B/D-HPP Newsletter

Biology/Disease- Human Proteome Project Newsletter | Issue 1, 2017

In This Issue

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HUPO 2016 in review

A huge thank you and congratulations to the Taipei organizing committee for HUPO 2016 and the HPP Workshop at Sun Moon Lake. The achievements of B/D-HPP initiatives were highlighted through the 6 joint B/D-HPP sessions and the pre-conference workshop. Several B/D-HPP initiatives have developed popular protein lists to facilitate research in biology/disease research. The post-conference workshop afforded additional opportunity for focused strategic planning in relaxed surroundings.

Two new features have been introduced to increase information flow. "Upcoming B/D-HPP workshops" and "B/D-HPP Hot Papers" which will highlight recent B/D initiative papers published in non-proteomics journals. Calls and submissions for these news items will be made via HUPO Secretariat.

Upcoming B/D-HPP Workshops

Mitochondria-HPP
16-17 Feb 2017, Como Italy

HPP Workshop @ US HUPO
20 March 2017, San Diego USA

Cardiovascular Initiative
1 April 2017, Potsdam Germany

Proteomics Standards Initiative
24-26 April 2017, Beijing China

Immuno-peptidome-HPP
4-5 May 2017, Zurich Switzerland

Brain-HPP
9-10 May 2017, Bochum Germany

Food and Nutrition HPP
12 June 2017, Lecce Italy

B/D-HPP HOT PAPERS

J Liepe et al. (2016). A large fraction of HLA class I ligands are proteasome-generated spliced peptides. ***Science*** 354, 354-358
Using advanced proteomics, the **Human Immuno-Peptidome Project (HIPP) team** found that a large fraction of peptides bound to class I MHC on multiple human cell types are spliced together by the proteasome from two different fragments of the same protein. Such merged peptides might turn out to be useful in vaccine or cancer immunotherapy development.

X Zhang et al. (2016) MetaPro-IQ: a universal metaproteomic approach to studying human and mouse gut microbiota. ***Microbiome*** 4(1):31
Food and Nutrition (FaN) initative investigators report a novel workflow for gut metaproteome identification and quantification. The approach uses the close-to-complete human or mouse gut microbial gene catalog as database and an iterative database search strategy.

B/D-HPP Newsletter

2

Biology/Disease- Human Proteome Project Newsletter | **Issue 1, 2017**

Growing HUPO through Early Career Researchers …..

Burcu Ayoglu, Ferdinando Cerciello and Justyna Fert-Bober (ECR Executive Committee)

Launched at HUPO 2015 in Vancouver under the auspices of the B/D-HPP EC, the Early Career Researcher (ECR) Initiative aims to provide a solid link between generations of proteomics scientists to be inspirational for the career of young researchers along the HUPO ideals of translating the code of life. The ECR Mentoring Day and the yearly ECR Manuscript Competition taking place at the international HUPO meetings are examples on how the ECR Initiative is concretizing these goals.

The missions of the ECR initiative are:

1. To foster awareness of the HUPO ideals among young researchers,
2. To identify the needs and create opportunities for the career development of young proteomics and allied omic researchers,
3. To provide platforms for continuous interactions between generations of proteomics researchers.

ECR Mentoring Day 2016

The 2016 ECR Mentoring Day involved approximately 25 participants, including mentors from academia and industry. Organized under the mentorship of *Jennifer Van Eyk* (Cedars-Sinai), the day consisted of morning lectures and afternoon roundtable workshop. The lecture topics addressed fundamental challenges which are typical for an ECR, and we asked the mentors to base the lectures on their personal experiences in order to transmit concrete advices to the ECRs.

Ruedi Aebersold (ETH Zurich) and *Paola Roncada* (Istituto Spallanzani) presented their personal experiences on "**How to start my lab**" and gave important suggestions about the first steps and the long-term strategy for career planning. They highlighted the importance of defining your research direction and your vision early on, avoiding shortcuts, and perceiving your lab as your "team".

David Herrington (Wake Forest School of Medicine) conducted us through the "race" of "**How do I write a fundable grant proposal**", presenting the process of writing a research grant in analogy to Formula One race, noticing how "sometimes drivers work 15 hours a day at the race track and then spend their nights thinking how to do it even better...whoever has already written grant proposals know exactly this feeling!".

