgery, (iii) surgery on Friday and sample processed Sunday night and (iv) surgery on Thursday but too late for Thursday night's processing run so is processed Sunday night. We evaluate the effect of these four scenarios on yield and integrity of DNA and RNA.

**METHODS:** Clinical tissue biospecimens (n = 6) were each cut into 36 blocks, fixed in formalin to represent the scenarios i - iv above (n = 72 for i and ii, n = 36 for iii and iv) then processed into FFPE blocks. DNA and RNA was extracted, quantified and integrity-assayed using Illumina FFPE QC Assay and DNA Integrity Numbers (DIN) for DNA, and RNA Integrity Numbers (RIN), DV200 and qRT-PCR for RNA.

**RESULTS:** The differences between scenarios i, ii and iii were small in magnitude and inconsistent between patients. However, scenario iv caused a large and statistically significant reduction in integrity of DNA and RNA. Compared to scenario i, average declines were as follows: for DNA, a reduction of 1.9 DIN units and a higher  $\Delta Ct$  in the Illumina FFPE QC Assay of 1.6 units; for RNA, DV200 reduced from 60% to 32% and Ct numbers increased by 6.8 units in qRT-PCR. All these changes denote a decline in integrity.

**CONCLUSIONS:** The fixation times in the existing clinical workflow had a limited effect on DNA and RNA integrity, with the exception of scenario iv, which had a considerable effect. So, samples collected on a Thursday should be processed on Thursday night, not left until Friday. The Illumina FFPE QC Assay is a QC tool for DNA sequencing, with  $\Delta Ct > 2$  denoting samples less amenable to sequencing. 50% of the samples in scenario iv had  $\Delta Ct > 2$ , meaning > 50% of patients destined for personalised medicine would need to return to clinic to provide a second biopsy when this QC threshold is applied. For DV200, the reduction induced by scenario iv equates to a decline in RNA quality from "intermediate" to "poor", denoting an increase in the amount of RNA required for trans





*Keywords: tissue processing, tissue processor, FFPE, stability, DNA, RNA, fixation time, formalin, DIN, FFPE QC assay*

#### **P-14. Homogenization Methods Have a Direct Impact on the Distribution of the Microbiome in Soil Sample Aliquots**

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**Background:** Soil is one of the most heterogeneous environments, especially regarding the distribution of different soil particles and the associated soil microbiome. This makes it challenging to obtain replicable results from aliquots of soil samples collected for microbiome research. The micro-heterogeneity of soil samples has significance for a wide range of fields including agriculture, forestry, medicine, and biobanking. Therefore, the aim of this study was to compare intra-sample microbiome variability after the application of different homogenization procedures.

**Methods:** Soil samples from five different switchgrass fields were collected and separated into three groups. The samples of group 1 were aliquoted directly and used as a control. The samples of the two other groups were homogenized with a blender to mix and disaggregate the soil aggregates. The samples of group 2 were aliquoted at this point; the samples of group 3 were aliquoted after the additional use of the two-dimensional Japanese slabcake technique as described in the Incremental Sampling Methodology. This technique reduces the effects of stratification during sample size reduction. Genomic analysis was conducted upon three aliquots of each group and field to identify bacteria and fungi, followed by bioinformatics and biostatistics analysis.

**Results:** Significantly less microheterogeneity was observed between aliquots in groups 2 and 3 than between aliquots in the control group. For bacteria, there was no difference between groups 2 and 3; while for fungi, group 2 showed significantly less microheterogeneity than group 3. The use of the two-dimensional Japanese slabcake was neither more nor less effective for the homogenization of the bacterial microbiome, but it was less effective when the fungal microbiome was the desired target.

**Conclusions:** Homogenization of samples resulted in aliquots which demonstrated less variability in the diversity of the bacterial and fungal taxa present in their microbiome in contrast to the control aliquots. This opens the door to conducting further studies to clarify and establish which homogenization methods work best for different soil types and target organisms. This may lead to the creation of new guidelines to obtain more

homogeneous aliquots of soil microbiome samples which can be stored by biobanks.

