In Person Lecture: Pathways to Psychosis: Integrating Rare and Common Variants Approaches

Heterogeneity of the genetic architecture of psychosis implicates both common and rare genetic variants, the former allowing generation of polygenic risk scores (PRS) that confer small effect sizes, while the latter can help identify rare variants with large effect size that can point to more specific mechanisms. Together they may enhance discovery of biomarkers for early identification and intervention. The seminar will first highlight multimodal lines of research examining the psychosis dimension in the population at large and in 22q11.2 deletion syndrome (22qDS) that confers a 25-fold increased risk for psychosis. Topics reviewed will include clinical presentation and course, neurobehavioral functions, and multimodal neuroimaging. Dr. Gur will then focus on 22qDS as a translational window to advance underlying biology and therapeutics. Rodent models probing neurobehavioral domains impacted in humans and iPSC investigations will be highlighted. The final part will discuss challenges and promises of such convergent efforts with special emphasis for Medical Scholars.