The outcome of spinal cord injury depends on the extent of secondary damage produced by a series of cellular and molecular events initiated by the primary trauma. Secondary injury is a combination of several factors contributing to cell death, including glutamatergic excitotoxicity, free radical damage, cytokines, and inflammation. Since secondary injury is a multi-dimensional disorder resulting from numerous interdependent molecular and biochemical events, its treatment is associated with a number of challenges. Current therapeutic strategies include the use of anti-apoptotic drugs, free radical scavengers, and anti-inflammatory agents. Each of these approaches focuses on only one of the aspects of the entire process. Thus, a need exists for the development of innovative multi-task strategies, which would be able to block key reactions on cellular and molecular injury cascades, thus reducing secondary tissue damage, minimizing side effects, and improving functional recovery.

Applications of nanotechnology in basic and clinical neuroscience are only in the early stages of development. One of significant achievements was demonstration that functionalized nanoparticles can penetrate through blood-brain barrier and be used for drug and gene delivery to central nervous system (CNS). Other studies, including our own research, showed that multiple biological molecules and other bioactive compounds can be physically adsorbed or covalently attached to nanoparticles without significant loss of function. Thus, nanotechnology provides a platform for both delivery of therapeutic agents to CNS and creation of multitask therapeutic devices. The ultimate goal of this project is design, preparation and characterization of nanodevices for treatment of secondary spinal cord injury based on attachment of several functional enzyme molecules to polymeric nanoparticles. In the first prototype systems the enzymes will be chosen to simultaneously address two different aspects of secondary injury, and will include glutamate receptor ligand peptides (anti-apoptosis), and free radical scavengers such as superoxide dismutase and catalase (anti-oxidative injury). The nanoparticle serves as a carrier and maintains autonomy of the entire system by preventing entropy-driven diffusion of the components away from each other.

A number of fundamental issues must be addressed to make possible the engineering of such biomedical nanodevices. These issues determine the specific aims to be achieved in this study. First, we plan to determine optimal conditions for the preparation of protein-nanoparticle conjugates suitable for applications as nanodevices for treatment of secondary spinal cord injury. Such parameters as nanoparticle size and material, density of surface coverage by the enzyme, and type of the enzyme binding to the nanoparticle will be used to tailor the activity of enzymes in their conjugates with nanoparticles to the desired level. Second, free radical scavenging properties of proteins conjugated to nanoparticles and their ability to bind to glutamate receptors will be characterized in vitro in the absence of cells. Third, we plan to demonstrate effectiveness of nanodevices in neural cell culture.