#### **P-15. Impact of specimen age on its DNA quality for Formalin-Fixed Paraffin-Embedded HPV specimens**

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Formalin fixation and paraffin embedding (FFPE) allows the storage of diagnostic and surplus tissue in archival banks. Therefore, FFPE is now a standard method for long-term preservation of tissue biopsies as FFPE of samples preserves the morphology of tissue. Unfortunately, the FFPE process engenders chemical changes and degradation in tissue macromolecules that can pose threats to reliable subsequent analysis. DNA, while more resistant to FFPE in comparison to RNA and protein, is also subject to such chemical formations and degradation. This study provides robust findings about the relationship between DNA quality and specimen age from 10252 FFPE HPV specimens. This paper suggests that there is a perceptible degrading effect in DNA quality as specimens age. This study suggests that the biospecimen may begin to take on new characteristics after certain storage years, and such changes may result in inaccurate determinations of the molecular characteristics of the biospecimen during analysis. Results from this study demonstrate that older HPV specimens are more inclined to be tested negative or inadequate from commercial HPV genotyping assays. Same findings are conferred when multiple genotyping assays are involved with HPV testing. Also, older HPV samples typify fewer HPV types compared to younger HPV samples. The results from this study will be useful to enhance potential scope for next fixation methods such as ethanol fixation that may be equally useful for both molecular profiling and histology as FFPE.

#### **P-16. Implementation Of A Software Framework for Data Validation According To CEN/TS – A Proof Of Concept**

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**Background:** Prior to the release of the first Biobank-dedicated ISO-Standard in August 2018, the European Committee for Standardization (CEN) published nine technical specifications (TS) covering the handling, processing and documentation of certain specimen during the pre-analytical phase. Hitherto those CEN/TS were the only binding norms for implementation in biobanking processes. Ensuring the conformity of the specimen's documentation with the respective CEN/TS is a cumbersome manual task. To facilitate



the process of data validation, the goal was to implement a supporting software tool.

**Methods:** Firstly the different CEN/TS were evaluated to extract the required and recommended data entries. Following the data fields were grouped by the steps of the pre-analytical phase to derive a suitable data model thereof. A software framework, consisting of database, validation layer and a web application, was designed and implemented. The database was realized as a document store (MongoDB) to offer a flexible data model. The validation layer was implemented in Ruby and contains validation rules and schemas for the individual CEN/TS. A simplified web application was written in Ruby to provide the user with a graphical user interface. A Java program for generating dummy data sets was implemented.

**Results:** Data sets were generated for the different specimen types as well as varying data field values and types. The implemented software framework validated the data sets for all suitable CEN/TS and stored the results and possible error messages in the database. Test cases were created for each type of validation rule and subsequently the expected result manually compared to the realized result. All test cases passed the verification. Missing data fields, faulty data and inconsistencies were detected by the validation algorithm and displayed in the web application accordingly.

**Conclusion:** The implemented framework compared the generated dummy data with the requirements of the different CEN/TS successfully. The exhibition of the validation results and error messages for the user via the web application demonstrates that such a tool provides a suitable support for data quality control. As a next step, the software should be refactored and expanded to be tested with real data sets, subsequently preparing it to be released as open source project for the biobanking community.

*Keywords: CEN/TS, IT, Data Validation, Quality Control*

## P-17. Is it the Amount of Tissue or the Quality of Tissue that is Important for Genetic Testing?

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Histopathology of a patient's tumour is heavily reliant on the use of fixed tissue. Fixation methods vary between institutions, and although fixation ensures sample integrity, it also causes substantial chemical modifications to the DNA. During fixation, nucleotides are cross-linked with proteins and DNA is degraded into small fragments, all of which create issues in the isolation of DNA for genetic testing. In addition the use of archived samples can also increase the complications. The Wales Cancer Bank (WCB) sent banked tissue samples for

genetic testing and initial studies yielded high failure rates. In a bid to identify the causes, WCB undertook a project looking for correlations between sample quantities and qualities and the failure rates.

Formalin-fixed paraffin embedded (FFPE) samples were collected from 55 patients diagnosed with prostate cancer. Sections were cut from each block at either 4µm or 10µm thickness and mounted onto glass slides. Sections were macrodissected using a corresponding H&E stained section. DNA was extracted and concentration measured using the QuBit spectrophotometer. DNA quality was assessed and library preparation was carried out using the Qiagen Clinically Relevant Mutations panel and sequenced on an Illumina MiSeq.

Out of the 55 samples sent for DNA analysis, 13 samples (26%) completely failed the sequencing run. Partial failures of some genes were observed in all samples. Two genes, AR and STK11, failed in all samples. Thickness of each sample was recorded along with the area of the tissue section and were used for correlation with the failure rates. The percentage of nuclei present was also recorded and is currently being analysed along with other variables such as quality of DNA. This presentation will detail the results of the correlation project.

Initial findings have suggested that DNA analysis using FFPE prostate tissue is difficult to perform. Correlations between the thickness of the tissue sections, the area of tissue or the concentration of DNA (ng/µl) with sequencing success rates are difficult to ascertain. With the increase in genetic testing for cancers, more work is needed to understand the pre-analytical variables influencing successful sequencing of prostate FFPE samples.

