Dr. Mugdha Deshpande, the Blazeman Foundation Postdoctoral Fellow for ALS Research in Avital Rodal's lab at Brandeis University, will be presenting her work at the **Neurodegenerative Diseases: Biology & Therapeutics Meeting** at Cold Spring Harbor Laboratory (December 3rd – 6th, 2014).

Her poster, titled "Mechanisms for misregulation of membrane traffic and growth factor signaling in animal models of Amyotrophic Lateral Sclerosis", focuses on how signals promoting growth and survival are transported within neurons, and how these processes are affected in ALS. Motor neurons control muscle contraction, and one of the early events in ALS is the loss of connections between these neurons and their target muscles. For many years, it has been known that growth factors secreted by the muscle control both neuron-muscle connections and the survival of the motor neuron. These growth factor molecules bind to receptors on the surface of the neuron and are transported, in membrane bound packets called "endosomes", to the neuronal cell body in the spinal cord, relaying a pro-survival signal. The type of endosome into which these growth factors and receptors are sorted is thought to determine the strength of the pro-survival signal.

Fruit flies that express a human ALS gene have previously been shown to mimic several aspects of ALS pathology, including neuronal death, motor dysfunction and reduced lifespan. In these flies, Dr. Deshpande and coworkers have identified a profound defect in growth signaling at the neuromuscular junction (NMJ), which is the point of contact between a neuron and the muscle. This signaling defect correlates with mis-sorting of growth receptors, such that fewer receptors are found in signal-permissive endosomes and the proportion of receptors in recycling endosomes is increased. They then used genetic tools to shunt the receptors back to the correct, signal-permissive endosome, and rescued neuronal defects in the fruit flies. Their results suggest that drugs targeting these endosome sorting pathways may be able to restore pro-survival signals in ALS patients.

In parallel, Dr. Desphande is working with Suzanne Paradis at Brandeis to develop a system to study growth receptor signaling in rodent neurons expressing human ALS genes. She has found that growth of these neurons is severely affected when they are modified to express ALS genes, similar to the fruit fly system. She is now testing if these defects are related to deficits in specific growth factor signaling and endosome sorting pathways in mammalian neurons.