

Molecular mechanism of innate signalling in the immune and nervous system.

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Name of Fellow

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Institution

Funder

Wellcome Trust

Contact information of fellow

Country

United Kingdom

Title of project/programme

Molecular mechanism of innate signalling in the immune and nervous system.

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01/03/13

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7.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Neurodegen | Parkinson

Research Abstract

My goal is to take an inter-disciplinary approach to address two major objectives. Firstly I aim to

understand the supramolecular organization of innate immune signaling platforms, their dynamics and the molecular basis of cooperative assembly and signaling crosstalk with reference particularly to the Toll and Toll-like receptors (TLR). We will define the protein-protein interfaces between receptors, ligands and adaptors that are critical to TLR signal transduction using an integrated structural biology approach. We will also study the molecular basis of signalling cross-talk from the TLR pathway with reference to the adaptor BCAP, that links to PI3 kinase and TRIF which couples interferon beta and apoptotic signals. Our second objective is to study the role of Toll and TLRs in neurogenesis and neurodegeneration. Specifically we will determine how LRRK2, a protein kinase that is a genetic risk factor for Parkinson's disease, and TLRs are activated in microglia and how activation is linked to neurotoxicity. Specifically we will analyse what cellular factors activate TLRs in the absence of infection and what proteins associate with LRRK2 in the presence and absence of signalling. We will also use transcriptomic and proteomic approaches to identify which genes are expressed when microglia are activated and what proteins are substrates for the LRRK2 kinase. An understanding of the events that initiate and maintain neurodegeneration will lead to the development of novel therapies aimed at inhibiting these processes.

Types:

Fellowships

Member States:

United Kingdom

Diseases:

Parkinson's disease & PD-related disorders

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