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## P-18. New and Traditional Biomarkers of Liver Cancer Process

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**Background:** Prognosis and overall survival for primary hepatocellular cancer (HCC) and metastatic liver cancer have improved recently. Regarding the primary liver cancer it seems to be important to identify the risk group of patients to be involved in screening programs. Metastatic liver process will require the optimal follow-up proposal in order to make a good decision whether to perform the surgery resection instead of palliative therapy or chemotherapy. Serum biomarkers may help in early diagnostics of cancer and differential diagnosis between benign and malignant processes. Serum alpha-fetoprotein (AFP) has been routinely used as a tumour biomarker for HCC detection and for monitoring the disease course. But it has not





yet become an optimal biomarker for diagnostic purposes. A protein induced by vitamin K absence (PIVKA-II) has been described in relationship with HCC. It is released in association with vitamin K deficiency and in the presence of HCC. The aim of this study was to evaluate the clinical contribution of PIVKA-II for HCC diagnostics and compare it with AFP.

**Methods:** A total of 332 participants were enrolled in this study: 64 with HCC, 48 with liver metastases of colorectal cancer origin, 42 with liver cirrhosis and 178 healthy individuals. Serum levels of PIVKA-II were measured using the chemiluminescent assay of the Architect 1000i System (Abbott, USA) and AFP levels using the chemiluminescent assay by Dxl 800 (Beckman Coulter, USA).

**Results:** Both biomarkers were found at the highest serum levels in the group of patients with HCC and the lowest levels were found in the control group. PIVKA-II achieved better sensitivity than AFP and the difference in this sensitivity was statistically significant. PIVKA-II achieved the best sensitivity (96.9%) in distinguishing between the HCC and control groups with the proposed cut-off value of 60 mAU/ml. The AFP sensitivity varied over the range 34.3-50.0%. AFP achieved the best sensitivity (50.0%) in distinguishing between the HCC group and the group with metastatic colorectal cancer with the proposed cut-off value of 6 IU/ml.

**Conclusions:** PIVKA-II achieved better sensitivity in our study than AFP, traditionally used a marker of HCC. Our recommendation is to add PIVKA-II to the routine panel of HCC tumour markers.

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## P-19. Nightingale experience - Blood sample quality control alongside NMR metabolomics in large biobanks

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**Background:** The importance of a biobank rests on the availability of large number of high-quality samples and associated big data. However, our analyses of more than 500,000 blood samples show that over 10% of blood samples are of poor quality. This result and all other data published on the quality issues of biobank samples suggest that millions of low-quality samples are not only stored in vain, but also compromise the scientific validity of the downstream research. Here, we suggest a way for biobanks to simultaneously increase their QC standards and obtain enriched biomarker data, which is applicable to multiple diseases.

**Methods:** We have developed a high-throughput NMR based

metabolomics platform, which simultaneously measures sample quality and biomarker concentrations. Importantly, the obtained sample quality metrics provide the rationale for compromised quality which in turn enable implementation of adequate process improvements. Moreover, the biomarker platform has been applied to study various conditions ranging from CVD, diabetes and cancer to neurological and kidney diseases. To date the platform has resulted in over 150 publications.

**Results:** Our metabolomics platform is transformational because it enables the combination of biomarker profiling and quality control at the biobank scale - both in terms of throughput and cost. These features are spurring large-scale metabolic biomarker profiling initiatives involving entire biobank collections. As a recent example, our platform was selected as the first biomarker omics assay to profile the entire UK Biobank collection of 500,000 samples.

**Conclusions:** The availability of large-scale profiling tools enables the evolution of biobanks from sample repositories into drivers of clinical translation and personalized medicine.

**Keywords:** Quality control, metabolomics, phenotyping, large-scale, biobanks

## P-20. NMR Based Quality Control in Biobanking

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Quality control is vital for input of specimens into biobanks. There are many parameters, that should be checked before releasing a specimen into the biobank inventory. Categories of high relevance include for example:

- control of sample generation and storage, does it followed agreed standard operation procedures
- identity of the sample to avoid wrong labeling: e.g. EDTA plasma, Citrate Plasma, Serum, Urine
- impurity detection
- agreement between meta-parameters given and the sample provided, e.g. drug intake, food intake

QC-Methods should be comprehensive and easy to use. Nuclear Magnetic Resonance (NMR) qualifies under the criteria given. Being used increasingly as a screening method in Metabolomics, it can deliver targeted analysis and non-targeted analysis in one measurement. Considering the fact, that NMR can handle very different polarity compounds in one analysis renders it a tool to consider for biobanks. NMR spectra generated and the analysis thereof (quantification results) can be stored in the biobank together with the specimen and associated metadata. Based on its high reproducibility spectral data can be compared if produced at different biobanks under identical SOPs, which can support for example clinical trials by reducing the need to collect new specimen. This allows



to reduce cost and time in such trials and clinical research studies. All aspects mentioned will be covered with examples in this contribution.

