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Th17 lymphocyte spearheads the immune attack in Parkinson's disease: New evidence for neuronal death.

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The exact etiology for Parkinson's disease (PD) continues to remain complex and elusive. Several lines of etiologies have been investigated including gene mutations, exposure to environmental toxins, mitochondrial dysfunction and increased oxidative stress to the neurons. There continues to be mounting evidence to support an immune dysregulation and an aberrant inflammatory process contributing to pathogenesis.[1] Recent studies have shown that, despite the dogma that peripheral immune cells do not cross the blood brain barrier, in fact, there is infiltration of peripheral immune cells into the central nervous system and autoreactive T cells are directed against alpha-synuclein as plausible associations of significant neurodegeneration.[2] However most data has emerged from animal models with no clear understanding on the exact pathogenic role of lymphocytes and how they contribute to progression of human PD.[3] Furthermore it is unclear whether the immune attack in PD is led by the innate immune cells or the reactive immune cells.[4]

In this study by Sommer et al,[5] peripheral blood T cells are co-cultured with autologous fibroblasts. The fibroblasts are reprogrammed into human induced pluripotent stem cells, which then further differentiate into midbrain neurons. The investigators find the midbrain neurons to succumb to death if co-cultured with T cells that are drawn from PD patients whereas they survive when the source for T cells is age-matched controls. Neuronal death is noted to accelerate when co-cultured with IL17 producing CD4+ T (Th17) lymphocytes. Whereas these neurons are rescued from dying when IL17 receptor is blocked or when

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human anti-IL17 antibody (Secukinumab) is applied to the culture. The effects of IL17 are PD specific considering a substantially increased gene dysregulation upon exposure to IL17 in the midbrain neurons of PD patients compared to the healthy controls. The IL17 expression for the lymphocytes is also not affected by addition of primary astrocytes.

Validation of Sommer et al findings will require further testing in a PD model that in vivo captures the complexity of pathogenesis. Future studies will need to focus on antigen specificity for Th17 cells considering the current study does not implicate alpha-synuclein as the primary antigen and the role of microglia are also important to investigate.

While the study findings suggest Secukinumab (an FDA approved drug for treatment of psoriasis) may have a potential neuroprotective role in PD, many further tests will be necessary prior to a successful clinical application. Nevertheless, a direct evidence for immune attack led by Th17 lymphocytes in PD is no doubt exciting and indisputably pushes the envelope.

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