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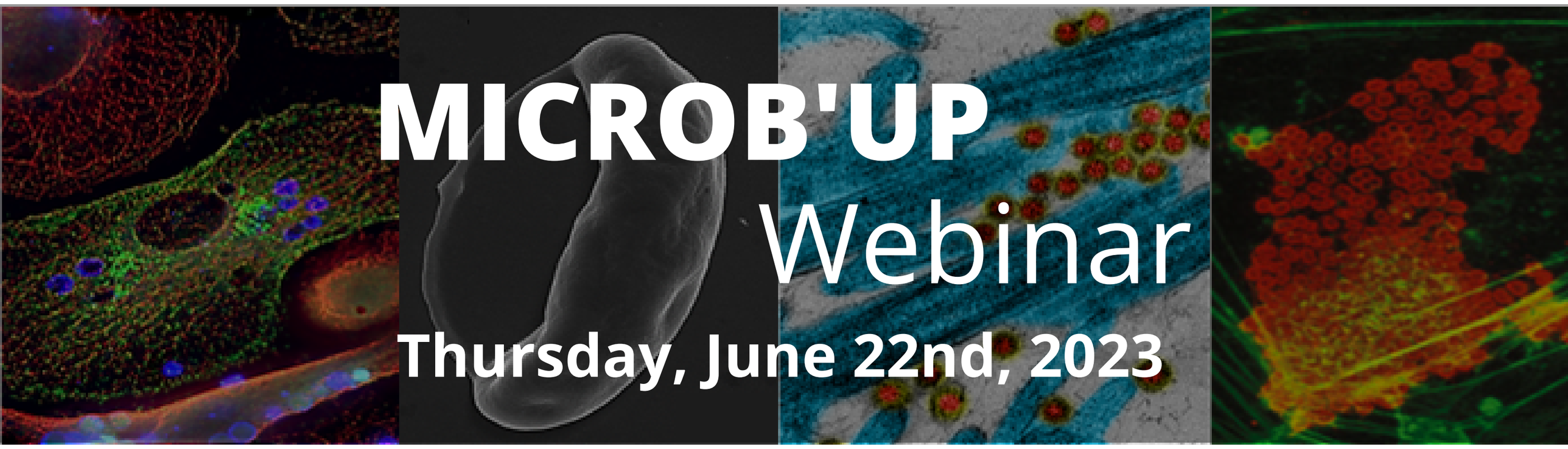

MICROB'UP Webinar

Thursday, June 22nd, 2023

"Pathogen sensing, inflammation and cell death"

Host Laboratory : Niedergang Lab, Biology of phagocytes, infection and immunity

22nd June 2023

At 11 am
Paris Time (GTM +2)

ZOOM, follow the link bellow

Registration
https://microb-up.u-paris.fr/webinar-22nd-june-2023/

11H00

Petr Broz

UNIL, Lausanne

Pyroptosis, a Lytic Cell Death Coordinating Host Defense and Inflammation

@broz_lab @unil

Petr Broz received his PhD in Microbiology in 2006 from the University of Basel working on the structure of bacterial type 3 secretion systems with Guy R. Cornelis. He joined Denise Monack at Stanford University in 2008 as postdoc, where he started to work inflammasome complexes in the context of bacterial infections. After working as an SNSF Assistant Professor from 2013-2017 in Basel, he joined the Department of Immunobiology at the University of Lausanne as an Associate Professor in October 2017 and he became Full Professor in February 2022.

11H50

Delphine Bonhomme

Institut Curie

The atypical LPS of Leptospira interrogans : from TLR4-TRIF escape to pyroptosis prevention

@institut_curie @DelphineBonhom

Delphine Bonhomme obtained her Ph.D in Institut Curie and is currently a postdoc in Insitut Curie. Her research focuses on Toll-Like-receptors and caspases. During her thesis, she worked on escape mechanisms of Leptospira interrogans, and she is now investigating novel TLRs signaling partners identified by homology with bacterial defense mechanisms.

12H05

Cécile Arrieumerlou

Institut Cochin

Spatio-temporal dynamics of ADP-heptose sensing during bacterial infection

@InstitutCochin @ArrieuLab

Cécile Arrieumerlou is a group leader at Institut Cochin. During her carrier, she has studied the spatio-temporal dynamics of several mechanisms of signal transduction involved in T cell activation, chemotaxis and bacterial infection. She is currently focusing on pathogen recognition mechanisms using Shigella flexneri infection as the main model system.