*Keywords: Biobank QC, NMR, validation, standardization*

## P-21. OPTIMARK project: search for quality markers for paraffin-embedded tissue samples

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**INTRODUCTION:** Quality of tissue samples is a critical factor affecting the reproducibility of biomedical research results and the development of disease biomarkers. The multicentric OPTIMARK project, developed in the context of the Spanish Biobank Network, is focused on trying to find sensitive quality tissue markers, to evaluate pre-analytical factors, to gain a precise knowledge on the real quality of tissue samples, which will contribute to render not only robust scientific analytical results but an accurate biomarker development and analysis. To this end, we are testing a number of biomarkers by immunohistochemistry in paraffin-embedded tissues, trying to correlate the expression level with the time of storage of the samples from the time of collection to the final analytical use.

**MATERIALS AND METHODS:** We first established the criteria to select biomarkers to be tested for antigenicity analysis. The first set of markers was selected among the most used in clinical practice; then we analyzed ki67, vimentin and CD31 in 374 non-tumoral tissues from lung, colon, stomach, breast

and brain. We only found a significant negative correlation between ki67 intensity and the time of storage in specific tissues (colon and stomach).

To try to get a universal quality marker, we focused on biomarkers related to structural proteins and cellular metabolism, present in as many tissues as possible. To allow automatic evaluation, we selected those with a nuclear moderate-intense intensity of staining, to avoid signal saturation.

**RESULTS AND CONCLUSIONS:** According to the mentioned criteria, we selected MSH2, MSH6 (DNA repair pathway) and Lamina (nuclear membrane) for further testing. Although the expression was ubiquitous, the expression of lamina did not show a correlation with the time of storage in the tissues analyzed.

Preliminary results suggest that MSH2 and MSH6 showed association among the loss of antigenicity and sample age, so they could potentially be used as quality biomarkers for long-term storage samples.

We also built a small number of tissue microarrays including a representative number of the analyzed tissues to easily test new biomarkers in relation with the time of storage. In conclusion, although we have found quality markers for specific tissues (ki67 for colon or stomach non-tumoral tissue) it is necessary to carefully establish the selection criteria to find a universal quality marker for tissue samples.

*Keywords: Biospecimen research, FFPE, quality, biomarkers, antigenicity*

## P-22. Optimization of DNA Extraction for Zoonotic Fish Parasites: Preparing the Barcoding for the Seafood Safety Challenge

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**Background:** The Fish PARASITE Biobank (FPB) was constructed on 2013 as a traceable high-quality sampling platform for the largest surveillance plan ever conducted in EU fish production value chains. The Biobank collects and records fish zoonotic parasite samples and their associated information. Since 2016, the FPB is certified with the quality management system standard ISO 9001. One distinguishable promising future challenge for the FPB is to provide high-quality genomic DNA (gDNA) stored under strict conditions of traceability. The different species of zoonotic fish parasites must be identified by molecular methods, therefore, gDNA included in the Biobank can be suitable for the development of DNA barcodes, DNA-signature sequences that will allow an accurate identification of these pathogens. Nowadays, few barcoding studies are available about zoonotic marine fish parasites. Here, we establish a suitable procedure to obtain high-quality DNA of zoonotic parasites and review the barcode sequences disposable in public databases for them.



**Methods:** Anisakis specimens were recovered from fresh and frozen hakes by visual inspection and artificial peptic digestion, as well from hakes processed by UV Press Method. gDNA of ten parasites of each condition were obtained used three commercial kits. The gDNA quantity, purity, integrity and functionality were also evaluated. BOLD and GenBank database were searched to find all the sequences anisakid parasites disposable.

**Results:** The best results of gDNA quantity, purity, integrity and functionality were obtained with Wizard Genomic DNA Kit, whereas lower DNA concentration and integrity were obtained with NucleoBond and QIAamp DNA Micro Kits. Differences in quantity and quality of DNA of the nematodes obtained from hakes of different conditions were observed. The sequences disposable in public databases means that the DNA barcodes are poorly developed for anisakid parasites. For nematode species, there are deposited 46,508 nucleotide sequences in the GenBank, of them only 379 (0.81%) are barcode sequences. In the BOLD platform, the available records are even lower, with only 92 sequences of the COI gene.

**Conclusions:** The optimization of DNA extraction will provide the FPB of high-quality gDNA of zoonotic parasites. It will help to construct new reliable barcode sequences for their specific and sensitive identification in isolated parasite forms, in processed seafood matrices or to perform epidemiological studies.

