THE HARTWELL FOUNDATION

2006 Individual Biomedical Research Award
2008 Biomedical Research Collaboration Award

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Discovery of Small Molecules Having Neurogenic Efficacy for Treatment of Childhood Schizophrenia

Schizophrenia is a chronic, debilitating mental illness that causes people to experience the world in a way that is very different from most people. Interpersonal communication appears to be disorganized and illogical, with behavior often detached, imaginary or paranoid. Childhood schizophrenia is rare, affecting an estimated one in 40,000 children under the age of 13, with prognosis poor if onset occurs before age 10. However, by age 18, the prevalence is 1.1% of the population. It appears schizophrenia results primarily from a genetic predisposition combined with environmental stress. Although structure-function abnormalities in the part of the brain (hippocampus) responsible for controlling autobiographical memories are known to exist in schizophrenic patients, the nature of the abnormality has until recently, remained unclear. In 2003, a family with schizophrenia was described with a unique disruption in the human NPAS3 gene, which controls postnatal appearance of new nerve cells in the hippocampus. Subsequently, Dr. Pieper published (2005) on a mouse model with a deletion in the NPAS3 gene that impaired hippocampal neurogenesis and appeared to cause the behavioral and anatomical abnormalities seen in schizophrenia. Given the compelling link between NPAS3, postnatal hippocampal neurogenesis, and schizophrenia, Pieper proposes to use his unique animal model to identify molecular target-drugs that will promote neurogenesis as a novel treatment option for this form of mental illness.

Dr. Pieper also shares a Hartwell Collaboration Award with Guoping Feng, Ph.D., from Duke University for “Rapid Discovery of Small Molecules for Drug Development in an Animal Model of Obsessive-Compulsive Disorder.” Their collaborative approach is designed to identify new compounds for OCD drug development that are both pharmacologically active and non-toxic in living animals, quickly elevating promising candidates to a very early stage of discovery.