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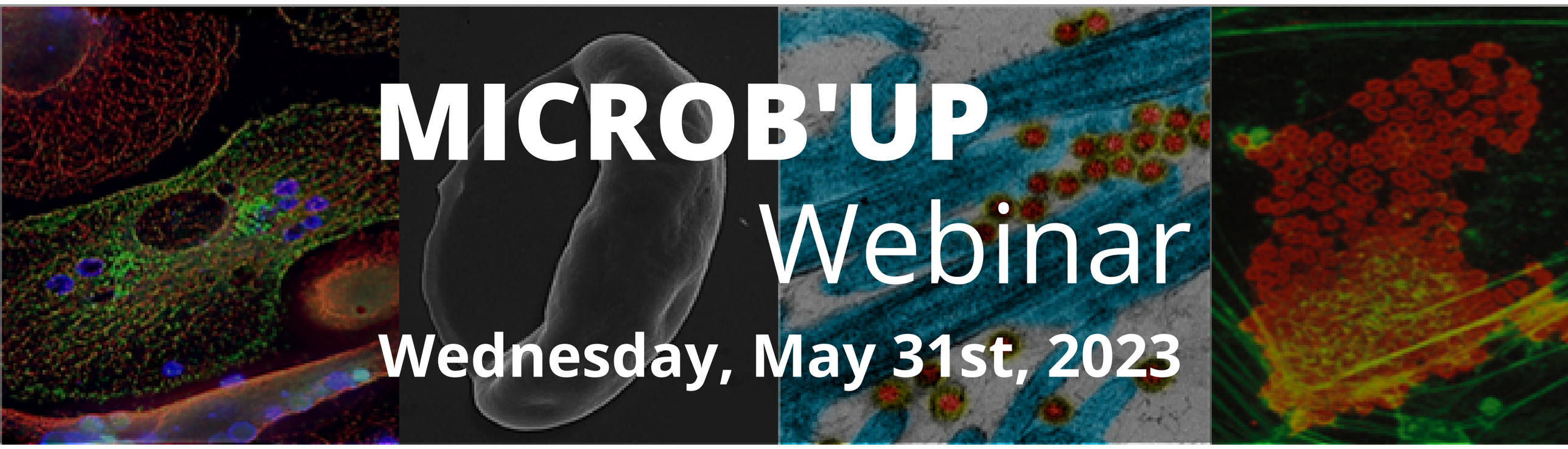

MICROB'UP Webinar

Wednesday, May 31st, 2023

Sex in parasites

Host Laboratory : Bastin Lab, Trypanosome Cell Biology

31st May 2023

At 11 am
Paris Time (GTM +2)

ZOOM, follow the link bellow

Registration
https://microb-up.u-paris.fr/webinar-31st-may-2023/

11H00

Wendy Gibson

University of Bristol, UK

Sex in trypanosomes: seeing the light

Professor Wendy Gibson now holds an honorary position at the University of Bristol, UK. During a career spanning 40 years, she focussed on research into the genetics, epidemiology and evolution of the pathogenic African trypanosomes using molecular tools. A major theme has been the elucidation of the sexual cycle of Trypanosoma brucei, a task still not complete.

11H50

Ludivine Royer

Institut Cochin

How to prevent the circulation of Plasmodium falciparum gametocytes in the blood stream?

Ludivine Royer is a second year PhD student in the Lavazec's lab at the Institut Cochin. Herfocus is on understanding the signaling pathways that regulate the mechanical properties of erythrocytes infected with Plasmodium falciparum circulating stages, the rings and stage V gametocytes. She studied pharmacy and joined the INSERM Liliane Bettencourt School.

12H05

Isabelle Louradour

Institut Pasteur

In vitro crossing, a powerful tool to investigate the elusive mechanisms of Leishmania hybridization

After a PhD in Toulouse focused on Drosophila immune response to wasp parasitism, Isabelle did her post-doctoral period at the NIH (USA), studying Leishmania parasites and their insect vectors. She joined the Institut Pasteur in 2021. Her areas of interest are Leishmania hybridization and interaction with their sand fly vectors.

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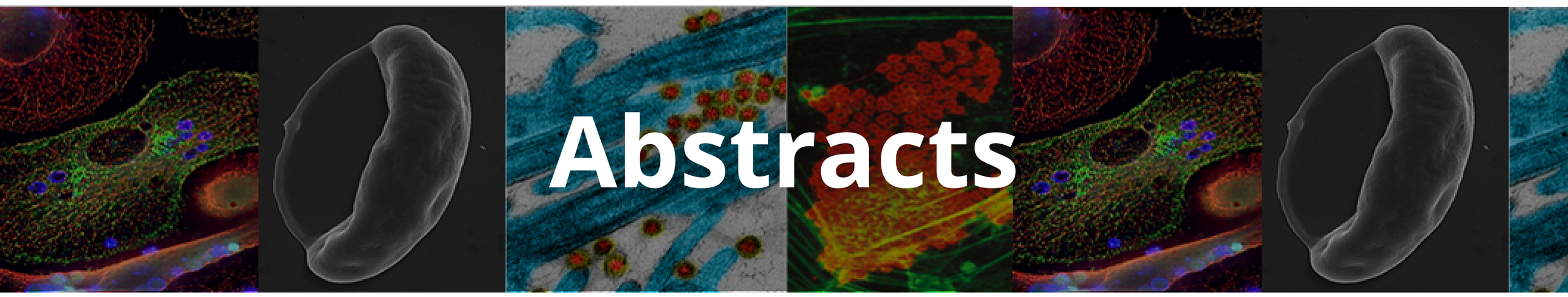

