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Developing New Methods to Answer Old and New Questions in Neurodegenerative Diseases:

21st Workshop of the HUPO Brain Proteome Project (HBPP) 23–24 January 2014, Honolulu, Hawaii

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From 23 to 24 January 2014 the 21st Workshop of the Human Proteome Organization's (HUPO) Brain Proteome Project (HBPP) took place in the conference room of the Aston Waikiki Beach Hotel, Honolulu, Hawaii, USA. During this spring workshop the participants discussed intensively their strategies to employ neuroproteomics in the study of neurological diseases and the outcome of their work. In line with HBPP goals all members and associates of the HUPO BPP community share the idea to bring all the data and ideas together to really understand the complexity of brain related diseases

After a warm welcome address by Helmut E. Meyer, the first session titled "Neuropathology" was initiated. Lea T. Grinberg, neuropathologist and Chairwoman of the

The HUPO Brain Proteome Project (HUPO BPP) held its 21st workshop in Honolulu, Hawaii. During the 23–24 January 2014 the island became the center of the open workshop of the scientific community.

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HUPO Brain Proteome initiative talked about common features of neurodegenerative diseases, the progress of neuron loss in Alzheimer's diseases (AD) and the project to create an interactive imaging brain map associating neuroimaging and histology in a voxel to voxel fashion. The protocol is already optimized and now her group is working on tools to allow the project to be scaled up. Once it is concluded, new analytical tools such as proteomics will be incorporated in the pipeline.

Helmut Heinsen, a Professor of Neuroanatomy from the University of Würzburg, talked about the correlation between genotype and phenotype of the neurological diseases choreaacanthocytosis and Chorea Huntington. Despite presenting the same clinical phenotype, these diseases differ in genetic basis, pathogenesis and brain vulnerability. It calls attention for the need of studies with human tissue to elucidate neurodegenerative diseases. The third talk of the session was given by PerAndrén, a neurobiologist from the Uppsala University. In the first part of his presentation he shared his data about Peptidomics of Parkinson's disease (PD) including a neuropeptide database SwePep.org and novel identified endogenous neuropeptides. In the second part he presented data from a project focusing on Parkinson's disease using MALDI Imaging. He put special emphasis in absolute quantification of drug concentrations in tissue sections, the comparison of different normalization methods and importing such data into the standard format imzML.

Fouzi El Magraoui, biochemist from the Ruhr-University Bochum, talked about the differential proteome of the human hippocampal regions CA1, CA2, CA3 and fascia dentata. He demonstrated an approach to analyze the differences of the proteomic composition of these regions early vulnerable to Alzheimer's disease. Taken together with several other immune based strategies he is trying to identify relevant autoantigens associated to Alzheimer's disease

Inaugurating the second session titled "Biomarkers", Helmut E. Meyer, Proteomics expert from the Ruhr University Bochum talked about the search for early onset biomarkers in AD and PD. Currently, no treatment is available for curing, delaying or stabilizing both diseases. All attempts to use the beta amyloid plaques as drug targets were so far unsuccessful. Therefore, other hypotheses like the role of autoimmune antibodies as potential trigger of AD and PD should be evaluated. The main question which must be answered in the near future is "What triggers the start of these diseases?" which is believed to start 25 years before the first clinical symptoms become obvious. Another hypothesis which might be worth to be evaluated is that the blood of affected individuals carries neurotoxic extracellular vesicles due to changes in their lipid and/or protein composition. Peter Nilsson, 'Affinity Proteomics' expert at SciLifeLab, KTH Royal Institute of Technology, Stockholm, Sweden, talked about antibody, antigen and peptide microarrays for Proteomic Profiling in Neurodegenerative Diseases and Psychiatric Disorders, including the ProteinAtlas project that lists approx. 22,000 antibodies with their immunohistological staining behavior in diverse human tissues, confocal microscopy and subcellular localization.

Anna Häggmark, researcher at the SciLifeLab, KTH Royal Institute of Technology, Stockholm, Sweden, presented data from cerebrospinal fluid (CSF) and plasma protein profiling project in multiple sclerosis.

Katja Kuhlmann, from the Ruhr-University Bochum (Cellular Proteomics), talked about a collaborative project with Gerd Schmitz (University Clinics Regensburg, Germany) regarding the Proteomics analysis of platelet-derived extracellular vesicles as potential neurotoxic agents contributing to the onset of AD.

Peter Verhaert, analytical biotechnology expert from Delft University of Technology, presented “The peptidomics of the human eye”. He first talked about peptides for cell cell communication including the secretome as cellular language used for diagnostics and potentially as therapeutics. He also showed his efforts with the “dry-eye project”, including the characterizing of tear and saliva proteome/peptidome.

The session “Bioinformatics and General Aspects” was chaired by Martin Eisenacher. The Bioinformatics and Biostatistics expert talked about established and new methods for analyzing Proteomics-specific data and about basic and advanced Biostatistical algorithms for all kinds of quantitative data evaluation.

Christoph Borchers, Proteomics expert at the Genome BC Protein Center at the University of Victoria, Canada, gave a lecture about Multiple Reaction Monitoring (MRM). He demonstrated the performance of this method by using stabile isotope label standard peptides to quantify more than 150 different plasma proteins in human plasma samples.

Jong-Shin Yoo, researcher at the Basic Science Institute of the Republic of Korea, presented data about the identification of human brain proteins. In a further step he analyzed for posttranslational modification in these proteins. He was able to identify several glycosylated, acetylated and phosphorylated proteins and to characterize them.

Bong-Hee Lee talked about the role of advanced glycation end products (AGE) in the pathology of the neurodegenerative disease like AD and PD. Using cell cultures of neuronal cells he was able to show that the rate of AGE-albumin synthesis in human microglial cells is markedly increased by amyloid-β exposure and oxidative stress. Exogenous AGE-albumin upregulates the receptor protein for AGE (RAGE) and augments calcium influx, leading to apoptosis of human primary neurons.

The next HBPP workshops will take place during October 2014 in Madrid as part of the Annual HUPO World Congress. Participant registration at www.hbpp.org is welcome!

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