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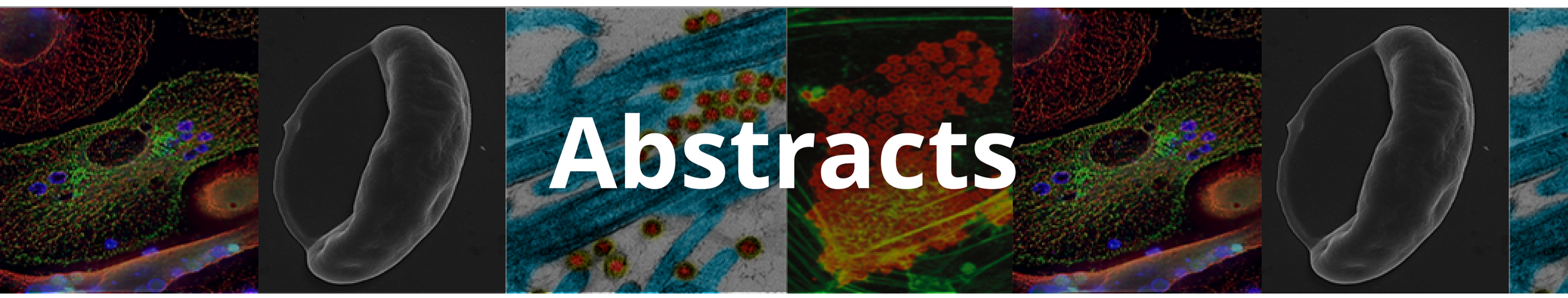

Abstracts

Petr Broz

UNIL, Lausanne

Pyroptosis, a Lytic Cell Death Coordinating Host Defense and Inflammation

Pyroptosis is a necrotic form of cell death that was initially found to be induced upon activation of inflammatory caspases by inflammasome complexes. Inflammasomes are cytosolic signaling complexes that are assembled by pattern recognition receptors in response to infection, damage or noxious insults. Mechanistically, pyroptosis induction requires cleavage of the caspase substrate gasdermin D (GSDMD), and the release of the GSDMD N-terminal fragment, which targets the plasma membrane to form large β-barrel pores.While induction of cell death has been assumed to be the main function of the gasdermin pores, increasing evidence suggests that these pores have non-lytic functions, such as releasing cytokines or alarmins and regulating intracellular signaling via ionic fluxes. Recently, it was also found that GSDMD-induced cell lysis is an active process requiring plasma membrane disruption by the protein ninjurin-1 (NINJ1). Here we will discuss new insights into the regulation of pyroptosis and the mechanism of NINJ1-driven cell lysis.

Delphine Bonhomme

Institut Curie

The atypical LPS of Leptospira interrogans : from TLR4-TRIF escape to pyroptosis prevention

Leptospirosis is a re-emerging zoonosis caused by pathogenic bacteria Leptospira interrogans. These bacteria are transmitted by asymptomatically infected rodents and can provoke acute and/or chronic infections in animals, including humans. The innate immune response against these pathogens relies mainly on the recognition of Microbial Associated Molecular Patterns (MAMPs) by host Pattern Recognition Receptors (PRRs). Among others, the lipopolysaccharide (LPS), an essential component of diderm bacterial membranes, is traditionally recognized extracellularly by TLR4 and in the host cell cytosol through inflammatory caspases (4-5/11). Activation of these two pathways leads respectively to the production of cytokines and to inflammatory pyroptotic cell death. Interestingly, the leptospiral LPS has been shown to be peculiar in terms of both structure and signaling. Indeed, we demonstrated that the LPS of L. interrogans escapes efficiently not only the TLR4-TRIF pathway (Bonhomme et al., 2020), but also the cytosolic activation of caspase 11 in murine macrophages (Bonhomme* et al., 2023). In both cases, we described a key role of the full-length O antigen of L. interrogans and we showed that the shorter LPS of saprophytic species L. biflexa was not as efficient in escaping receptors activation. Finally, our data suggest that these escape mechanisms could be instrumental for the stealthiness of leptospires, hence potentially contributing to the chronicity of the disease in mouse.

Cécile Arrieumerlou

Institut Cochin

Spatio-temporal dynamics of ADP-heptose sensing during bacterial infection

During infection by invasive bacteria, epithelial cells contribute to innate immunity via the local secretion of inflammatory cytokines. These are directly produced by infected cells or by uninfected bystanders via connexin-dependent cell-cell communication. However, the cellular pathways underlying this process remain largely unknown. Here, we identify TIFA and TRAF6 as central players of Shigella flexneri-induced interleukin-8 expression and show that threonine 9 and the forkhead-associated domain of TIFA are necessary for the oligomerization of TIFA in large structures named TIFAsomes, in both infected and bystander cells. Subsequently, this process triggers TRAF6 oligomerization and NF-κB activation. We demonstrate that TIFA/TRAF6-dependent cytokine expression is induced by the bacterial metabolite ADP-heptose (ADPH) and depends on alpha-kinase 1 (ALPK1). We show that TIFAsomes form within minutes of ADPH detection and last for several hours in infected cells. Single TIFAsome tracking by live cell imaging reveals sequential mechanisms of TIFAsome fusion and degradation. This last process depends on the proteasome and the E3 ubiquitin ligase activity of TRAF6. Altogether, our results provide the first insights into the spatio-temporal regulation of the ADPH/ALPK1/TIFA axis during infection and contribute to better characterize this newly identified pathway of innate immunity against Gram-negative bacteria.

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