*Keywords: zoonotic parasites, barcodes, biobank, high quality data*

## P-23. Optimizing Deparaffinization Process From FFPE Tissue : Employ a Commercial Solution or Xylene Protocol ?

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**Background:** The deparaffinization process is the first step in extractions from formalin-fixed paraffinembedded (FFPE) tissue that many times can affect the nucleic acids quality. However, it is quite necessary to optimize this process. In this study we evaluate the quality and yield of RNA in FFPE tissues using two different deparaffinization process in an automatic extration platform.

**Methods:** FFPE blocks made in 2015(n=16,12 tissue-types) were sectioned (10µm). In both procotolos were used 2

and 5 sections each samples. In xylene protocol the samples were placed in 1,5-ml tubes whit 1 ml xylene then ethanol washes were performed. In the other protocol was used only the commercial solution called deparaffinization solution. After to the deparaffinization process, all samples were treated with proteinase k then extracted using an automatic platform. The quality and yield were performed used an spectrophotometer.

**Results:** We show that commercial solution provides best results because had an good yield and quality using 2 or 5 sections moreover is not necessary to use a toxic reagent. In the xylene 50% of the samples using 5 sections had a good quality and no one samples using 2 sections had good quality. Therefore, this novel method can be a good solution to obtain RNA from biopsies tissues that have limited material to RNA extraction. However, commercial method have a higher cost when comparing with xylene protocol.

**Conclusions:** In conclusion was possible to identify that commercial protocol associating with automatic nucleic acid

extraction wokstation seems to be a best strategy to desparaffinization from FFPE tissue in RNA extraction and may be applied in a routine of biobanks because provides best results using few sections of FFPE tissues.

## P-24. Performance Comparison between Micro Electro Mechanical Systems Tracking Tags and Other Labelling Strategies for Cryotubes

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Reliable and efficient methods of identification can be extremely useful for ensuring the quality of samples, maintaining integrity of procedures and improving productivity in biobanking. There are many methods of identification available for use in cryopreservation procedures (handwritten markings, human readable printed labels, barcoded label, RFID tags, and Micro Electro Mechanical Systems (MEMS) tracking tags). The MEMS tracking tag is a mechanical device based on mechanically resonating micro-structures used to encode an identification number and measure temperature at the individual sample level.

The objective of the present study is to compare the performance of MEMS chips-based method for identifying cryotubes with the currently printed label method used in the biobank as well as some other methods during day-to-day process and other low temperature storage conditions.

Four different labelling methods were compared: handwritten markings, human readable printed labels, barcoded printed labels and MEMS tracking tags. The performance of each method was compared using 3 tests: i) sample registration: compared the time spent in registration process of 10 aliquots (3 replicates each method); ii) identification of heavily frozen tubes: compared time to read 10 aliquot labels covered by a thick ice layer (3 replicates each); iii) ultra-low and cryogenic temperature storage sample identification: reading 5 aliquots at two different extremely low (-80°C and -196°C) temperatures (3 replicates each). The MEMS chip vials were sterilised



using three different methods: steam at 132°C (5 vials), steam at 134°C (5 vials) and H<sub>2</sub>O<sub>2</sub> (300 vials).

All MEMS-enabled vials operated successfully after each sterilisation procedure. The less time-consuming method to tag vials was the MEMS based one (96 vials/h.) followed by barcoded labels (57 vials/h.), handwritten markings (53 vials/h.) and human readable printed labels (51 vials/h.). Regarding to manual reading time of heavy frozen vials, MEMS based method also slightly outperformed the rest of the methods (3.5 s. per vial vs. 5.0 s., 4.5 s. and 5.0 s. respectively). The MEMS tracking tag acquired a positive read at the two ultra-low reading scenarios (-80°C and -196°C).

The use of MEMS tracking tags can reduce our biobank labeling time from 55 to 33 minutes (40%) per donation event. MEMS tracking tagged vials can be sterilized using at least two of the more common used methods, H<sub>2</sub>O<sub>2</sub> and autoclave.

*Keywords: cryotubes, labelling, micro, electro mechanical systems MEMs, tracking, tag*

## P-25. Quality Control in Cryopreserved Samples Applied in Exome Analysis

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Background: The Biobank from Barretos Cancer Hospital have around 200.000 frozen samples

collected from 38.000 patients of several cancer types. To molecular downstream analysis the quality of the samples is crucial. The aim of this study is to determine the percentage of samples that are excluded by low quality to be applied in exome analysis.

Methods: We analyze the quality of 586 paired tumor tissue and matched buffy coat samples from esophagus, colorectal, lung and breast cancer. Initially, the tissue samples were macrodissected and the tumor percentage was determine by the pathologist considering at least 60% of tumor and to 20 % of necrosis. After to the macrodissection, the tumor and blood DNA was extracted using an automatic platform. The buffy coat samples were extracted using a comercial kit. To determine the quality and yield from DNA was used a spectrophotometer and a fluorimeter methods respectively. Finally, the STR (Short Tandem Repeat) analysis of each pair was made to determine the percentage of match considering tumor tissue and blood from the same patient.