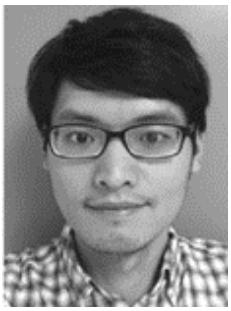
Christine Hunter (SCIEX), *Michael MacCoss* University of Washington), *Ken Miller* (Thermo Fisher Scientific) and *John Yates III* (Scripps) led a roundtable on "**Building a long term relationship between academia and industry**", highlighting strategies for ECRs to develop mutually beneficial and effective industry partnerships.

The workshop session in the afternoon started with an introduction by *Dr Justyna Fert-Bober* (Cedars-Sinai) from the ECR team on how to prepare an **elevator pitch**. All participants practiced their personal elevator speeches in smaller groups and then received feedback from the audience! The afternoon continued with a **brainstorming round-table session about conflict resolution in the lab of an early-career PI**. For that, we had prepared different case scenarios and the audience was distributed in different groups around round-tables, where mentees and mentors were mixed. To give examples, one scenario was about an early-career PI, who was part of a collaborative project where one of the co-authors was refusing to share his/her data for publication. Another scenario was about an early-career PI who was confronted with tension among two of his/her students disturbing the dynamics within his/her entire group.

Mentees and mentors worked together in teams to create solution strategies to such case scenarios and then each team presented their strategy to the audience, which led to exciting discussions. These conflict resolution exercises highlighted that young PI's should realize early on that they have a leadership responsibility, they should foster open and clear communication among the members of their lab and they should try to address problems early on and consider receiving help e.g. from more experienced and independent authorities like senior faculty. At the end of the Mentoring Day, we felt that the day was a truly valuable and interactive learning experience with a positive influence on various aspects of our research careers.

ECR Manuscript Competition

Initiated at HUPO 2015, the ECR Manuscript Competition serves as a platform to highlight the research excellence and important contributions of junior researchers. In 2016, we received a total of eleven high quality manuscripts from ECRs affiliated to institutions across the world: Australia, Brazil, Canada, China, Denmark, Ireland, Switzerland, Taiwan and USA. After having redacted all author and institution information, the manuscripts were randomly assigned among five proteomics experts for scoring. Authors of the top three manuscripts were invited to give oral presentations in a dedicated session at HUPO 2016, where a jury including senior proteomics leaders selected a winner. We would like to use this opportunity to briefly introduce the three finalists.



ECR Manuscript Winner
Dr Cheng-Kang Chiang
(University of Ottawa, Canada)
"*Altered intestinal microbiota-host mitochondria crosstalk in new onset Crohn's disease*"
Cheng-Kang obtained his PhD from National Taiwan University under the supervision of Dr Huan-Tsung Chang and is currently pursuing postdoctoral training with Prof Daniel Figeys. His current research interests include using quantitative mass spectrometry to understand the cellular mechanisms of the circadian clock underlying environmental factors in metabolic processes, as well as deciphering key regulators between gut microbiota and host proteome at the mucosa-luminal interface of new-onset pediatric IBD patients.

B/D-HPP Newsletter

4

Biology/Disease- Human Proteome Project Newsletter | **Issue 1, 2017**

ECR Manuscript Runner-Up
Dr Stefan Kempf
(University of Southern Denmark) "*Chronic low-dose rate ionising radiation affects the hippocampal phosphor-proteome in an ApoE-/- Alzheimer mouse model*"
Stefan is a biologist working on Alzheimer´s disease in Prof Martin Larsen's group. He is particularly interested in post-translational modification profiles that are associated with synaptic plasticity triggered by Alzheimer´s disease mutations, but also via exogenous stimuli, such as ionising radiation.

ECR Manuscript Runner-Up
Dr Hannes Röst
(Stanford University & ETH Zurich) "*Reproducible protein quantification with TRIC: An automated alignment strategy for comprehensive data matrices in targeted proteomics*"
Hannes' is a bioinformatician focused on high-throughput systems technologies. He wrote the first software for targeted analysis of SWATH-MS data during his PhD under Prof Ruedi Aebersold. Hannes is now applying his knowledge to personalized medicine with Prof Mike Snyder.

