

EuReCa International PhD Program
PhD thesis project
2022 Call for application

**Role of intracellular pathways exploited by viruses in tumor cell
secretion of extracellular vesicles and their immune functions**

General information

Call	2022
Reference	2022-14-THERY_MARTIN
Keyword(s)	Extracellular vesicles; Tumor microenvironment; Immune responses; Virus; Immunotherapy

Director(s) and team

Thesis director(s)	Clotilde Théry & Lorena Martin-Jaular
Research team	Extracellular vesicles, immune responses and cancer
Research department	U932 – Immunity and Cancer

Description of the PhD thesis project

Cells release membrane-enclosed extracellular vesicles (EVs), which act as intercellular messengers, by transferring surface or internal signals into surrounding cells. The host laboratory aims at unraveling the diversity of EVs, with a goal to identify EVs able to induce anti-tumor immune responses. It has identified two proteins whose expression in virus-infected cells may change the downstream immune functions of their EVs. This project will explore this hypothesis in human cancer. Expression of the identified targets will be manipulated in breast cancer cell lines, and the consequences on EV release, tumor growth and immune responses will be evaluated. A long-term goal is to identify EVs with potential as anti-tumor immunotherapies in breast cancer.

International, interdisciplinary & intersectoral aspects of the project

The project involves an international collaboration with a long-term collaborator, who is also involved in development of a biotech company in his country. This collaborator will mentor the PhD student, and thus provide strong international and intersectoral exposure. This biology project will require the student to acquire expertise in bioinformatics, to analyse independently the -omics dataset generated, and to interact with physicians of the Institut Curie, to obtain and analyse clinical samples, thus to develop his/her interdisciplinary skills.



Recent publications

1. M Mathieu, N Névo, M Jouve, J I Valenzuela, M Maurin, F Verweij, R Palmulli, D Lankar, F Dingli, D Loew, E Rubinstein, G Boncompain, F Perez, **C Théry** (2021). Specificities of exosome versus small ectosome secretion revealed by live intracellular tracking of CD63 and CD9. *Nat Commun* 12: 4389.
2. **L Martin-Jaular**, N Nevo*, J Schessner*, M Tkach, M Jouve, F Dingli, D Loew, K W. Witwer, M Ostrowski, G H. H. Borner *, **C Théry** * (2021). Unbiased proteomic profiling of host cell extracellular vesicle composition and dynamics upon HIV-1 infection. *EMBO J* e105492.
3. F Cocozza*, N Névo*, E Piovesana*, X Lahaye, J Buchrieser, O Schwartz, N Manel, M Tkach, **C Théry**, **L Martin-Jaular**. (2020). Extracellular vesicles containing ACE2 efficiently prevent infection by SARS-CoV-2 Spike protein-containing virus. *J Extracell Vesicles* 10: e12050.
4. L Liao*, **L Martin-Jaular***, E Soueidi, M Jouve, D C. Muth, T H. Schoyen, T Seale, N J. Haughey, M Ostrowski, **C Théry***, K W. Witwer* (2019). Acetylcholinesterase is not a generic marker of extracellular vesicles. *J Extracell Vesicles*, 8: 1628592.
5. M Tkach, J Kowal, A E. Zucchetti, L Enserink, M Jouve, D Lankar, M Saitakis, **L Martin-Jaular**, **C Théry** (2017). Qualitative differences in T cell activation by dendritic cell-derived extracellular vesicle subtypes. *EMBO J*, 36: 3012-3028.

Expected profile of the candidate

Applicants should have a strong desire to explore cell biological phenomena, and should show solid capacity for independent and creative thinking. Background in cell biology, and/or immunology is strongly recommended. Background in extracellular vesicles and bioinformatics is a plus but not compulsory. The project highly relies on biochemistry and flow cytometry techniques, for which the applicant should have either experience or a strong motivation to learn.