Results: A total of 338 pairs of tissue and blood were qualified for analysis of whole-exome sequencing. A total of 248 pairs from samples (tissue and blood) (42%),

because 143 (57%) samples tumor presented macrodissection due to the low percentage of tumor or hight necrosis percentage, arround 102 (41%) cases were excluded due to

low quality of DNA and only 3 (2%) cases were excluded in the analysis of STR.

Conclusion: Our results showed that is necessary to improve the strategy for tissue tumor that are collected to biobank considering a macrodissection before cryopreservation ensuring a maximal of tumor tissue area avoid high costs and loss of samples that can be used to genomic downstream analisys.

## P-26. Spectral fingerprinting of biobanked fish-borne parasites

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Background: Marine parasites are an important health and quality threat in fishery products. There are a growing number of fish-borne parasitic infections and hypersensitivity reactions following intake of viable parasites. Anisakidae (Anisakis, Pseudoterranova and Contracaecum) are by far the most prevalent macroparasites in fish products worldwide and causes human parasitic infections commonly associated to this consumption.

In 2013, the Fish Parasite Biobank (FPB) developed within the EU-granted PARASITE Project collected fish zoonotic parasite samples and recorded their associated data, to accomplish with the Data Collection, Management and Sharing EU-strategy. As proof of concept of the many uses of biobanked samples we checked different responses of these parasites to variable exciting lights, to explore a non-destructive spectral technology of detecting nematodes in fish.

Methods: Nematodes from different fish species caught in European waters were identified microscopically at genus level and biobancarized. Anisakidae (Anisakis, Pseudoterranova and Contracaecum) and Raphidascaridae (Hysterothylacium) were selected and divided in two fragments: one half for spectral analysis, and the other for molecular identification. Spectral analysis was carried out with a confocal microscope in a double-step: firstly, exciting the sample with a UV laser at 364nm and analyzing the fluorescence emission from 405nm until 600nm; then, we used the 488nm laser for exciting and recovering the fluorescence signal from 500nm until 700nm.

Results and Conclusions: Exciting the samples with the UV laser we found that for all the specimens, fluorescence was no homogenous along the body. When the spectrums were analyzed, we found that Hysterothylacium aduncum have a different emission profile to those from Anisakidae, in agreement with the fact of being from a different family. Anisakis and Contracaecum had an intense and similar emission profile. Pseudoterranova had lower fluorescence emission that the other Anisakidae, although a similar profile. With regards to the differences between species, tested with Anisakis simplex and Anisakis pegreffii, they were not detected.





In several samples a peak in the emission signal was detected between 500-550nm. As the UV light use have a number of limitations for its use at industries (such as cost and security), the possibility of detection of differences in this range of the visible spectrum could be of interest

*Keywords: fish borne parasites, Anisakidae, Raphidascaridae, confocal microscopy*

## P-27. Strengthening Quality Metrics for Human Biospecimens Through the Use of Data Science: A Case Study

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Background: Quality of biospecimens is essential to the success of any biorepository. However, equally important is a robust IT system that can support the Quality Management activities of the biorepository. Categorizing the key performance metrics for quality control within the system are necessary to the identifying the data elements that will be key to tracking and reporting the biospecimen quality. The Cooperative Human Tissue Network Eastern Division (CHTNED), a National Cancer Institute (NCI [USA]) supported program, compiled and reviewed 20-plus years of data that evolved through multiple legacy data systems to set benchmarks for the quality standards of their biosamples. Using the data-science concepts set forth by Mason and Wiggins (2010) of Obtaining, Scrubbing, Exploring, Modeling and iNterpreting data (OSEMN), the CHTN-ED was able to construct multiple views of their data as part of a quality audit. As noted in the ISBER Best Practices (4th ed), data quality audits are a requirement of a Quality Management System.

Methods: The five steps of OSEMN data science are:

1. Obtaining the Data: CHTNED developed and maintains its own databases and data management applications. All data within these datasources is within the sole domain of CHTNED. Review of 20+ years of data, identified the selected data elements to be incorporated into the QC metrics.
2. Scrub: Evaluated data within multiple datasources to minimize irreconcilable data that could not be migrated into current practices.
3. Explore: Analyzed data to determine a benchmark of QC standards (Technician accuracy; % of tumor; necrosis, etc.)
4. Model: Creation of reports/views that allow technicians at various collection sites to monitor performance against expectations
5. Interpret: Real time audits of performance metrics and underlying factors (annotated data elements) allows prompt responses to modify procedures or techniques as necessary and address deficiencies with retraining.