All three finalists received monetary prizes generously sponsored by HUPO and B/D-HPP. They opined that the ECR Manuscript Competition is an excellent platform to increase the recognition and visibility for ECRs across a wider community. As one of our finalists put it: "Opportunities to get awards are rare and we should continue this (competition)." The ECR Initiative will continue its various efforts in promoting the visibility of ECRs within the proteomics community and facilitate exchange between senior and young proteomics researchers to realize the HUPO ideals of translating the code of life.

Success Story – Cancer Moonshot at HUPO

A real success story of international collaboration through HUPO was the launch of the International Cancer Proteogenome Consortium (ICPC) during the 2016 HUPO Congress in Taipei.

This exciting development was grounded on ongoing collaboration between the Cancer Initiative of the B/D-HPP and the Clinical Proteomic Tumor Analysis Consortium (CPTAC) of The United States National Cancer Institute (NCI), and nurtured through years of work at HUPO Congresses. Following the first announcement in Australia in July 2016, an additional 7 countries now joins the initiative to form the International Cancer Proteogenome Consortium (ICPC). This is a real success story of international collaboration catalyzed by HUPO. Two of the leaders tell of the story.

Some of the ICPC representatives at HUPO 2016 in Taipei. From left: Daehee Hwang (South Korea), Ruedi Aebersold (Switzerland), Christoph Borchers (Canada), Henry Rodriguez (USA), Albert Sickmann (Germany), Mark Baker (Australia), Chia-Jung Yu, Yu-Ju Chen, Min Daw Tsai, Chen-Yang Shen (Taiwan).

B/D-HPP Newsletter

5

Biology/Disease- Human Proteome Project Newsletter | **Issue 1, 2017**

The NCI journey from TCGA, CPTAC to ICPC ……..

Henry Rodriguez

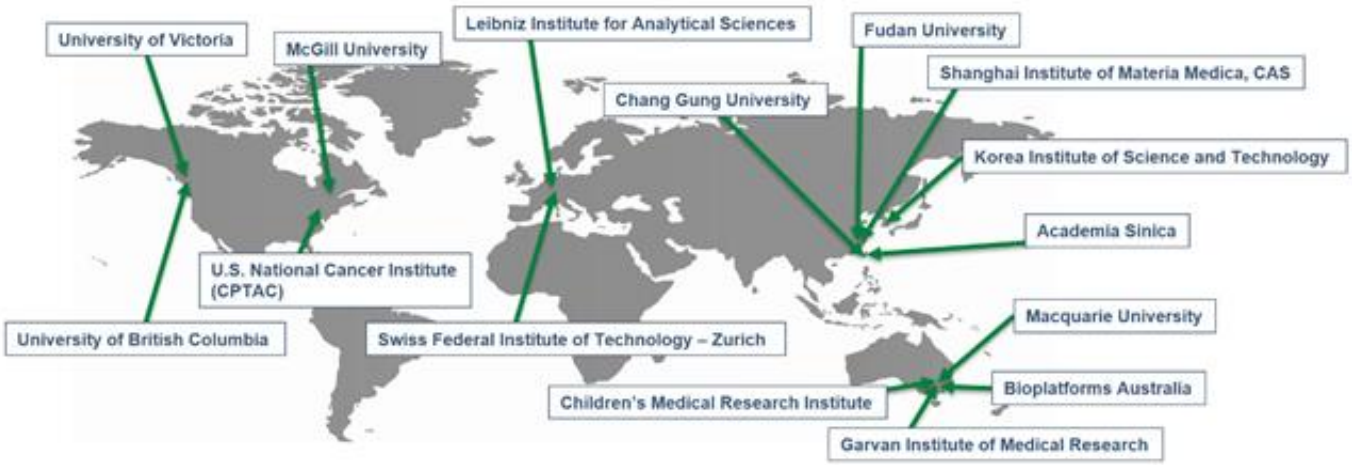
The United States National Cancer Institute (NCI) leadership recognizes the tremendous opportunity to transform cancer research and the central role that advanced technologies will play in the successful translation to the cancer patient. To this end, NCI launched clinical omic-based flagships in clinical molecular biology towards understanding the molecular basis of cancer, notably The Cancer Genome Atlas (TCGA) initiative followed by The Clinical Proteomic Tumor Analysis Consortium (**CPTAC**).

