Even though there are millions of neurons in our brain, in neurodegenerative diseases only a select set of neurons show vulnerability and progressively degenerate. In amyotrophic lateral sclerosis (ALS), motor neurons in the cortex and spinal cord show selective vulnerability. Their progressive degeneration results in lack of control over voluntary movement, without affecting memory and cognitive function. We are developing novel approaches to understand cellular and molecular mechanisms responsible for motor neuron degeneration. Our findings will allow cell-based therapeutic interventions in the near future.