

Investigating the contributions of inflammation and antigen depot to adjuvant function

James Brewer, Sharon Hutchinson, Abigail Pollock and Paul Garside

Centre for Biophotonics, Strathclyde Institute for Biomedical Sciences, University of Strathclyde, Glasgow, G4 0NR.

T. 0141 548 4022

F. 0141 548 4887

E. james.brewer@strath.ac.uk

Although we may think that we understand how vaccine adjuvants work, we cannot satisfactorily explain why certain vaccine adjuvants and/or delivery systems are more or less effective at inducing immune responses, or indeed why they promote the induction of particular types of response. A number of *in vitro* studies indicate that T cell activation, differentiation and function are regulated by APC factors, specifically the phenotype and activation state of APCs as well as the magnitude and duration of their antigen presentation. While it appears that adjuvants mediate their effects indirectly via APCs, it is unclear how, or if, any of the APC parameters noted above are influenced by vaccine adjuvants. Generalising the relationships between adjuvants and APC function is confounded by the diversity of adjuvant formulations available, for example various combinations of depot forming and inflammatory adjuvants. Importantly, few if any, of the APC factors defined above have been defined for these agents *in vivo*. This is a significant omission, as it is clear that the component parts of the immune system do not work in isolation and their interactions are dynamic and occur in distinct and specialised micro- and macroanatomical locations that can only be fully determined in real time, in the physiological context, *in vivo*. Therefore, we have analysed the impact that inflammatory and depot-forming adjuvants have on the phenotype, activation state, processing and presenting capacity of APC and the subsequent consequences of this for T cell activation, differentiation and function. Such studies have generally been performed *in vitro*, however, only by performing such detailed and fundamental studies *in vivo* can we fully understand the cellular and molecular interactions that control the immune response. This information is a prerequisite if we are truly to design, build and target vaccines and therapeutic strategies effectively.