# DEPARTMENT OF CHEMISTRY AND ENVIRONMENTAL SCIENCE SEMINAR SERIES SPRING 2022

# DATE: WEDNESDAY, APRIL 13, 2022 LOCATION: TIERNAN HALL – LECT. HALL 2 TIME: 1:00PM-2:20PM

### **GUEST SPEAKER**

Dr. Bin Xu Assistant Professor Columbia University Medical School New York, NY

#### <u>TOPIC</u>

Understanding Genetic Contribution to Neuropsychiatric Disorders Using Patient iPSC Derived Models

## **ABSTRACT**

Neuropsychiatric disorders (i.e. autism, schizophrenia etc.) present a huge burden to the patient, their family, and society. Our understanding of the underlying pathophysiologic mechanisms is largely limited by a lack of functional validation in patients. We established state-of-the-art patient induced pluripotent stem cell (iPSC)-derived organoid models to gain cellular and molecular insights of the patients carrying high risk genetic lesions. This patient iPSC-based disease modeling system proposed has strong translational potential for developing novel therapeutic strategies for this debilitating mental illness.

## **BIO**

Dr. Bin Xu. I have a broad background in genetics, neurobiology and bioinformatics, with specific training and expertise in key research areas for neuropsychiatric diseases. During my postdoc training at the Department of Physiology, Columbia University Medical Center, I developed analysis methodologies to show, for the first time in the field, that the frequency of de novo copy number variations (CNV) is collectively higher in people with schizophrenia without family history than that in health controls (Xu et al., 2008). Meanwhile, using mouse models, I studied the neurobiological aspects of the 22q11.2 microdeletion, a recurrent human CNV associated with high risk of schizophrenia and other mental disorders. I laid the groundwork for the proposed research by establishing the direct pathogenic evidence of abnormalities in miRNAs and their contributions to the neuronal and behavioral deficits associated with 22q11.2 microdeletion (Stark, Xu et al., 2008). As an Assistant Professor of Clinical Neurobiology at Department of Psychiatry, Columbia University Medical Center, I am continuing to study the functional impact of various genetic mutations identified through human genetic studies because I believe that identification of recurrent rare genetic variants embedded in patient genomes and understanding their impact on the clinical phenotypes holds great promise for identification of novel treatments of these debilitating disorders. Recently I developed new research strategy to analyze exome sequencing data from a schizophrenia patient cohort which demonstrated that protein altering *de novo* mutation rate, especially the number of nonsynonymous mutations, is significantly higher in the schizophrenia cohort than in the general population (Xu et al., 2011).

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Furthermore, I was able to demonstrate that the *de novo* mutations are part of a larger brain developmental framework and showed that many mutated genes play a critical role during the prenatal stage of brain development (Xu et al., 2012). Finally, I identified MIRTA22, a key novel molecule that contributes to neuronal morphology deficits in the mouse model of 22q11.2 microdeletion by combining gene expression profiling technology at molecular level and neuroimaging technology at cellular level (Xu et al., 2013). A key bottleneck of the field is to understand the underlying disease mechanism in patients with neuropsychiatric disorders that can lead to novel, targeted treatments. In this proposal, we assemble a new interdisciplinary team. We aim to establish a clinically relevant pre-clinical platform to evaluate the mechanisms that underlie various genetic mutations.