

FULL SPEAKER BIOGRAPHY and ABSTRACT

Stewart Anderson, MD Weill Cornell Medical College

Stewart Anderson, MD, is currently an Associate Professor of Psychiatry in Neuroscience at the Weill Cornell Medical Center in New York City. Dr. Anderson received his MD degree from the University of Connecticut, and his undergraduate degree in Neuroscience from Amherst College. He completed his residency training in Psychiatry at the University of Pittsburgh, where he conducted research on the neuropathology of schizophrenia with Dr. David Lewis. Dr. Anderson continues to supervise the outpatient care of people with schizophrenia in the Paine Whitney Clinic of New York/Presbyterian Hospital.

Building upon research started during his postdoctoral fellowship in the laboratory of John Rubenstein at UCSF, Dr. Anderson's laboratory at the WCMC focuses on the molecular and cellular mechanisms that govern the development of the mammalian forebrain. Of particular interest are the molecular underpinnings behind the fate determination of subclasses of GABAergic interneurons implicated in the neuropathology of schizophrenia. With guidance from the Lorenz Studer lab at the neighboring Sloan Kettering Institute, Dr. Anderson's laboratory is also engaged in a major effort to generate cerebral cortical interneurons from mouse and human stem cells. ES-derived interneurons are being applied to normative studies on interneuron development as well as to develop cell-based therapies for medication-intractable seizures. Dr. Anderson will be directing future studies on the use of patient-derived stem cells to conduct hypothesis-driven research on the causes of neuropsychiatric diseases that may be related to interneuron maldevelopment, including schizophrenia and autism.

Derivation of cerebral cortical interneurons from mouse and human ES cells and their application to normative and preclinical studies

Progress in generating forebrain neurons from embryonic stem cells (ESC) has lagged behind that from more caudal regions of the neuroaxis, particularly when their potential to survive and mature is evaluated after long-term survival following transplantation. GABAergic interneuron precursors have the remarkable ability to migrate extensively and survive after transplantation into postnatal cortex, making them attractive candidates for use in cell-based therapy for seizures and other neurological disorders. We have modified a mouse ESC line with an Lhx6-GFP reporter construct that allows for the selection of newly generated cortical interneuron precursors. Transplantation of these cells into postnatal cortex reveals robust migratory behavior as well as morphological, neurochemical, and physiological characteristics of mature interneurons. Variations in administration of Sonic Hedgehog alter gene expression at the interneuron progenitor stage and interneuron fates evaluated after transplantation. Preliminary evidence suggests that a similar approach may be useful for isolating interneurons from human ES cells. In sum, we present a novel approach for the study of cortical interneuron fate and for the development of cell-based therapies for neuropsychiatric disease.

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What is the central hypothesis of your presentation?

Can functional inhibitory interneurons be generated from embryonic stem cells.

What is the most important observation you will discuss?

An Lhx6-GFP bacterial artificial chromosome, transfected into mouse embryonic stem cells, permits the isolation of interneuron-fated neuronal precursors and their identification long after transplantation into mouse cerebral cortex.

What is the translational significance?

Interneuron transplants can reduce seizure activity in both neonatal (Baraban et al., 2009) and adult (this presentation) models of epilepsy. The generation interneurons from embryonic stem cells raises the possibility that a similar approach can be used to generate an essentially limitless supply of interneurons from human pluripotent stem cell sources for use in cell based therapy for medication resistant seizure disorders.