

C-HPP PIC
HPP Workshop
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HUPO-2017
JPR Special Issue Update
NeXt-50 MP Update
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Highlights of the HUPO-2017 C-HPP 5th Special Issue of Journal of Proteome Research

Guest Editors: Young Ki Paik, Gil Omenn, Eric Deutsch, Jennifer VanEyck
Associate Editor: Chris Overall

- 2016 18 papers; **2017: potentially 26 papers**
- 2017 SI: C-HPP, B/D-HPP, Pillars (but only 3 BD/HPP)
- 11 of 22 teams have a paper in JPR SI
- 11 Accepted and online in JPR in time for Dublin HUPO
- 9 Under review
- 6 Awaiting resubmission
- October 1 ACS deadline for December 2017 Issue
- The Wiki has proven successful in reporting these papers and NeXt-50 MP progress

NeXt-MP50

- 2016: 216 PE1 MPs passed Guidelines v2.1
- 17 of 25 Ch teams reported by 2:55 am today
- PE1: 15 MPs confidently identified
- + ~ 37 that may survive review = 52 PE1 MPs
- Silver MPs: 267 additional candidate MPs
- Discuss two finish targets:
 - PE1
 - Silver category (i.e. Candidate MPs in papers)
e.g. One peptide >9 aa as per guidelines
or 2 peptides of 7 or 8 amino acids long
And found in >3? biological replicates

[ftp://ftp.nextprot.org/pub/current_release/custom/hpp/
HPP entries with unconfirmed MS data.txt](ftp://ftp.nextprot.org/pub/current_release/custom/hpp/HPP_entries_with_unconfirmed_MS_data.txt)

Human Proteome Project Mass Spectrometry Data Interpretation Guidelines 2.1.

Deutsch, E. W.; Overall, C. M.; Van Eyk, J. E.; Baker, M. S.; Paik, Y. K.; Weintraub, S. T.; Lane, L.; Martens, L.; Vandenbrouck, Y.; Kusebauch, U.

J. Proteome Res. 2016, DOI: 10.1021/506 acs.jproteome.6b00392.

- The rigour of the 15 Guidelines for Mass Spectrometry Interpretation v2.1 adopted by the EC-HPP for high confidence protein identification especially of MPs undoubtedly slowed progress
- In 2017 JPR SI Digging more missing proteins using an enrichment approach with ProteoMiner. By Yan Ren et al.
 - 2 non-nested proteotypic peptides with 9+ aa
 - Passed the Uniqueness checker screen
- 8302 of the 8432 proteins detected in kidney
7845 of the 7985 proteins detected in bladder
6740 of the 7598 proteins detected in colon

JPR SI Strategies Learned

- Careful selection of specimens for those with highest expressed mRNA for MPs (rare tissues)
- Combinations of Triton-X100 and various buffers for solubilization and release of hydrophobic and membrane-proteins
- Enrichment/equalization of low-abundance proteins with ProteoMiner hexapeptide beads
- Maximal use of the neXtProt uniqueness checker to help avoid claims based on matches of peptides to abundant proteins

JPR SI Strategies Learned

- Use of alternative proteases (Albert Heck) that can generate non-tryptic proteotypic peptides from highly homologous proteins. [LysargiNase](#) identified a MP not possible with trypsin.
- Stimulate expression of undetected proteins (and transcripts) with epigenetic inducers, etc.
- MPs may be disease responders. Integrates with B/D-HPP inflammation-associated proteins and transcripts might be detected if specimens were obtained with infection/inflammatory etc.
- Collaborate with the B/D-HPP to seek responder MPs in disease (discussed later)

Discussion Points Deeper Collaboration with B/D HPP

- Distal fluids of diseased tissues as well as the tissues themselves are promising sources of disease-linked MPs
- Such MPs may only be induced on microbiological, pathological, or physical / chemical challenge
- SNP variant MPs that are associated with disease, and disease-associated PTMs, may render MPs tractable to identification where traditional MS approaches struggle
- Thus, B/D- and C-HPPs teams can further dovetail for a more united HPP effort in MP identification