

INCREASED GENE MUTATION RATE IN THE NFKBIA PROMOTER REGION IN PERIPHERAL LYMPHOCYTES OF THE PATIENTS WITH MULTIPLE SCLEROSIS

J. Yan¹, M.P. Pender², P.A. McCombe¹, J.M. Greer¹

¹*UQ Centre for Clinical Research & ²School of Medicine, the University of Queensland, Brisbane, Australia*

j.yan@uq.edu.au

Increased activation of the transcription factor NF- κ B has been implicated in development of many diseases, including multiple sclerosis (MS), and may relate to dysfunction of some of the multiple inhibitory molecules that normally act to keep the NF- κ B pathway under tight regulation. We have investigated whether genes encoding some of these inhibitory molecules are different in people with MS compared to healthy individuals.

Preliminary data suggested an increased frequency of mutations and polymorphisms in the promoter region of the NFKBIA gene, which encodes one of NF- κ B inhibitors, I κ B- α , in people with MS compared to healthy controls. To confirm this finding, we investigated the frequency of NFKBIA mutations and polymorphisms in 560 MS DNA samples from the ANZgene bank (180 relapsing–remitting MS; 180 secondary progressive MS; 200 primary progressive MS), and additional healthy individuals as controls. Sequencing was successful for 554/560 ANZgene samples. Overall, the frequency of mutations or polymorphisms was increased in people with MS compared to healthy controls ($P=0.03$; $OR=2.2\{1.1-4.8\}$); however, this effect was largely due to a significantly higher frequency (12.7%) in patients with primary progressive MS compared to healthy controls ($P=0.005$; $OR=3.0\{1.3-6.7\}$).

The results suggest that mutations or polymorphisms in the promoter region of NFKBIA may contribute to the development of MS in some individuals, particularly in a subgroup of patients with primary progressive MS.

We are currently investigating how these changes to the NFKBIA promoter that are found in MS patients affect the expression of I κ B- α within immune cells.