CPTAC began in 2006, seeking to build an integrated foundation of standardized technologies and community resources to advance the application of proteomics in basic and clinical cancer research.

Program highlights include the standardization of mass spectrometry (MS) for untargeted protein analyses; standardization of multiple reaction monitoring (MRM) MS in targeted protein analyses; adoption of a thyroglobulin MRM assay by clinical reference labs; development of an open-source computational tool Skyline; development of mock 510(k) device clearance documents for approval of multiplexed protein-based *In Vitro* Diagnostics (IVD) assays/platforms in a clinical setting, in coordination with the U.S. Food and Drug Administration (FDA) and the American Association for Clinical Chemistry (AACC); and development of Open Data sharing policies (Amsterdam Principles) in proteomics. CPTAC's public resources include Data Portal, Assay Portal, and Antibody Portal.

The second phase of CPTAC initiated in 2011 aimed to apply CPTAC's standardized proteomic workflows to three genomically-characterized tumors from the TCGA. By integrating proteomics and genomics, the CPTAC was successful in producing a more unified understanding of cancer biology and possibly therapeutic interventions for patients, as reported in recent publications for colorectal cancer, breast cancer, ovarian cancer. CPTAC was unanimously reissued in 2016, to include additional cancer types, and to elucidate biological mechanisms in support of NCI-sponsored clinical trials (a first for the NCI).

CPTAC paved the way for the White House International Cooperation and Investments as part of the Cancer Moonshot announced on 21 September 2016 by Vice President Joe Biden, which followed the Memorandum of Understanding (MOU) the Vice President announced on 17 July 2016 in Australia. These MOUs represent an unprecedented international collaboration in medical research.



International Cancer Proteogenome Consortium Partners

By aligning efforts through these MOUs, multiple institutions and nations will establish a new collaboration (International Cancer Proteogenome Consortium - ICPC) to facilitate the sharing of cancer-associated clinical and molecular data (DNA, RNA, and proteins), targeted tests, medical imaging through NCI's Genomic Data Commons, NCI's CPTAC Data Portal, and NCI's Cancer Imaging Archive.

The ultimate goal of reducing cancer mortality will be achieved through public dissemination of products and data for use by cancer researchers and physicians around the world. To ensure harmonization within the partnership, regular consultation and discussions will be organized, with the first meeting to occur during the US HUPO Conference in San Diego, March 2017.

Moonshot Down Under Paves the Way .....

An interview with Mark Baker

Hill: How did you come to set up the Cancer Moonshot Australia?
Baker: I had been working with Henry Rodriguez during previous HUPO Congresses on how Australian cancer research could partner with the NCI. A mechanism of implementation crystallized during HUPO 2014 in Madrid, with the maturation and planned expansion of the CTPAC. The White House Moonshot initiative announcement in April 2016, the Vice President Biden's visit to Australia coinciding with the opening of the Victorian Comprehensive Cancer Centre (VCCC) in Melbourne with similar mandates (to double the rate of translation of proteogenomics), provided an opportunity to officially launch the collaboration.

Hill: Who are the major partners of the Australian Moonshot?
Baker: As a start, I approached two cancer-focused research institutions in Sydney with complementary strengths in genomics and proteomics, respectively. Garvan Institute of Medical Research has strong next-generation sequencing platforms with established genomics research in rare cancers. The Children's Medical Research Institute had committed to profile 6000 proteomes of cancer tissues through the ProCan Project funded by Australian Cancer Research Foundation. The independent body Bioplatforms Australia was recruited to manage data streams, co-ordinate transparency and governance. My own institution, Macquarie University, is involved in the development of blood biomarkers for early detection, predicting response to therapy. It is an open group and we welcome additional partners. Funding support was also committed by the New South Wales state government.

Hill: What were the main challenges in organising such a consortium?
Baker: The biggest difficulty is that the researchers have different objectives for their research, diverse clinical goals and technical challenges. Funding the collaborative was another challenge. Australia was in the middle of a election mid-2016, with no governing body to approach. We were thankful the New South Wales state government committed $6 million seed funding to assist integration of tissue proteomics and genomics data.

