Novel Regulatory Mechanisms In Innate Immune Signalling

Dr Endre KISS-TOTH
Reader in Cell Signalling
Department of Infection, Immunity and Cardiovascular Disease
University of Sheffield

Abstract
Appropriate regulation of inflammatory cell signalling is critical to physiological responses; dysregulated signalling underpins the development of disease. Our group have discovered several novel regulators of inflammatory signalling and have been involved in characterising the physiological importance of some of these novel genes. This journey has started with describing basic cellular regulatory mechanisms, mostly using mammalian cell lines and recently led us to develop murine models of disease to understand the physiological action of our favourite genes.

In my talk, I will first review our work on the discovery and initial characterisation of the tribbles family of pseudokinases as regulators of innate immune signalling, followed by the recent extension of these studies into investigating how macrophages and their inflammatory phenotypes influence plasma lipid homeostasis and will summarise some lessons we learned about the complexity of inter-tissue communication that drives the development of hyperlipidaemia and atherosclerosis.

In the second part of the seminar, I will describe the recent discovery of a novel transmembrane protein, which appears to be an important regulator of STING, thus shaping innate immune responses against a range of pathogens.

About the speaker
I joined the University of Sheffield in 1988 as a postdoctoral researcher and was working on the development and implementation of a novel genetic screening approach. This is based on detecting the bioactivity of proteins, which are transiently overexpressed in mammalian cells. We used this approach to identify novel components of signalling pathways key in innate immunity. I have kept interest and association with this screening platform ever since and have recently been leading research identifying novel inflammatory regulators of macrophages.

In 2000, I was awarded a Career Development Fellowship by the Arthritis Research Campaign (now AR-UK) to characterise the mode of action of a novel family of proteins, tribbles.

In 2002, I joined the Cardiovascular Research Group as a Lecturer and developed my interest in tribbles further, by investigating their biological importance in vascular cells.

I am currently a Reader in the Department of Cardiovascular Science with the same overall focus around regulation of innate immune signalling.