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The burden of neurodegenerative disorders on the health care systems, on patients and on their families is immense as no effective therapies exist. ALS is the most common and fatal motor neuron disease. Most cases of ALS are sporadic with unknown etiology or risk factors. However, 10% are inherited in a dominant manner. Mutations in eight genes have been identified to cause typical ALS with different mechanisms. RNA-mediated proteinopathy is increasingly being recognized as the major cause of neurodegenerative disorders. FUS was identified as a primary cause of familial ALS.

In order to modeling FUS-ALS in a dish, we will start from fibroblasts obtained from ALS patients with different *FUS* mutations and from controls. Induced pluripotent stem (iPS) cells will be generated from these fibroblasts using reprogramming vectors. Thereafter, iPS cells will be induced to differentiate into motor neurons. We will look for differences between mutant and control cells. Initially, we will focus on differences in gene expression, on neuronal survival/apoptosis, on neurite outgrowth and on subcellular FUS localization. In addition, we will evaluate their resistance to a variety of stresses (excitotoxicity, heat shock, oxidative stress). Furthermore, these differentiated cells will also be used to test the effectiveness of potential novel treatments for ALS.