

Biological Sciences Division

Firsts in mouse and mammalian brain proteomic research featured in journal

Scientists from Pacific Northwest National Laboratory (PNNL) and the University of California-Los Angeles have completed the first comprehensive characterization of the whole mouse brain proteome and the most comprehensive proteome coverage for the mammalian brain to date. The results are described in the article "Characterization of the mouse brain proteome using global proteomic analysis complemented with cysteinyl-peptide enrichment," which appeared in the February 2006 issue of the *Journal of Proteome Research*.

Most proteomic studies of the mammalian brain have been based on two-dimensional electrophoresis separations coupled with in-gel protein digestion and mass spectrometric (MS) identification, but limitations of this approach have prevented extensive coverage of the mouse brain proteome.

In their study, the PNNL-UCLA team took a global proteomic approach for comprehensive profiling of the brain tissue using liquid chromatography-tandem mass spectrometry (LC-MS/MS) and an extensive protein database for the whole mouse brain. They incorporated a highly efficient cysteinyl-peptide enrichment (CPE) technique to complement a global enzymatic digestion method, which resulted in significantly increased proteome coverage. Both sample types were analyzed by strong cation exchange (SCX) fractionation coupled with reversed-phase LC-MS/MS analysis. This extensive analysis identified 48,328 different peptides and 7792 nonredundant proteins, or ~34% of the predicted mouse proteome. The identified proteins provide a broad representation of the mouse proteome with little bias evident.

The mouse brain peptide/protein database generated from this study will be the basis for future quantitative brain proteomic studies using mouse models. The proteomic approach presented here may have broad applications for rapid proteomic analyses of various mouse models of human brain diseases. Ultimately, the researchers hope to achieve a 3-D view of the mouse brain proteome and to produce images of specific brain regions.

The PNNL research team includes Haixing Wang, Wei-Jun Qian, Vladislav Petyuk, Richard Barry, Tao Liu, Marina Gritsenko, Heather Mottaz, Ron Moore, Dave Camp, and Dick Smith. The UCLA team members are Mark Chin, Arshad Khan, and Desmond Smith of the David Geffen School of Medicine.

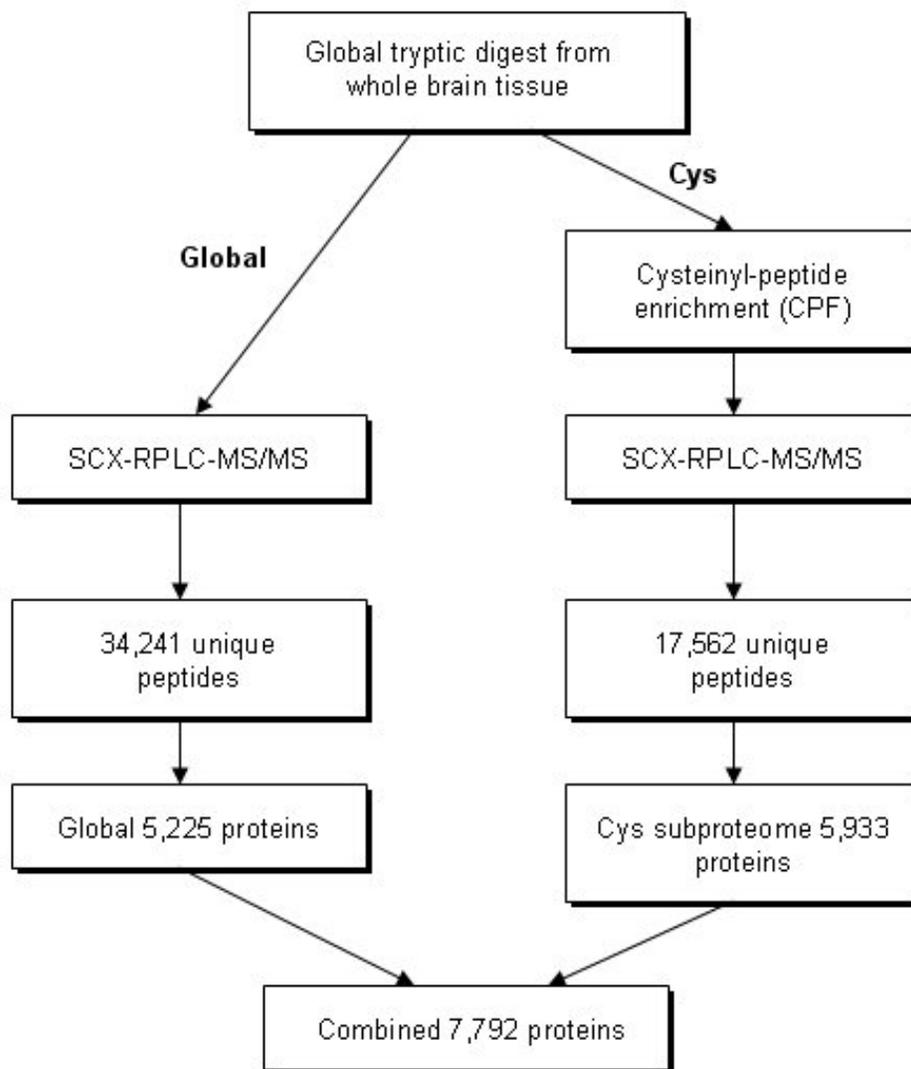


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Experimental strategy: preparation of the whole mouse brain using a combination of global tryptic digestion and cysteinyl-peptide enrichment (CPE) methodology, followed by SCX fractionation and LC-MS/MS analysis of each fraction, and the peptide/protein identification results from both preparation methods.

Reference

Wang H, W-J Qian, MH Chin, VA Petyuk, RC Barry, T Liu, MA Gritsenko, HM Mottaz, RJ Moore, DG Camp II, AH Khan, DJ Smith, and RD Smith. 2006. "Characterization of the mouse brain proteome using global proteomic analysis complemented with cysteinyl-peptide enrichment." *J. Proteome Res.* 5(2):361-369.