The role of adaptive immunity in Parkinsonian syndromes

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Neuronal surface-directed antibodies (NSAbs) have pathogenic potential. This project aims to determine the presence and target(s) of NSAbs in patients with idiopathic Parkinson's disease (PD). We aim to ask if novel and established antibody-targets are present at onset of PD and whether they develop during the disease course in varying phenotypic severities. These antibodies may be pathogenic but, more likely, could modify disease course and prognosis.

We will examine binding to cultured live hippocampal and dopaminergic neurons using 64 available paired sera and CSFs from PD patients at diagnosis, 198 patients with extreme endophenotypes of PD, and IgG extracted from PD-patient brains. Also, to study patient-specific neuronal antigen expression, we will determine binding of patient IgG to their own inducible-pluripotent stem cell-derived dopaminergic neurons. The presence of NSAbs in one culture system will initiate the proteomic methods to detect novel antigens. In addition, autoantibody binding to the our primary candidate antigen in PD, alpha-synuclein, will be tested using cell-based assays under development in Oxford.

This study aims to establish the presence of disease-relevant autoantibodies in neurodegeneration, and inform novel mechanisms of disease initiation or perpetuation with potential for novel biomarker development and disease-modification with immunotherapies.