# PrgmNr 2631 - Schizophrenia risk mediated by microRNA target genes in 22q11.2 deletion syndrome

**View session detail**

**Author Block:** **S. Ying**[1], Z. Zhang[1], R. K. Yuen[2], A. S. Bassett[3]; [1]Univ. of Toronto, Toronto, ON, Canada, [2]The Hosp. for Sick Children, Toronto, ON, Canada, [3]Univ of Toronto, Toronto, ON, Canada
**Disclosure Block:** **S. Ying:** None.
**Background**: 22q11.2 deletion syndrome (22q11.2DS) is associated with an over 20-fold increase in risk for schizophrenia. The 22q11.2 deletion region contains *DGCR8*, encoding a protein in the miRNA biogenesis pathway; global miRNA dysregulation imparted by *DGCR8* haploinsufficiency may play a role in mediating increased risk for schizophrenia. There is also evidence that rare genome-wide copy number variants (CNVs) increase schizophrenia risk in 22q11.2DS, and in the general population. We hypothesized that, within 22q11.2DS, in those with schizophrenia, there would be an enrichment of miRNA target genes that are overlapped by rare genome-wide CNVs.
**Methods**: We derived experimentally supported miRNA target genes (n=8464) from DIANA-TarBase, and obtained data available on rare genome-wide CNVs that overlapped genes in 22q11.2DS. We compared results for the miRNA target genes overlapped by these CNVs in 218 individuals with 22q11.2DS, with and without schizophrenia.
**Results**: Consistent with our hypothesis, among the 22q11.2DS cohort, we found a higher proportion of subjects in the schizophrenia group to have one or more miRNA target genes overlapped by a rare CNV (odds ratio (OR)=2.29, p=0.004). The miRNAs whose target genes contributed most to this differential target gene burden included miR-17-5p, miR-124-3p, and miR-342-3p, miRNAs with previous evidence for differential expression in 22q11.2DS experimental models and/or in schizophrenia and related neuropsychiatric disorders. Gene set enrichment results supported a role for miRNA target genes that belonged to several sets previously implicated for schizophrenia in the general population, including targets of FMRP and post-synaptic density (PSD)-related, when compared to all genes in the genome (FDR**Conclusion**: These data are the first to support a possible synergistic disruption of gene expression involving the target genes of dysregulated miRNAs and genome-wide rare CNVs as part of the complex mechanisms that increase risk for schizophrenia in 22q11.2DS. A comparable mechanism may be relevant to individuals with idiopathic schizophrenia and could therefore have implications for proposed novel miRNA-based therapeutics.