Searching for novel Cdk5 substrates in brain by comparative phosphoproteomics of wild type and Cdk5-/- mice

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Protein phosphorylation is the most common post-translational modification that regulates several pivotal functions in cells. Cyclin-dependent kinase 5 (Cdk5) is a proline-directed serine/threonine kinase which is mostly active in the nervous system. It regulates several biological processes such as neuronal migration, cytoskeletal dynamics, axonal guidance and synaptic plasticity among others. In search for novel substrates of Cdk5 in the brain we performed quantitative phosphoproteomics analysis, isolating phosphoproteins from whole brain derived from E18.5 Cdk5+/+ and Cdk5-/- embryos, using an Immobilized Metal-Ion Affinity Chromatography (IMAC), which specifically binds to phosphorylated proteins. The isolated phosphoproteins were eluted and isotopically labeled for relative and absolute quantitation (iTRAQ) and mass spectrometry identification. We found 40 proteins that showed decreased phosphorylation at Cdk5-/- brains. In addition, out of these 40 hypophosphorylated proteins we