Role of complement classical pathway protein C1q in neuroinflammation and neurodegeneration

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C1q is the first subcomponent of the complement classical pathway. Classically, it is known to bind to immune complexes containing IgG and IgM and trigger the complement cascade leading up to the generation of membrane attack complex and C3a and C5a fragments that cause cellular infiltration. In addition, C1q is also known as a charge pattern recognition molecule which is involved in the clearance of non-self and altered self. It has become increasingly evident that C1q (and other complement proteins) can be made locally by microglia, neurons and astrocytes within the central nervous system. Thus, C1q can bind beta amyloid aggregates and precipitate neuroinflammation and neurodegeneration in Alzheimer’s Disease (AD) via classical pathway as well as microglia activation. It turns out that developmental expression of C1q is essential for synaptic pruning and C1q deficiency can have aberrant neuropathological consequences. Therefore, under pathological conditions, regulating C1q expression and its target binding can have therapeutic benefits. We have identified two recombinant inhibitors of the classical pathway that interfere at the C1q function level. We have also immunologically characterised a natural model of AD, a Chilean rodent called *Octodon degus*, and found a direct link between complement activation (via C1q upregulation) and burrowing behaviour.

Biography

Uday Kishore completed his PhD from University of Delhi and did post-doctoral training at the Salk Institute (California) and University of Oxford. He is currently the Director of Centre for Infection, Immunity and Disease Mechanisms at Brunel University London. Prof Kishore’s research interests include understanding role of innate immunity in human health and disease. He is a recipient of fellowships from NASA, Wellcome Trust, Medical Research Council UK, and Humboldt Foundation. He was recently awarded the prestigious Mother Teresa Excellence Award in 2014.

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