UCDAVIS HEALTH | MIND INSTITUTE

2018- 2019 Distinguished Lecturer Series

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Dr. Lewis is a Distinguished Professor of Psychiatry and Neuroscience, the Thomas Detre Professor of Academic Psychiatry and Chair of the Department of Psychiatry at University of Pittsburgh. He also serves as Director of the Translational Neuroscience Program and of a NIMH Conte Center for Translational Mental Health Research, which is focused on understanding the role of cortical circuit dysfunction in the pathophysiology of schizophrenia. He received his medical degree from the Ohio State University, completed residencies in internal medicine and in psychiatry at the University of Iowa, and received his research training at the Research Institute of the Scripps Clinic. Dr. Lewis has published over 480 scientific articles. In recognition of his research accomplishments, he has received the American Psychiatric Association's Research Award, NIMH Senior Scientist and MERIT Awards, and the Lieber Prize for Schizophrenia Research from NARSAD. He is an elected member of the National Academy of Medicine and of the Association of American Physicians.

Presentation Title: A Neural Circuitry Substrate for Cognitive Dysfunction in Schizophrenia

Deficits in cognitive control, the ability to adjust thoughts or behaviors in order to achieve goals, are now considered to be a core feature of schizophrenia and to be the best predictor of long-term functional outcome. Cognitive control depends on the coordinated activity of a number of brain regions, including the dorsolateral prefrontal cortex (DLPFC). Subjects with schizophrenia exhibit altered activation of the DLPFC, and reduced power of frontal lobe gamma band (~40 Hz) oscillations, when performing tasks that require cognitive control. Gamma oscillations require robust activity in the reciprocal connections between the parvalbumin-containing basket cell class of cortical GABA neurons and neighboring pyramidal neurons. Thus, alterations in either the excitatory or inhibitory synapses in this circuit could contribute to impaired gamma oscillations and cognition in schizophrenia. This presentation will review the evidence for alterations in components of this circuit in the DLPFC of subjects with schizophrenia. Current findings converge on the hypothesis that the primary disturbances are in pyramidal neurons with the changes in parvalbumin neurons representing compensatory responses to maintain excitatory-inhibitory balance in DLPFC networks. In concert, the findings provide both a circuity-based explanation for gamma oscillations impairments and cognitive disturbances in schizophrenia and a possible mechanistic substrate for the emergence of psychosis.