Results and Conclusion: Data audits, while necessary to ensure accuracy of the data sources, can be equally important to the establishment of Standard Operating Procedures and support the overall Quality Management system of an operation. A biorepository that has the ability to view data in myriad ways can bolster the ability to support the physical biospecimens' quality through accurate data annotation.

*Keywords: Quality Management, Data Audit, OSEMN Data Science*

## P-28. Testing the quality and stability of plasma protein and whole blood RNA in archived loggerhead sea turtle blood, *Caretta caretta*

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Sample storage conditions can affect the accuracy and reproducibility of biological measurements. Storing samples at lowest available temperatures as fast as possible is considered ideal, but not always feasible during remote or logistically challenging field sampling events. Sampling sea turtles during in-water studies poses logistical challenges at sea in frequently rough and limiting conditions. Here, we examined the quality and stability of plasma proteins and of whole blood RNA from loggerhead sea turtle blood collected as part of an eighteen-year-long curated specimen collection at NIST in Charleston, South Carolina. These variables are often used to assess sea turtle health; therefore, it is necessary to maintain the integrity of these components during storage. Protein electrophoresis was conducted on plasma from individual turtles collected in 2018 (n = 3), 2008 (n = 3), and 2001 (n = 3). Plasma was also pooled from four turtles and subjected to various temperatures. Whole blood was collected in blood collection tubes containing sodium heparin or PAXgene tubes with an RNA preservative. These were subjected to different storage treatments that can likely occur during logistically difficult field sampling. Following the various treatments, plasma proteins showed minor differences among collection years, and no differences among storage treatments even when exposed to 38 °C for three h. RNA quality was preliminarily assessed from whole blood using an RNA Integrity Number (RIN). Whole blood collected in sodium heparin tubes and frozen and from PAXgene tubes after extended thaw resulted in poor quality samples with low RINs. High quality RNA was obtained from a sodium heparin tube that was never frozen (RNA isolated within 48 h) and from PAXgene tubes even when freezing was delayed by up to 264 h. Overall, these results indicate that plasma proteins remain stable over time when exposed to undesirable storage conditions, and RNA degrades rapidly in sea turtle samples after freezing. These aspects are important





to consider when planning logistics and optimal sample preservation ahead of sampling and long-term storage.

*Keywords: plasma electrophoresis, RNA quality, biorepository, marine turtle, reptile; pre-analytical variables*

## P-29. The Effect of Pre-analytical Conditions on Blood Metabolomics in Epidemiological Studies

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Background: Serum and plasma are commonly used biofluids for large-scale metabolomic-epidemiology studies. However, their metabolomic profile is susceptible to changes due to variability in pre-analytical conditions and the impact of this is unclear.

Methods: Matched EDTA-plasma and serum samples were collected from 37 non-fasting volunteers and profiled using a high-throughput targeted nuclear magnetic resonance (NMR) metabolomics platform (N=151 metabolic traits). Metabolic concentrations were compared between reference and four (pre-storage) blood processing conditions, where samples were incubated at (i) 4°C for 24h; (ii) 4°C for 48h; (iii) 21°C for 24h; (iv) 21°C for 48h; and two (post-storage) sample processing, for NMR analysis, conditions in which samples (i) thawed overnight, then left for 24h before addition of sodium buffer followed by immediate NMR analysis; (ii) thawed overnight, addition of sodium buffer, then left for 24h before profiling. Univariate and multivariate methods were used to assess the impact of these six pre-analytical conditions on EDTA-plasma/serum metabolome.

Results: Fatty acids, beta-hydroxybutyrate, glycoprotein-acyls and most lipids and lipoproteins, in serum and plasma, are robust to the tested pre and post-storage conditions. Pre-storage sample processing conditions impacted most glycolysis metabolites, acetate, albumin and amino-acids concentrations by levels that could importantly bias research results (up to 1.2SD difference). Post-storage conditions affected histidine, phenylalanine and LDL-particle-size, with changes up to 1.2SD from reference.

Conclusions: Most metabolic traits are stable to the pre- and post-storage conditions tested and which might commonly occur in large-scale cohorts. However, results for glycolysis metabolites, and amino-acids may be compromised.

*Keywords: metabolomics, serum, plasma, NMR, lipids, metabolites, pre-analytical phase*

## P-30. The influence of long-term cryopreservation on human peripheral blood cells

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Collection, processing and preservation of human peripheral blood cells (PBMCs) gain more and more importance in supporting clinical and basic research. However, unlike other biospecimens (e.g. DNA or serum) little is known about PBMCs. Certain aspects of processing, freezing, storage and transport have been studied over the past years. We investigate the influence of long-term storage at -190 °C on the vitality of PBMCs. As part of the Competence Network Multiple Sclerosis (KKNMS), blood of more than 400 Patients has been collected and processed in 6 centers. A comparative cohort of 100 healthy subjects has been collected and processed in 1 center. Those samples have been thawed and investigated after different time points. These time points vary from several months to 8 years. Our first results show very stable sample quality, even after 8 years of storage.

