36-month postdoctoral offer in cell imaging, cell biology and immunology in the context of host-pathogen interaction

Principal Investigator

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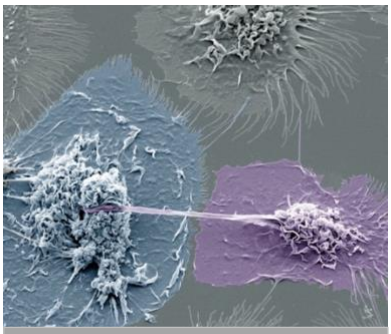
Title of the Project

Cellular and molecular mechanisms involved in tuberculosis-mediated exacerbation of HIV-1 infection in macrophages: focus on Siglec-1 and tunneling nanotubes

Context and Project

Co-infection with *Mycobacterium tuberculosis* (Mtb), the etiological agent of tuberculosis (TB), and HIV-1 is major health issue in the world. The synergistic relationship between HIV-1 and Mtb is known to result in increased pathogen proliferation and associated pathogenesis. In this context, we recently demonstrated that tunneling nanotubes (TNT) are cellular structures induced by a TB-associated microenvironment that favors HIV-1 spread among macrophages, enhancing virus load as observed in HIV/TB co-infected patients. TNT are thin connections that gained international scientific attention as a novel mechanism of intercellular communication for providing a continuous cytoplasmic bridge between cells. **We will now determine the cellular and molecular mechanisms driven by Mtb that enhances the cell-to-cell transfer of HIV-1, in particular in the context of TNT.** Innovative microscopy approaches will be used to study the dynamics of TNT and of HIV-1 transfer in macrophages both *in vitro* and *in vivo*. Based on solid preliminary data, we will focus on the cell-surface lectin receptor, Siglec-1 (CD169), a factor that is crucial in the synergy between Mtb and HIV-1**.**



TNT between macrophages
Scanning electron microscopy

This project will identify mechanisms involved in HIV/TB co-infection pathogenesis, including in HIV-1 transmission and spread. Understanding how HIV-1 and Mtb interact is crucial to ameliorate the prognosis and treatment of co-infected patients. Finally, we will generate novel fundamental knowledge on the biology of TNT, that have been associated with a wide range of pathological conditions, but also with physiological processes.

Job description

We are looking for a highly motivated post-doctoral researcher with a specific interest in cell imaging in the context of host-pathogen interactions, and excellent track record to identify and solve scientific problems. The employment is for 3 years, aiming to better understand the HIV-1/Mtb co-infection. General responsibilities include design, implement, and to interpret experiments, both independently and in collaboration, and communicate research and findings in a clear and concise manner. Applicant is expected to perform a short-term internship with Dr. Luciana Balboa, CONICET (Buenos Aires, Argentina), at least once during postdoctoral tenure.

Team consortium and environment

The project is a full collaboration between two teams at IPBS (http://www.ipbs.fr/index.php/)/CNRS, Toulouse (France), supported by a framework of an international collaborations, including a *Laboratoire International Associé* (LIA, #1167) with Dr. Luciana Balboa, CONICET (Buenos Aires, Argentina). The state-of-the-art imaging technology in the Biological Safety Level 3 (BSL-3) facilities at IPBS and the combination of expertise between the two teams (*e.g.,* HIV-1, TB, macrophage biology, cell imaging and TNT) assure the success outcome of this project.

Qualification required

- A PhD degree preferably in cell biology or immunology.
- Scientific excellence evidenced by publication track record as well as track record of presenting at national and international meetings.
- Hands-on experience of biological imaging, including wide-field and spinning-disk confocal imaging, and a solid theoretical understanding of all current and emerging microscopy technologies.
- Exhibit strong computer literacy including experience with image analysis, FlowJo, Prism, and Excel.
- High levels of initiative, autonomy and the ability to assume a high level of responsibility.
- Strong interpersonal skills needed to effectively deal with different people and groups, both scientific and non-scientific.
- Proficiency in English in order to manage our LIA partnership with Argentina; oral communication in Spanish would be a plus.

Additional qualification desired

- Experience of mammalian cell culture of primary cells and cell lines, and basic immunology assays such as multi-color flow cytometry, immunofluorescence and ELISA.
- Knowledge of histology, quantitative PCR, and general lab protocols and methodologies used in the biological sciences.
- Experience in working in BSL-3 facilities.
- Previous mentoring of Master or PhD students.
- Experience in editing and writing original research articles and grant applications is an asset!

Employment

The appointments will be funded for three years (36 months), starting no later than April 1st, 2020, by an ANRS (*Agence Nationale de la recherche sur le SIDA et les Hépatites*) grant.

The application should be written in English and include:

1. Letter of motivation with a short description of your previous research and why you consider you are a good match for the position (1-2 pages).
2. Curriculum vitae, including a description of relevant skills and experiences, as well as a full publication list.
3. Copy of PhD diploma.
4. Names, e-mail addresses and telephone numbers to 2-3 reference persons.

Contact

Application should be sent to Christel Vérollet (verollet@ipbs.fr) and Geanncarlo Lugo-Villarino (lugo@ipbs.fr)

Main Publications

- *Dupont et al., "Tuberculosis-associated IFN-I induces Siglec-1 on tunneling nanotubes and favors HIV-1 spread in macrophages", In revision,* ***eLIFE****, since Jan 16th, 2020;* ***BioRxiv*** *preprint: https://doi.org/10.1101/836155*
- *Genoula et al., "Mycobacterium tuberculosis Modulates the Metabolism of Alternatively Activated Macrophages to Promote Foam Cell Formation and Intracellular Survival". In revision,* ***mBio****, Jan 16th, 2020;* ***BioRxiv*** *preprint: https://doi.org/10.1101/2019.12.13.876300*
- *Souriant et al., "Tuberculosis Exacerbates HIV-1 Infection Through IL-10/STAT3-Dependent Tunneling Nanotube Formation in Macrophages",* ***Cell Reports.*** *2019, 26(13):3586-3599.e7*
- *Raynaud-Messina et al."Bone degradation machinery of osteoclasts: An HIV-1 target_that contributes to bone loss"* **Proc Natl Acad Sci U S A.** 2018 Mar 13;115(11):E2556-E2565
- *Dupont et al., "Tunneling Nanotubes: Intimate Communication Between Myeloid Cells",* ***Front Immunol.*** *2018, 9:43.*
- *Genoula et al., "Formation of Foamy Macrophages by Tuberculous Pleural Effusions Is Triggered by the Interleukin-10/Signal Transducer and Activator of Transcription 3 Axis Through ACAT Upregulation",* ***Front Immunol.*** *2018, 9: 459.*
- *Lugo-Villarino et al., "The C-type lectin receptor DC-SIGN has an anti-inflammatory role in human M(IL-4) macrophages in response to Mycobacterium tuberculosis."* ***Front Immunol.*** *2018, 9: 1123.*
- *Lastrucci et al., "Tuberculosis is associated with expansion of a motile, permissive and immunomodulatory CD16(+) monocyte population via the IL-10/STAT3 axis."* ***Cell Research****. 2015, 25(12): 1333-51.*
- *Vérollet et al., "HIV-1 Reprograms the Migration of Macrophages",* ***Blood****, 2015, 125 (10): 1611-22*
- *Balboa et al., "Diverging biological roles among human monocyte subsets in the context of tuberculosis infection."* ***Clin Sci****. 2015, 129(4): 319-30.*
- *Lugo-Villarino et al., "Macrophage polarization: convergence point targeted by M. tuberculosis and HIV".* ***Front Immunol.*** *2011, 2: 43.*