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/ **STRENGTHEN THE BRAIN**

**Project ALS Commitment:** \$1.8M

**Investigators:** Kevin Eggan/Harvard University; Elizabeth Engle/Children’s Hospital Boston, Harvard Medical School; Esteban Mazzoni/New York University; Lorenz Studer/Memorial Sloan Kettering Cancer Center; Hynek Wichterle/Columbia University

**Background:** ALS destroys almost all types of motor neurons. Yet some—including those that control eye movements—survive the disease. In the past, researchers have postulated that differences in genetic makeup, motor circuitry, and cell size/position might make ocular motor neurons resistant to ALS, but this important phenomenon has never been studied rigorously. Thanks to recent advances in genetics and genomics, developmental and stem cell biology, and drug screening, this consortium is now able to identify specific differences in ocular motor neurons. Project ALS has put together a team including an expert in ocular motor neurons (Engle), the scientist who first differentiated a stem cell into a motor neuron (Wichterle), a leader in motor neuron subtype differentiation (Mazzoni), and an expert in developing specific neuronal subtypes in Parkinson’s disease models (Studer) to understand, for the first time, why the eyes are unaffected in ALS.

**Summary of Progress:** Directed by Elizabeth Engle, the Project ALS ocular motor neuron consortium has successfully differentiated stem cells into ocular-like motor neurons and purified these; identified key genetic differences between ocular motor neurons and spinal motor neurons; and initiated studies into how ocular motor neurons respond differently to ALS-like stressors. Now in its second phase, the main goal of this effort is to identify which of these identified differences is responsible for ocular motor neurons’ survival in ALS—and to successfully confer this resistance onto vulnerable motor neuron populations.

**Relevant publications:**

[Mazzoni: Differentiation of stem cells into motor neuron subtypes](#)

[Wichterle: Differentiation of stem cells into motor neurons](#)

[Studer: Derivation of dopaminergic cells from iPS cells](#)

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