

## Membrane traffic and cytoskeleton: relevance for host-pathogen interactions

### Soldati lab website:

[http://www.unige.ch/sciences/chimie/?enseignants/soldati\\_fr.php&port=etu&hl=1?port=last](http://www.unige.ch/sciences/chimie/?enseignants/soldati_fr.php&port=etu&hl=1?port=last)

The major aim of the Soldati group is to understand the integration, the cooperation of signalling, cytoskeleton and membrane trafficking in phagocytosis and its relevance to host-pathogen interactions. To this end, they use the social amoeba *Dictyostelium* as a model organism as it is a professional phagocyte very similar to mammalian phagocytes of the innate immune system in morphology and behaviour, but which is genetically and biochemically tractable (Cosson & Soldati, 2008). In recent past, their work has concentrated on the lipidomic and proteomic characterisation of phagosomal components (Gotthardt et al, 2006; Dieckmann & Soldati, 2009), as well as on the molecular dissection of the role of actin and class I myosins in the formation and closure of the phagocytic cup, and in the flux of membrane during maturation and recycling from endosomes/phagosomes (Soldati & Schliwa, 2006). The projects are being extended to include other major regulators of the specificity and efficiency of membrane transport such as the Rab GTPases and the Exocyst tethering complex.

Crucially, the group has established *Dictyostelium* as a model host to study infection and dissemination of pathogenic mycobacteria (Hagedorn & Soldati, 2007). Interestingly, pathogenic mycobacteria such as *M. tuberculosis*, *M. marinum* and *M. leprae* utilise common strategies to invade phagocytes of the innate immune system, manipulate their otherwise bactericidal phagocytic apparatus and increase the success of cell-to-cell transmission. *M. marinum*, a fish pathogen, is the closest relative to the tuberculosis group of mycobacteria and provides a powerful model to study the pathogenesis of tuberculosis in genetically tractable model organisms, such as *Drosophila* and zebrafish (Hagedorn & Soldati, 2009). In particular, the Soldati group discovered that both *M. marinum* and *M. tuberculosis* can escape from their vacuole into the cytosol, and are then ejected from the cell through an F-actin structure, they named the ejectosome (Hagedorn et al, 2009). Ejection is crucial for the maintenance of an infection and is a concerted process that requires both host and pathogen factors. They propose that this specific strategy evolved as a necessity for the release of a cytosolic pathogen in a mutually beneficial manner, and discuss its evolutionary origin and relevance for dissemination of a mycobacterial

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