Kristen Brennand, Ph.D., is a biologist who has pioneered stem cell studies in the field of schizophrenia research. She is an Associate Professor of Genetics and Genomics in the Neuroscience and Psychiatry department at the Icahn School of Medicine at Mount Sinai in New York. She trained in developmental and stem cell biology at Harvard University and in neurobiology during her postdoctoral research at the Salk Institute for Biological Studies. By combining expertise in stem cell biology and neurobiology, she has helped to pioneer a new approach in the study of psychiatric disease.

Due partly to the lack of live patient material for study, the cellular and molecular mechanisms in brain cells associated with the initiation and progression of schizophrenia remain unknown.

Postmortem studies of the brain tissue of deceased patients typically reveal defects in mature neurons, such as reduced neuronal size and reduced density of small features called dendritic spines that enable neurons to communicate. These abnormalities have been observed in neurons of the prefrontal cortex and hippocampus, in addition to abnormalities of neuronal organization, particularly in the cortex. Yet the processes that result in these changes are not understood in the context of the living, developing brain.

Dr. Brennand has obtained skin samples from well-characterized cohorts of children and adults with schizophrenia as well as from healthy controls. Her team has reprogrammed these skin cells so that they revert to an earlier developmental state in which they acquire the ability of stem cells to develop into other cell types. Called human induced pluripotent stem cells (hiPSCs), they are directed to differentiate into neural cells and their progenitors. By identifying differences between healthy and diseased neurons, Dr. Brennand and colleagues hope to clarify the mechanisms that result in schizophrenia and to screen for new drugs with which to reverse the cellular defects contributing to disease.

“Dr. Brennand’s work is critically deepening our mechanistic insights into how specific types of DNA mutations or sequence variants contribute to the neurobiology of schizophrenia. The long-term importance of such work can hardly be underestimated, given that schizophrenia is in genetic terms extremely heterogeneous and complex, while at the same time access to the diseased organ, the brain, is limited.”

—Schahram Akbarian, M.D., Ph.D., 2018 recipient of the Lieber Prize