Hill: What are the immediate and longer term future plans for expansion?
Baker: Recruiting high quality proteomics researchers, increasing technical exchange (MRM, immuno-MRM and SWATH-MS). We are in the planning stage for a symposium. Globally, we would like to increase the link with HUPO and HPP, to grow Cancer-HPP initiative and translational cancer research.

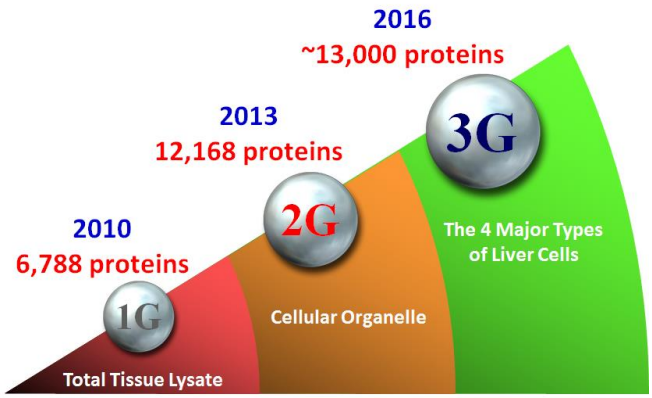
B/D-HPP Newsletter

7

Biology/Disease- Human Proteome Project Newsletter | **Issue 1, 2017**

Spotlight on - Liver Human Proteome Project

The liver is a central organ of human body that controls metabolic homeostasis, and detoxifies xenobiotics. In addition to its biological function, liver physiology is peculiar in different aspects, including its regeneration capacity. Despite the intense research over several decades, there are still many open questions in regards to the molecular mechanisms underlying liver function and, most importantly, liver disease. This constraint largely restricts the development of more effective diagnostic and therapeutic strategies. The Human Liver Proteome Project (**HLPP**) Initiative began in 2001 as a large-scale international collaborative aiming to define a comprehensive and dynamic human liver proteome.



HLPP Co-chairs Fernando Corrales and Pumin Zhang meeting in Beijing after HUPO 2016

Chaired by **Fernando Corrales** (Spain) and **Pumin Zhang** (China), the group has had regular workshops at HUPO congresses, and have steadily increased the proteomic coverage over the past 15 years.

The current goals of the L-HPP are:

- To define the liver proteome by characterization of all specific liver cell types and their interaction in health and disease.
- To define priority protein lists relevant in liver physiology and liver disorders.
- To develop targeted standardized methods for the quantification of clinically relevant proteins.
- To identify novel proteins relevant in liver biology and pathology by means of proteogenomics.

Spotlight on Mitochondria Human Proteome Project

The mitochondria human proteome project (mt-HPP) began in 2012, and has been chaired by **Mauro Fasano** (Italy, picture right). Currently more than 50 members contribute to the mt-HPP. The main goal of mt-HPP is to understand the integrative role of mitochondrial proteins in health and disease. Considering the broad role of mitochondria in regulating cellular energy and cell death, the mt-HPP initiative is working with several other HUPO initiatives including mitochondria C-HPP, food and nutrition B/D-HPP and neurodegeneration cluster.

mt-HPP Chair Mauro Fasano

B/D-HPP Newsletter

8

Biology/Disease- Human Proteome Project Newsletter | **Issue 1, 2017**

The St. Abbondio Cloister in Como is the location of the next mt-HPP workshop, in February 2017.

One of the first technical challenges faced by the team is to standardize mitochondrial enrichment methods. This was achieved by head-to-head comparison of three commonly used methods using several cell lines. Current and ongoing work of the mt-HPP include: mitochondrial interactomics and degradomics, and alteration of mitochondrial proteome in neurodegenerative diseases.

A recent publication from the mt-HPP team highlight the translational potential of proteomics. Chronic fatigue syndrome (CFS) is a debilitating and complex disorder characterized by unexplained fatigue not improved by rest. Defective mitochondrial function was previously connected with CFS development. F Ciregia et al. used bottom-up proteomics to report an association between CFS and the differential expression of 2 mitochondrial proteins in saliva. This work may potentially lead to new treatments for CFS.