Title
ALS-Like Spinal Cord Pathology in Transgenic Mice with a Mutation in the Valosin-Containing Protein Gene

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Kimonis et al. identified a human genetic syndrome, Inclusion Body Myopathy associated with Paget's disease of the bone and frontotemporal dementia (IBMPFD), and subsequently found it to be associated with mutations in the valosin-containing protein (VCP) gene (Watts, Nature genetics 2004). A knock-in VCP mouse model of IBMPFD (R155H) developed by this group exhibited muscle, bone and brain pathology characteristic of the human disease, including TDP-43 positive inclusions (Badadani, PLoS One. 2010). Recent studies have extended the list of diseases associated with VCP mutations to include ALS (Johnson, Neuron 2010). We have thus undertaken studies of spinal cord pathology in heterozygous R155H mice. Preliminary examinations of 18–24 month old R155H mice show degenerative changes in ventral horn motor neurons (MNs), and increased astrocyte activation. In addition, we find evidence for TDP-43 positive cytosolic inclusions in many damaged MNs. These studies suggest that the R155H VCP mouse may provide a valuable new animal model for ALS,

which reproduces key aspects of human disease, including the presence of MN cytosolic aaggregates, and pronounced astrocytic as well as MN pathology.

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