Exploring the Human Plasma Proteome: The HUPO Plasma Proteome Project,
A Foundation for Biomarker Studies

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Also, Poster #925, Wed PM
Scheme Showing Aims and Linkages of the HUPO Plasma Proteome Project–Pilot Phase

Serum vs Plasma

Reference Specimens

HUPO PPP Participating Labs

Technology Vendors

Technology Platforms–Separation and Identification

Development & Validation of Biomarkers

Liver and Brain Proteome, Antibody, Protein Stds Projects

Output From PPP Pilot Phase


Collaborative analyses & annotations, lab-specific analyses

Publicly-accessible datasets
- www.peptideatlas.org/hupo/hppp [ISB];
- www.ebi.ac.uk/pride [EBI]
- www.bioinformatics.med.umich.edu/hupo/ppp [UM]

Additional papers:
- *Nature Biotechnology* 2006;24:333-338 (States et al)
- *Genome Biology* 2006;7:35R (Fermin et al)

Numerous citations/comparisons of datasets
Numbers of Proteins Identified
(LC-MS/MS or FTICR-MS, 18 labs)

From 15,519 reported distinct protein IDs in IPI 2.21, we chose one representative/cluster:

(a) 9504 = 1 or more peptide matches
(b) 3020 = 2+ peptide matches (Core Dataset) (Proteomics 2005; 5: 3223-3519)
(c) 1274 = 3 or more peptide matches
(d) 889 = follow-up high-stringency analysis with adjustments for protein length and multiple comparisons (43,000) in IPI v2.21 (Nature Biotech 2006; 24:333-338)
New Phase of the PPP Launched Now

1. Quantitation and subproteomes (PTMs) with new methods and advanced instruments

2. HUPO Plasma Proteome Databases, with complementary partners, robust bioinformatics analyses, and distributed file sharing system

3. Convergence of HUPO organ-based and disease-related proteome studies to a common pathway in the plasma proteome
Agenda of the PPP Workshop, 7 Oct 2007

20:00-20:45 Panel on Advances in Technology Platforms and Analytical Strategies for Quantitation, Identification of PTMs, and Higher Throughput, Ruedi Aebersold (Switzerland)
   Christie Hunter (USA), Denis Hochstrasser (Switzerland), Bill Hancock (USA), Ole Jensen (Denmark), Richard Smith (USA), Rong Zeng (China)

20:45-21:30 Panel on Informatics and Databases for the PPP
   Henry Lam (USA), Lennart Martens (UK), Ron Beavis (Canada), Martin McIntosh (USA), Akhilesh Pandey (USA)

21:30-22:00 Panel on Plasma and Serum as Final Common Pathway for Biomarkers Emerging from Organ and Disease Proteome Initiatives, John Bergeron (Canada), moderator
   Fuchu He (China), Helmut E. Meyer (Germany), Jan Schnitzer (USA), Richard Simpson (Australia), Tadashi Yamamoto (Japan), Naoyuki Taniguchi (Japan)
1. Advanced Proteomics Technologies

LTQ, LTQ-FT, Orbitrap, ABI 4800, Triple-Quad 4000 offer greater sensitivity, much higher mass accuracy, quantitation, and detection of PTMs---for biomarker discovery & targets.

Proteotypic N-glycosite peptides with heavy isotope labeling, and multiple reaction monitoring (MRM) facilitate quantitation and throughput for informative biomarker candidates.

New informatics methods assign more of the high quality spectra to peptides, including PTMs.
2. Databases with Advanced Informatics: Insights for the PPP and Links across HUPO Initiatives

PeptideAtlas at Institute for Systems Biology, led by Eric Deutsch: comprehensive plasma proteome build from uniformly re-analyzing primary raw spectra using TransProteomic Pipeline from investigators’ submissions.

PRIDE at European Bioinformatics Institute, led by Lennart Martens: Repository for peptide and protein IDs, without the raw spectra; generic resources to facilitate a wide range of annotation; tied to data management standards from the HUPO PSI.

