Our lab studies the complex relationship between immune cells and viruses. Our projects are at the interface between cell biology, immunology and virology.

1. **How the innate immune system senses the presence of viruses at the molecular level.**

Evolutionarily conserved molecular patterns on microbes are recognized by Pathogen Recognition Receptors to induce a potent innate immune response and a tailored adaptive immune response. A subset of the Toll-Like Receptors (TLRs) specific for molecular patterns on nucleic acids are located in the endosome. Microbial nucleic acids are generally not directly accessible to cell surface receptors. They are present in apoptotic bodies of infected cells or can be exposed upon degradation of the microbes within the endocytic pathway. Therefore it is critical that nucleic acid-sensing TLRs bind their ligands and signal from the endocytic/phagocytic pathway. Endosomal TLRs have a poor intrinsic ability to discriminate between host- and pathogen-derived ligands and are therefore tightly regulated all along their intracellular trafficking. Elucidating at the molecular level how these TLRs are precisely directed into the compartments that define their downstream signaling will enable us to better understand their biology and help modulate their activity during immunotherapeutic strategies.
2. HIV and macrophages: a complex relationship.

Macrophages are critical for the detection of pathogens and can deal with many of them. However in the case of HIV, macrophages are used by the virus, which efficiently infects them and makes them produce new virions. HIV-infected macrophages can survive in many tissues and accumulate intracellular stocks of infectious HIV. HIV-infected macrophages represent therefore an important viral reservoir that should be treated to cure patients from HIV. Macrophages accumulate newly synthesized viral particles in internal compartments, the VCCs or Virus Containing Compartments. The VCC nature and origin remain elusive and very little is known about the molecular mechanisms allowing viral assembly and production.

Our general aim is to decipher at the molecular level how incoming HIV is sensed, how macrophages react to HIV, how HIV escapes this control and succeeds to replicate into macrophages. We are also developing new strategies to target these viral reservoirs.
Key publications

Year of publication 2017

Jérémie Decalf, Marion Desdouits, Vasco Rodrigues, François-Xavier Gobert, Matteo Gentili, Santy Marques-Ladeira, Célia Chamontin, Marylène Mougel, Bruna Cunha de Alencar, Philippe Benaroch (2017 May 12)
Sensing of HIV-1 Entry Triggers a Type I Interferon Response in Human Primary Macrophages.
Journal of virology : DOI : e00147-17

Year of publication 2013

Stefano Berre, Raphaël Gaudin, Bruna Cunha de Alencar, Marion Desdouits, Mélanie Chabaud, Nadia Naffakh, Marc Rabaza-Gairi, François-Xavier Gobert, Mabel Jouve, Philippe Benaroch (2013 Oct 21)
CD36-specific antibodies block release of HIV-1 from infected primary macrophages and its transmission to T cells.

Raphaël Gaudin, Bruna Cunha de Alencar, Nathalie Arhel, Philippe Benaroch (2013 Apr 8)
HIV trafficking in host cells: motors wanted!

Year of publication 2012

Critical role for the kinesin KIF3A in the HIV life cycle in primary human macrophages.
The Journal of cell biology : 467-79 : DOI : 10.1083/jcb.201201144

Alejandra Garcia-Cattaneo, François-Xavier Gobert, Mélanie Müller, Florent Toscano, Marcella Flores, Aurianne Lescure, Elaine Del Nery, Philippe Benaroch (2012 May 18)
Cleavage of Toll-like receptor 3 by cathepsins B and H is essential for signaling.
Proceedings of the National Academy of Sciences of the United States of America : 9053-8 : DOI : 10.1073/pnas.1115091109

Year of publication 2009

Matias Ostrowski, Nuno B Carmo, Sophie Krumeich, Isabelle Fanget, Graça Raposo, Ariel Savina,

**Rab27a and Rab27b control different steps of the exosome secretion pathway.**

*Nature cell biology* : 19-30; sup pp 1-13 : [DOI : 10.1038/ncb2000](http://dx.doi.org/10.1038/ncb2000)