Nearly 3 million Americans suffer from epilepsy. In one third of these patients available antiepileptic drugs or invasive surgical procedures are not effective. With an increased understanding of the molecular, electrophysiological and genetic bases of the epilepsies, hope for a cure emerges. Understanding the fundamental basis of epilepsies, especially those that occur in children, and using this information to develop novel treatments is the mission of our laboratory.

Research in the BarabanLab is based on a multi-disciplinary strategy. Techniques include the use of in vitro brain slices for electrophysiological recording of membrane properties and synaptic function (using visualized patch-clamp and optogenetics methods); molecular analysis of gene expression using in situ hybridization, qPCR and micro-array; immunohistochemical and morphological studies of neuronal structure and protein expression; pharmacological analysis including high-throughput drug screening in zebrafish; and progenitor-based cell therapies.

Zebrafish

With recent advances in our understanding of the genetic basis for many epilepsies, hope for curative treatments and effective prevention has increased. Unfortunately, this information has not resulted in significant clinical advances and where new drugs have emerged, the average cost of research and development for each new drug is estimated at greater than $800 million. To approach this challenge from a different direction, we leverage the distinct advantages offered by a simple vertebrate - zebrafish (Danio rerio) - as a template for a genetically tractable epilepsy model compatible with rapid, cost-effective and high-throughput drug screening. Our work with zebrafish began over 10 years ago with the first adaption of acquired seizure protocols (PTZ, pilocarpine, heat, etc.) and has progressed to include stable mutant lines generated with state-of-the-art gene editing technologies. As a form of "personalized medicine" these mutants mimic known gene mutations seen in children with catastrophic forms of epilepsy.

Cell therapy

Transplantation of neuronal precursors into the CNS offers great promise for the treatment of neurological disease. Reports of neural progenitor cells with the ability to disperse and differentiate into neurons following transplantation have further raised expectations that defective brain circuits can be repaired. Using transplanted progenitors from the embryonic medial ganglionic eminence (or MGE) we are exploring the possibility that these cells will influence synaptic function in the host brain and reduce seizures. Our work takes advantage of the unique ability of MGE progenitor cells to migrate and functionally integrate as inhibitory GABAergic interneurons following transplantation. Toward the development of a "stem cell
therapy" we are transplanting MGE cells into epileptic mice to directly explore the therapeutic potential of these cells in intractable forms of epilepsy.

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