BUSM **Research**

$2.5 Million Addiction Training Grant Awarded by Burroughs Wellcome Fund

Researchers from the BU Schools of Medicine and Public Health have been awarded a five-year, $2.5 million training grant by the Burroughs Wellcome Fund to support specialized, multidisciplinary PhD training for addiction scientists.

Lindsay Farrer, PhD, professor of medicine, neurology, ophthalmology, and genetics and genomics and chief of biomedical genetics at BU School of Medicine (BUSM), and Timothy Heeren, professor of biostatistics at BU School of Public Health (BUSPH), will lead the Transformative Training Program in Addiction Science (TTPAS). Farrer codirects the nation's largest genetics study of cocaine, opiates, alcohol, and nicotine addiction among Caucasians and African Americans. Heeren is currently studying the effects of maternal cocaine use on child development and the impact of alcohol addiction on HIV treatment outcomes.

"Addictions to smoking, alcohol, and illicit drugs are among the nation's most critical public health and societal problems," the proposal summary says. "The genetic vulnerability, environmental exposures, and individual behaviors that contribute to the brain dysfunction and compulsive tendencies that mark addiction make it one of the most complicated diseases to study and treat.

"Some researchers, especially at Boston University, have developed multidisciplinary collaborations, but training addiction scientists still proceeds in disciplinary silos, preventing emergence of the broad skill set needed for genuine breakthroughs. TTPAS will prepare investigators to apply diverse approaches to addiction research using tools from bench science, medicine, population studies, statistics, and computational biology."

TTPAS will have three core components: a biweekly seminar focusing on how different disciplines approach a similar issue on addiction; multiple mentors from different disciplines for each trainee and multidisciplinary dissertation committees; and a clinical module enabling trainees to interact with people in addiction treatment and recovery. To facilitate effective communication, the program includes a concentrated effort to achieve student diversity and to assure that all trainees have a thorough understanding of the intellectual bases, techniques, and languages of reporting in all the disciplines.

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The coleaders will be supported by a large group of established BU addiction scientists in medicine, psychology, neuroscience, pharmacology, biology, psychiatry, social work, engineering, biostatistics, informatics, health services research, and public health who are already linked through multidisciplinary faculty seminars.

BU faculty investigators currently direct more than 50 funded addiction-related research projects, including pharmacological and neurocognitive mechanisms regulating drug withdrawal and relapse in animal models; the relationship between long-term alcohol abuse and decrements in brain structure and cognitive-emotional functioning; and the efficacy of pharmacological treatments of alcoholism in a clinic population.

The Burroughs Wellcome Fund is an independent private foundation dedicated to advancing the biomedical sciences by supporting research and other scientific and educational activities. Within this broad mission, the fund has two primary goals: To help scientists develop as independent investigators early in their careers, and to advance fields in the basic biomedical sciences that are undervalued or in need of encouragement. ■

Research in Brief

■ Largest case series of CTE published introduces four-stage disease classification

Investigators at the BU Center for the Study of Traumatic Encephalopathy (CSTE) and the Veterans Affairs Boston Healthcare System, in collaboration with the Sports Legacy Institute (SLI), have described 68 new cases of chronic traumatic encephalopathy (CTE) among deceased athletes and military veterans whose brains and spinal cords were donated to the VA CSTE Brain Bank. Of the 68 cases, 34 were former professional football players, nine had played only college football, and six had played only high school football. The results, published in the December issue of the scientific journal *Brain*, represent the largest case series of CTE published to date, doubling the number of published CTE cases internationally.

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Ann McKee, MD, BUSM professor of neuropathology and director of the Neuropathology Service for VA New England Healthcare System and co-director of the CSTE, led the study, which is the first to characterize the pathology of the disease into four stages of severity.

CTE is a degenerative brain disease associated with repeated brain trauma—including concussions and multiple subconcussive exposures such as those in contact sports and military combat—and appears to be slowly progressive in most individuals. In the early stages, CTE is characterized by the presence of abnormal deposits of a protein called tau in the form of neurofibrillary tangles, glial tangles, and neuropil threads throughout the brain; these tau lesions eventually lead to brain cell death. Currently, CTE can only be diagnosed postmortem.

The report provides specific pathological criteria for the diagnosis of CTE and divides CTE into four stages of disease. "This study extends our knowledge concerning the spectrum of the clinical and pathological abnormalities associated with CTE," said McKee, who also is director of the Brain Banks for BU's Alzheimer's Disease Center and the CSTE, which are based at the Bedford VA Medical Center in Bedford, Massachusetts. "However, further studies are needed to investigate critical aspects of this trauma-induced neurodegeneration, including the incidence and prevalence of CTE; whether the symptoms of CTE are distinctive from other conditions; how genetics influence susceptibility or resistance to CTE; and whether other environmental exposures play an additive role in the development of CTE."

■ Potential of Differentiated iPS Cells in Cell Therapy without Immune Rejection Shown

A study by BUSM researchers showed that tissues derived from induced pluripotent stem (iPS) cells in an experimental model were not rejected when transplanted back into genetically identical recipients. The study, published online in *Cell Stem Cell*, demonstrates the potential of utilizing iPS cells to develop cell types that could offer treatment for a wide range of conditions—including diabetes, and liver and lung diseases—without the barrier of immune rejection. Ashleigh Boyd, DPhil, and Neil Rodrigues, DPhil, the study's senior authors, are assistant professors of dermatology at BUSM and researchers at the Center for Regenerative Medicine (CReM) at BU and Boston Medical Center (BMC). By returning them to a stem cell state using genetic manipulation, iPS cells can be developed from adult cell types, such as skin or blood. The study results suggest that using patient-specific iPS cells should overcome issues of immune rejection in transplantation, which will be a significant problem for potential embryonic stem cell-derived therapies. Immune rejection in transplantation is treated clinically by immunosuppressive drugs, but they can have serious side effects, including the risk of developing cancer. "If the use of immunosuppressive drugs can be avoided, as may be the case for patient-specific, iPS cell-based therapies, it would be preferable. Our results are very promising, and future work should be directed at assessing whether tissues derived from human iPS cells will similarly lack immunogenicity," said Boyd. Research reported in this release was supported by an Institutional Development Award (IDeA) from the National Institute of General Medical Sciences of the National Institutes of Health (NIH).

Using patient-specific iPS cells should overcome issues of immune rejection in transplantation.

■ Genetic Variants' Role in Increasing Parkinson's Disease Risk Studied

BUSM investigators have led the first genome-wide evaluation of genetic variants associated with Parkinson's disease (PD). The study, which is published online in *PLOS ONE*, points to the involvement of specific genes and alterations in their expression as influencing the risk for developing PD.