AS23-01 - TRAVELLING WITH HIGH-SPEED THROUGH THE FOREST OF SCHIZOPHRENIA GENETICS: FROM GWAS TO BIOLOGY

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Genome-wide association studies (GWAS) have been successful in identifying replicable susceptibility loci for schizophrenia. The most replicated GWAS association is at chromosome 6p (MHC). However, identifying the causal gene networks, the specific genes, and functional variants has proven difficult for schizophrenia, just like for most other complex disorders. Since almost all GWAS associated SNPs are either intergenic or intragenic but uncorrelated with obvious candidate functional variation such as missense or nonsense SNPs, it is likely that gene regulation is involved in schizophrenia susceptibility. This suggests that an integrative systems biology approach, one that combines DNA sequence and structural information with functional data, will be useful to study the biological mechanisms underlying the GWAS statistical associations and to identify new disease genes. To this end, we are investigating the genetic etiology of SZ by generating transcriptional profiles under conditions designed to reveal biological mechanisms involved in conferring risk, for example, by using environmental perturbations of etiological and pharmacological relevance on simple cellular models. This strategy, by refocusing transcriptional activity towards targets of specific environmental perturbations, is also useful for testing specific hypotheses of schizophrenia pathophysiology independently of GWAS results. I will be presenting transcriptional profiles at baseline that show association with schizophrenia, and the results of applying a number of external stimuli.

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