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2001 Program  
New Investigator (3-year project)

**Project Title:** Neuronal plasticity of the hippocampus following ischemic stroke injury

**Project Summary:** Millions of Americans that smoke are disabled as a result of cardiac arrest induced stroke. Stroke leads to loss of oxygen “called ischemia” and a secondary hemorrhagic damage to specific brain regions. In order to restore function to the neuronal connections will need to be re-established, and understanding the molecules that regulate these functions is paramount to promoting recovering. The ephrins and Eph receptors are a family of molecules that have been implicated in controlling growth in the developing brain. The project hypothesizes that ephrins and Eph receptors also function to promote connections between neurons in the adult injured brain. Innovative technologies will be employed to examine the function of ephrins and Eph receptors in the brains of living animals. Gene-targeted knockout mice are animals that are genetically engineered to grow in the absence of a specific gene. Aim 1 will examine ephrin and Eph receptor knockout mice for their ability to form neuronal connections in the hippocampus. Aim 2 will examine the expression and function of these molecules in the cells that makeup the scar tissues and employ knockout mice to examine whether the absence of these molecules in the scar can promote recovery. In summary, these studies provide cutting edge technologies to investigate the mechanisms that function in the wiring of the nervous system, and potentially lead to mechanisms to promote rewiring and restoring of brain function.

**Project Successes:** The project found that ephrinB3 functions to regulate synaptic plasticity in the adult hippocampus through activation of its Eph receptor(s). In particular, ephrinB3 knockout mice have reduced learning and memory behavior and long-term potentiation in the hippocampus, which is supported by morphological changes in the synaptic densities. These changes are supported by biochemical alterations in the expression of numerous pre- and post-synaptic proteins, adaptor proteins, and signaling proteins in the synapse. The project also found that ephrins and Eph receptors are up regulated following injured, which may contribute to the underlying defects in regeneration.

**Selected publications from BRP funded research in Peer Reviewed Journals:**

Blitz-Huzinga C, Nelersa CM, Malhotra A, Liebl DJ. Ephrins and their receptors: Binding versus Biology. *IUBMB Life*. 2004;56(5):257-265.

Liebl DJ, Morris C, Parada LF, Henkemeyer M. mRNA Expression of B-class Ephrins and their receptors in the neonatal and adult mouse CNS. *J Neurosci Res*. 2003;71:7-22.

**Presentations from BRP funded research:**

Rodenas-Ruano A, Green EJ, Perez-Pinzon M, Liebl DJ. The Role of EphrinB3 in Synaptic Function. American Psychological Association/ Diversity Program in Neuroscience Predoctoral Fellowship. 2004

Rodenas-Ruano A, Huizinga C, Wu E, Perez-Pinzon M, Green E, and Liebl DJ. Ephrin-B3 and EphB1 receptor deficiencies leads to defects in synaptic functions in the hippocampus. Soc. Neurosci. Abstr. 2003