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Epilepsy at Every Angle: A Systems Biology Approach to a Cure

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Epilepsy at

by Amy Oprean

Caused by birth trauma, malformation, stroke, brain tumor or head injury and affecting as much as 1 percent of the population, epilepsy is one of the least understood human disorders in the most complicated of organs – the brain.

Groundbreaking work to unlock the disease's cure is in motion in the lab of Jeffrey Loeb, M.D., Ph.D., associate professor of neurology, member of the WSU/DMC Comprehensive Epilepsy Program and associate director of the Center for Molecular Medicine and Genetics in the School of Medicine. By applying a systems biology approach to the study of human epileptic brain tissue, Loeb and his team are working to identify a "final common pathway" of genes consistently induced at human epileptic foci. Using this pathway as a drug target, Loeb and his team will work to develop drugs that successfully prevent epilepsy, first in rats, then in humans.

This work is being performed with the Systems Biology of Epilepsy Project (SBEP), a multi-disciplinary collaboration between Wayne State experts in areas ranging from neurosurgery to information technology. The project catalogs donated human epileptic brain tissues into an integrative, one-of-a-kind database, using the power of systems and computational biology to understand the disease through its electrical, anatomical and molecular features. Funded by WSU's President's Research Enhancement Program and the National Institutes of Health (NIH), the goals of the SBEP are to find biomarkers – substances or other characteristics that can be used for diagnosis – and drug targets for epilepsy therapeutics.

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every Angle

A Systems Biology Approach to a Cure

The project has several distinct advantages over other epilepsy research, one being the ability to study the disease in human brain tissue. "With many diseases, particularly those of the brain, researchers treat animals and then try to bring the treatment to patients, and that doesn't always work," Loeb said. "That's why donated brain tissue is such an invaluable gift; it gives us the unique opportunity to start with the human disease and understand it at a level that we never could before."

Another unique aspect of the project is its use of systems biology – the ability to obtain, integrate and analyze complex data from multiple experimental sources using interdisciplinary tools. "From the neurosurgeons performing brain-removal surgery to the IT experts that maintain our database, it's the collaboration of first-rate researchers that makes this project work," Loeb said.

Donated from epilepsy patients who underwent brain surgery at Harper University Hospital and Children's Hospital of Michigan, each epileptic tissue sample has a profile in the database that includes the patient's clinical information, genes and proteins expressed and a 3-dimensional computer rendering of the tissue with a heat map of hot spots of electrical activity. The map identifies the location of seizures as well as interictal spikes – the minor, more frequent electrical discharges in the brain that occur between seizures.

The database can then process common characteristics and other relational information about the tissues. "We don't look at one particular gene, pathway or protein, but at everything simultaneously and determine which variables are the most important to the diagnosis and treatment of epilepsy," Loeb said. "I am not aware of any other programs with a database that catalogs epileptic tissue so comprehensively."

From animal model to human medicine

Loeb recently received NIH funding for a drug development facility and is partnering with drug companies to develop human drugs from his animal model. If successful, the human version of the drug will prevent human epilepsy in its early stages, before seizures ever occur. "I call it the epilepsy morning after pill," Loeb said. "If you're out riding a bike without a helmet and you fall and hit your head, taking this drug after the accident could prevent you from developing epilepsy."

Loeb will also investigate if the same drug can be used to cure epilepsy in patients months or years after a brain injury, when seizures begin.

Another major goal of the SBEP is improving diagnosis. Current noninvasive EEG techniques can only detect very large interictal spikes, with the more subtle electric activity requiring surgery in which the scalp is removed and electrodes are placed directly on the brain. Loeb is working to develop more powerful noninvasive screening methods.

"By developing a method that gives us a higher resolution, we would dramatically improve our ability to treat epilepsy patients on a number of levels, from greater success in early diagnosis, to finding more biomarkers and developing better therapeutics," Loeb said.

About Dr. Jeffrey Loeb

Dr. Loeb received his M.D. and Ph.D. in biochemistry and molecular biology, his S.M. in biochemistry and his A.B. in chemistry from the University of Chicago. Following a neurology residency at Massachusetts General Hospital and postdoctoral work in the Department of Neurobiology at Harvard Medical School, he joined Wayne State University in 1998.

Loeb will continue to build and maintain the database of epileptic tissue with the ultimate goals of developing diagnosis and disease-curing treatment for epilepsy at every stage by building and maintaining the project's growing database of epileptic tissue. "We're hoping to be successful on all fronts of disease diagnosis and prevention," Loeb said. "This work would not be possible without the strong Wayne State expertise and the patients who allow us to study their brain tissue in hopes to put an end to this life-altering disease."

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PAGE 27