Tranche at University of Michigan, led by Phil Andrews: Repository accepts raw spectra and complete datasets, provides encrypted as well as open access, has backup on three continents, and provides distributed file sharing.
3. Convergence with HUPO Initiatives on Organ and Disease Proteomes

The PPP Next Phase invites each HUPO initiative to analyze EDTA-plasma alongside the tissue or biofluid analyzed (liver, brain, kidney/urine, saliva) or disease studied (CV, cancers)

The PPP Database and Bioinformatics unit will provide collaborative cross-analyses of these and other available datasets.
Invitation to HUPO Congress Participants

1. Indicate your potential interest in participating in the Next Phase HPPP.

2. Criteria for labs: substantial scope of funded work, advanced state of technology platforms, commitment to contribute datasets in timely fashion for collaborative analyses, and interest in active participation in PPP workshops and other forums and in generating significant publications.

3. Indicate your willingness to organize cross-initiative collaborative analyses if you are in the leadership of a HUPO initiative.

4. Contact Gil Omenn: gomenn@umich.edu.
Acknowledgements

Pilot Phase Corporate Sponsors

Johnson & Johnson       Abbott Labs
Pfizer                   Novartis
Invitrogen               Amersham
Procter & Gamble
BD Biosciences           BioVision
Ciphergen                Molecular Staging
Bristol Myers Squibb    Sigma-Aldrich
Agilent                  Dade Behring
September 2007 Report on the Plasma Proteome Project to the HUPO Initiatives Committee
(Submitted by Gil Omenn, 11 Sept 2007)

Major activities:
1. At the Long Beach HUPO 5th World Congress of Proteomics, Ruedi Aebersold, Gil Omenn, and Young-Ki Paik were named co-chairs of the HUPO Plasma Proteome Project. The PPP held a very well-attended Workshop, with lots of discussion about the Next Phase of the PPP and the use of standardized blood specimens (EDTA-plasma) with standardized specimen handling protocols. The Biomarker Work Group led by Marti McIntosh joined the PPP Workshop.

2. Omenn and Eric Deutsch represented the PPP for the entire six-day HUPO Initiatives Workshop in Barbados in January 2007, chaired and hosted by John Bergeron.

3. The HUPO PPP co-chairs and several leading investigators held a conference call on March 2.

4. The PPP had a workshop and several presentations at the U.S. HUPO Annual Meeting in Seattle March 5-8.

5. The PPP has organized a Workshop for the HUPO 6th World Congress in Seoul, October 7, 2007.


Outline of the Next Phase for the PPP:
1. Quantitation and subproteomes (PTMs) with new methods and advanced instruments
2. HUPO Plasma Proteome Databases, with robust bioinformatics analyses and distributed file sharing system (Tranche)
3. Convergence of HUPO organ-based and disease-related proteome studies to a common pathway in the plasma proteome

Request to HUPO Council and Participants in Buenos Aires Meeting, July 2007:
1. Indicate your potential interest in participating in the Next Phase HPPP. Criteria for labs: substantial scope of funded work, advanced state of technology platforms, commitment to contribute datasets in timely fashion for collaborative analyses, and interest in active participation in PPP workshops and other forums and in generating significant publications.
2. Indicate your willingness to organize cross-initiative collaborative analyses if you are in the leadership of a HUPO initiative.
3. Attend HUPO PPP Workshop in Seoul
4. Contact Gil Omenn: gomenn@umich.edu.

Program for the PPP Workshop in Seoul, Oct 2007:
20:00-20:45 Panel: Advances in Technology Platforms and Analytical Strategies for Quantitation, Identification of PTMs, Throughput
Aebersold, Mallick, Hunter, Jensen, Hochstrasser, Smith, Zeng

20:45-21:30 Panel: Informatics and Databases for the Plasma Proteome
Martens, Deutsch, Beavis, Kapp, Nesvizhskii, Pandey

21:30-22:00 Panel: Plasma as Final Common Pathway for Biomarkers Emerging from Organ and Disease Proteome Initiatives
John Bergeron (Canada), moderator; He, Ping, Schnitzer, Yamamoto