*Keywords: biobanking, long-term storage, cryopreservation, vitality, viability, PBMC*

## P-31. Validation of processing methods for an extraordinary specimen type: FFPE bone.

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Formalin Fixed Paraffin Embedded (FFPE) tissue blocks enable prolonged storage of clinical samples including tumour biopsies and surgical material, preserving tissue morphology for pathological examination and nucleic acids for molecular analysis. If a bone or bone marrow disease is being investigated, it is necessary to have access to a good quality FFPE bone material and, therefore, it is crucial to have established and optimised a processing protocol for bone samples. As mineralized bone is such a hard material, there are a limited range of techniques available to produce sections from it. Bone samples require not only standard formalin fixation, but also a specific decalcification procedure before preparation of the FFPE blocks. All these processing steps are potential source of pre-analytical variables, which may affect the quality and quantity of extracted nucleic acids.

We performed a formal method validation of two decalcification protocols applying different times (4 hours or 18 hours) and temperature (37°C or 50°C) using pig bone (*Sus scrofa domestica*) and a commercial instrument BoneStation (Milestone Srl.), in order to see which method fulfilled pre-defined acceptance criteria relative to yield and quality of

the extracted DNA and RNA. Molecular extraction efficiency was evaluated by both quantitative (total and dsDNA, RNA yields) and qualitative (DIN, RIN, DV200, whole genome amplification) methods, as well as H&E staining of FFPE bone tissue sections. Validation parameters included method reproducibility and robustness. The optimal settings of the processing method in terms of nucleic acid yield were 4 hours and 50°C temperature of decalcification. However, relatively lower yields with decalcification at 37°C for 18 hours can be partly attributed to variable cellularity of individual samples.

Overall, the validation work demonstrated that RNA and DNA can be recovered from bone FFPE tissue in sufficient quantity and quality. The results also demonstrated the most critical factors to be considered (decalcification time and temperature). As a result, we established and validated an optimised short decalcification protocol which can be implemented in a standard operating procedure for processing of bone and bone marrow samples.

### P-32. Virus Screening Test of Biosamples (Cell Line, Tissue, and DNA).

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Japanese Collection of Research Bioresources (JCRB) Cell Bank was established in 1985, which are collected mainly human cell lines. The cells are qualified by testing for microbial contamination, virus contamination, and cross culture contamination, and also confirming their karyotype and cell characteristics. And then the qualified cells are provided to researchers around the world (more than 4500 vials/year). Bacterial contamination is visually found in cell cultures through a conventional light microscope, and can be prevented using antibiotics. However, virus detection requires molecular analysis, and, once cells have become infected with a virus, they cannot be easily removed from the cells. Datasets from virus examination in cell lines contribute to the safe management of cell culture and characterization of cell lines. We have screened for 15 viruses in 844 human cell lines registered with the Japanese Collection of Research Bioresources (JCRB) Cell Bank and have detected 6 different viruses in 42 cell lines. By utilizing the know-how cultivated in the cell bank business, in addition to it, we are screening of human tissue (or tissue derived materials) and DNA of rare disease patient. These research resources are those that cannot be essential to the development of drug discovery and medical treatment, has been implementing projects in response to the support for Japan's Ministry of Health, Labor and Welfare.

### P-33. New Developments in Nucleic Acid Sample Quality Control

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Quality control (QC) of RNA and DNA samples is key for the success of any downstream experiment. Especially, Next Generation Sequencing (NGS) developed to a powerful tool in almost all genetic research and diagnostic areas. Since the downstream applications are often time-consuming and expensive, tight QC steps are required to avoid a "garbage in-garbage out" situation.

The ideal QC solution is easy-to-use, economical and provides fast and unambiguous results also for very low concentrated samples. Nucleic acid quality assessment can be standardized using automated electrophoresis systems to ensure that samples are "fit for purpose".

Quality scores enable impartial sample comparison and allow defining a quality threshold for specific types of samples or preparation. The DNA Integrity Number (DIN) was established for genomic DNA (gDNA). It represents gDNA integrity by assigning a numerical score from 1 to 10. The RNA integrity number equivalent (RINe) delivers an objective assessment of RNA degradation for eukaryotic or prokaryotic samples. Many tailored FFPE library protocols use an additional 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 across a wide quality range for nucleic acid samples originating from blood, fresh frozen tissue and FFPE material.

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