

Wednesday August 8 , 2018 - 10h30
Conference room AI 1153 (*)- EPFL - Lausanne

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“Mycolactone, a pathogen-derived inhibitor of Sec61 with immunosuppressive properties”

Host: Prof. Johan Auwerx

Abstract:

Mycolactone is a diffusible macrolide produced by the human pathogen *Mycobacterium ulcerans*, the causative agent of necrotic skin lesions called Buruli ulcers. In addition to displaying cytotoxic properties locally, mycolactone down-regulates the host immune responses. In vitro work had indicated that mycolactone blocks the co-translational translocation of secretory proteins into the endoplasmic reticulum (ER), leading to their cytosolic degradation by the ubiquitin:proteasome system. We demonstrated that mycolactone targets the alpha subunit of the Sec61 translocon (Sec61 α). Using quantitative proteomics, we showed that Sec61 blockade impairs key immune processes, such as antigen presentation by dendritic cells, T cell activation and migration. These global analyses also revealed that mycolactone-driven Sec61 blockade triggers ER stress responses, eventually causing apoptotic cell death.

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