Abstracts

Wendy Gibson

University of Bristol, UK

Sex in trypanosomes: seeing the light

No sexual stages are depicted in Vickerman's iconic diagram of the life cycle of Trypanosoma brucei from 1985, trypanosomes being believed to multiply only by binary fission. Soon afterwards, the production of hybrid trypanosomes in the first successful experimental cross showed that some form of genetic exchange could occur during the trypanosome's developmental cycle in the tsetse fly vector, and the hunt was on to discover how it worked. Progress was painfully slow at first, partly due to the inaccessibility of the relevant life cycle stages within the tsetse fly, but the introduction first of methods for genetic manipulation of trypanosomes and then expression of fluorescent reporter proteins, brought key findings. Now we know that trypanosomes undergo sexual reproduction with meiosis and the production of haploid gametes. Single cell RNA sequencing has allowed analysis of the transcriptomes of gametes and it is to be hoped that future technical advances will reveal more of the secrets of sex in trypanosomes.

Ludivine Royer

Institut Cochin (Paris, France)

How to prevent the circulation of Plasmodium falciparum gametocytes in the blood stream?

The persistence of mature Plasmodium falciparum gametocyte-infected erythrocytes (GIE) in the bloodstream is crucial for their transmission to mosquitoes. The estimated lifespan of circulating gametocytes is several weeks, during which mature gametocytes are able to avoid splenic retention, immune recognition and haemolysis. To this end, one of the strategies developed by gametocytes is to decrease both the stiffness and the permeability of infected erythrocytes. The regulation of these mechanisms is closely controlled by cyclic AMP (cAMP) which is hydrolyzed by phosphodiesterases (PDE). Thus, drugs targeting PDE activity are expected to increase both the permeability and stiffness of GIE, thereby promoting GIE haemolysis and their clearance by the spleen. Here, we address the effect of tadalafil, a marketed PDE inhibitor widely used to treat erectile dysfunction and pulmonary arterial hypertension, on GIE mechanical properties using in vitro assays and an in vivo humanized mouse model. Phosphoproteomic analysis of tadalafil-treated GIE reveals several proteins potentially involved in the regulation of GIE mechanical properties. These results validate that tadalafil is a novel drug lead potentially capable of blocking malaria parasite transmission by targeting GIE mechanical properties.

Isabelle Louradour

Institut Pasteur (Paris, France)

In vitro crossing, a powerful tool to investigate the elusive mechanisms of Leishmania hybridization

Phlebotomine sand flies are responsible for the transmission of Leishmania parasites, the causative agent of Leishmaniasis. In addition to their clonal reproduction, Leishmania can engage in a cryptic sexual cycle resulting in the production of hybrids. Experimental generation of hybrids was for long confined to parasites growing in the sand fly gut, which is associated with an inherent difficulty to identify and observe the process of hybridization. We developed a protocol enabling Leishmania hybridization in vitro. However, the frequency of hybrids generated in vivo is much higher than in vitro, showing that the vector gut environment is particularly adapted for this process. The mechanisms of Leishmania hybrid production and the parameters rendering the vector gut favorable are currently poorly understood. We showed that culture conditions inducing genotoxic stress, such as exposure to X-irradiation or to Reactive Oxygen species (ROS), lead to a drastic increase in Leishmania hybridization in vitro, suggesting a link between DNA damage repair and hybridization. We established the single cell transcriptome of Leishmania cultures exposed or not to irradiation, to identify hybridization-competent parasites and establish their gene expression profile. This approach identified clusters of cells enriched in irradiated cultures and marked by the expression of genes involved in meiosis or DNA damage repair in other organisms, such as the gamete-fusogen Hap2, the nuclear-fusion agent Gex1 or the DNA recombinase Rad51. Preliminary results show that Gex1 null mutant strains fail to produce hybrids in vitro, suggesting an essential role for this protein in hybridization that we are currently investigating. In conclusion, we established an in vitro system to investigate the mechanisms controlling Leishmania hybridization, which allowed us to identify genes involved in the production of hybrids, such as Hap2 and Gex1, and to investigate parameters influencing hybridization, such as DNA damaging conditions. Future challenges lie in describing the precise mode of action of Gex1 in hybridization, and analyzing the mechanistic link between DNA damage repair and hybrid formation.

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