Proteogenomic analyses of Lingo-1 and the Nogo receptor in schizophrenia

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Abstract

PROTEOGENOMIC ANALYSES OF LINGO-1 AND THE NOGO RECEPTOR IN SCHIZOPHRENIA

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Purpose: Schizophrenia is a severe neuropsychiatric disorder with an elusive aetiology, thought to result from abnormal brain development. Nogo, an oligodendrocyte bound molecule responsible for CNS myelin regulation, neurite outgrowth and plasticity during neurodevelopment, binds to its receptor NgR, located on axonal membranes and interacts with its co-receptor Lingo-1. This study investigated polymorphisms within the Lingo-1 and NgR genes in schizophrenia; and examined the Lingo-1 and NgR protein levels within the human dorsolateral prefrontal cortex (DLPFC) in schizophrenia.

Methods: Human matched case control DNA samples (n=268/group) from the Australian Schizophrenia Research Bank were purified and then genotyped to assess polymorphisms within the Lingo-1 and NgR genes using restriction fragment length polymorphism, and Multiplex MassARRAY genotyping assays. Human DLPFC matched case control samples (n=37/group) from the NSW Tissue Resource Centre were used to assess Lingo-1 and NgR protein levels by immunoblotting.

Results: One genetic marker, NgR rs701427, had a significant association with schizophrenia (p = 0.02). NgR protein expression was significantly decreased by 16% (p < 0.001) and Lingo-1 protein expression was significantly increased by 12% (p = 0.006) in the DLPFC of schizophrenia subjects. There was a significant correlation between NgR and Lingo-1 protein levels (p = 0.017).

Conclusion: This study shows strong evidence for NgR/Lingo-1 involvement in schizophrenia in both genetics and protein. The NgR and Lingo-1 gene mutations found to be associated with schizophrenia in this study may result in the dysregulated NgR and Lingo-1 protein expression. Further studies are required in order to investigate the implications of these genetic and proteomic alterations to the aetiology of schizophrenia.