The Role Of Apoptosis, Necroptosis And Microbiota In Skin Inflammatory Responses

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Abstract
TNF is a master regulator of inflammation. Until recently, it was believed that TNF functioned by promoting transcription of inflammatory mediators such as cytokines and chemokines, however we and others have revealed that TNF induced cell death can be a major driver of inflammation, presumably by promoting release of Danger Associated Molecular Patterns (DAMPs) from dying cells. This has led major pharmaceutical companies to develop inhibitors of TNF induced cell death that are currently in trials for a range of inflammatory diseases including psoriasis. I will discuss our results from a large number of genetically modified mice where we have explored the role of apoptosis, necroptosis and the microbiota in skin inflammation.

About the Speaker
John completed a law degree in King's College, London, before seeing the error of his ways and obtaining a second degree in Biochemistry at Churchill College, Cambridge (1992). He completed a PhD in Zürich, Switzerland, with Prof. Walter Schaffner, looking at the role of DNA methylation in the regulation of transcription (1997). A Swiss fellowship allowed John to do a post-doc with Prof. David Vaux in the WEHI, Australia (1997-2005), where he focused on cell death mechanisms and in particular the role of Inhibitor of Apoptosis proteins (IAPs) in regulating cell death. After a five year stint running a lab in La Trobe University, Australia, he returned to the WEHI (2011) where his lab focuses on the programmed cell death pathways: apoptosis and necroptosis, and their intersection with cancer and inflammation.

He has a strong interest in translational research and was a member of the Scientific Advisory Board of TetraLogic Pharmaceuticals Corporation for 5 years. In this capacity he has contributed to our understanding of how IAP antagonist drugs, now called Smac-mimetics, kill cancer cells and the development of a well tolerated Smac-mimetic, called birinapant (Vince, 2007; Lalaoui, 2016; Brumatti, 2016). Smac-mimetics such as birinapant work to kill cancer cells by inducing inflammatory cytokines such as TNF and simultaneously sensitising cells to cell death induced by these cytokines. They are widely used together with TNF to induce necroptosis and John's lab has a keen interest in exploring the mechanisms and consequences of this newly recognised type of cell death (Rickard, 2014; Hildebrand; 2015; Brumatti, 2016).