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The progress in Human Brain Proteome Project (HBPP) and some of the progress in brain proteomics studies are briefly reviewed in this article.

The human and mouse brain proteomics pilot studies attracted excellent researchers worldwide (Klose, 2005). Currently, 23 research groups are participated to have proteomic studies fall into five different areas: (1) total number proteomics (2) 2D gel based proteomics (3) multidimensional chromatography based proteomics (4) Peptidomics and (5) mRNA profiling. The most popular one were the total number proteomics and the 2D gel based proteomics studies. Main technology used in achieving these studies is 2D PAGE, besides, 2D-LC-MS-MS, Q-TOF-MS, LCQ-MS, ESI-MS/MS, FITCR, protein chips and multi-dimensional LC-MS-MS are used.

The highlighted BPP pilot study carried out during year 04/05 was the proteome analysis and expression profiling of 5-10 brain derived from female C57/b16 inbred mice of 3 different developmental age stages (fetal, juvenile and adult). There was no pooling allowed in these studies and having goals in feeding the brain proteome database and assessment of 2D or non-2D based analysis. Isoelectric focusing using protein extracted from 3 developmental stages was performed in the first dimension using the 20 cm 3-10 linear self-made IPG strips or 24 cm 3-10 non-linear commercial IPG strips with sample cup application. Focused proteins were resolved in 15% acrylamide gel and detected by silver-stains. In the linear pH gradient gels, they found 178 proteins of approximately 1000 detected spots that shown differential protein expression as a result of different developmental stages and analysis was carried out for 155 proteins so far. 276 proteins of approximately 1000 detected spots shown differential protein expression under non-linear first dimension and analysis was carried out for those 234 proteins differential expressed proteins. Some of the identified upregulated proteins in adult stage were glutamine synthetase, malate dehydrogenase, while proteins downregulated during adult stage were isocitrate dehydrogenase, stathmin and dihydropyrimidinase related protein 1, 3 and 4.

Some highlighted brain proteomics researches are done by Kim, Chen and Knofel's

groups. 2D DIGE coupled to LC/MS/MS analysis of 1 week old male SD rat brain under corticotrophin-releasing factor (CRF) stimulation, a kind of chronic restraint stress (CRS), by Kim's group revealed that several proteins correlated with stress response showed significantly different expressions.

Chen's research group developed a modified protocol for rat hippocampal plasma membrane isolation, by affinity labeling technique with immobilized streptavidin beads biotinylated on cell surface. One dimensional electrophoresis coupled with in-gel digestion of protein spots followed by LC-Q/TOF and MALDI-TOF using hippocampal plasma membrane proteins derived from different methods was compared. Entire tissue homogenate separated by sucrose density gradient centrifugation fractionation and cultural neuron cell purified by affinity enrichment are used in one dimensional electrophoresis. Several hundred proteins are identified by each method in which some of them are novel proteins or proteins located at apical and basolateral membranes.

Knofel's group has done a preliminary proteomics study on the cause and pathogenesis of multiple sclerosis (MS), an inflammatory demyelinating disease of central nervous system. 2D gel electrophoresis of cerebrospinal fluid (CSF) proteins from MS patients found that 27 additional protein spots expressed in 5-10 pH range with molecular weight of 30-35 kDa. Pentapeptide with sequence QYNAD was suggested to biological marker for MS recently. Western blot analysis of CSF proteins from MS patients using anti-QYNAD antibody revealed binding of several protein spots in MW range between 30 and 60kDa. The identification of CSF proteins may lead to new insights in multiple sclerosis pathogenesis and the discovery of disease biological markers.

References:

1. Chen et al. (2005) Proteomic analysis of rat hippocampal plasma membrane. Late breaking abstract of HUPO 4th Annual World Congress, P.13.
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3. Klose J. (2005) Presentation of HUPO 4th Annual World Congress.
4. Knofel et al. (2005) Proteomic analysis of cerebrospinal fluid from multiple sclerosis patients. Late breaking abstract of HUPO 4th Annual World Congress, P.13.