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STePS - Signalling compartmentalization and vesicle Trafficking at the Phagocytic Synapses

A key feature of the immune response is its specificity and macrophages must be able to discriminate precisely between an infectious stimulus and a non-infectious one and tune their response in accordance with the molecular context in which the target particle is recognized. In recent years, scientists have proposed the concept of the phagocytic synapse, to stress the fact that a particle does not engage only one receptor on the cell surface; instead, an array of receptors interacts with a specific pathogen, either sequentially or simultaneously. Indeed, the tightly controlled and specific responses of macrophages require the establishing of checkpoints for signalling and the phagocytic synapse represent an exquisite site for cross-talk among several signalling pathways. Although we can describe detailed signalling pathways for most of the single receptors acting at the phagocytic synapse, we still do not know how these pathways are integrated during the various phases of macrophage responses. An integrated view of phagocytic synapse signalling would allow us to understand the contribution of each ligand-receptor pair to macrophage dysfunctions in pathology and to design novel immunotherapeutic strategies. The aim of STePS is to provide a deeper understanding of the molecular interactions leading to the orchestration of phagocytic synapses for phagocytosis and activation, two events crucial for immune responses to pathogens as well as for inflammation. In particular, we will focus on three fundamental aspects that bring together the fields of immunology and cell biology: establishment of dynamic platforms for recognition and signalling at the plasma membrane; vesicle trafficking to the plasma membrane; signalling compartmentalization for specific cell functions. Importantly, these mechanisms will be analysed in the context of physiological and pathological conditions, thus providing answers to both basic and translational biomedical research questions.

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