

## Characterization of SOD1 Complexes from Transgenic Mice Spinal Cords

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Amyotrophic Lateral Sclerosis (ALS) is a neurodegenerative disease affecting motor neurons in which 10% of the cases are familial and of which about 20% of the familial cases are linked to a dominant mutation in the Cu,Zn Superoxide Dismutase protein (SOD1). Protein inclusions rich in SOD1 are a hallmark of pathology, and SOD1 aggregation, possibly with other proteins, is suspected to be involved in pathogenesis. In order to investigate the protein composition of these aggregates, high and low molecular weight SOD1 complexes were purified from the spinal cords of end stage ALS symptomatic hSOD1 transgenic mice through a two-step chromatographic method. Two ALS-related mutants were used as well as the human wild type SOD1 in these experiments. First, the presence and high abundance of SOD1 complexes varying in molecular weight was observed in diseased mice through western analysis.\* The complexes were then subjected to proteomic characterization by Electrospray Ionization Mass Spectrometry (ESI-MS) in order to identify the non-SOD1 components. The vast majority of the samples contained full length SOD1, along with small amounts of other proteins. Identification of these non-SOD1 proteins was confirmed by immuno-histochemical methods. In addition to analyzing the components, the SOD1 protein from the complexes is also now being examined for the presence of post-translational modifications using ESI-MS as well as Matrix Assisted Laser Desorption Ionization (MALDI) mass spectrometry.

\*Wang, J. et al., (2003) Copper-binding-site-null SOD1 causes ALS in transgenic mice: aggregates of non-native SOD1 delineate a common feature, *Human Molecular Genetics*, **12**, No 21, 2753-2764