Our team ("Immunoregulation, Chemokines and Viral Persistence" in the UMR996 INSERM-UPSaclay) is offering a PhD position accounting from September 2020 to 2023 (36 months) with generous funding in the context of an EU PhD Training Network named "ONCORNET2.0" for oncogenic GPCR networks **(see below)**. The selected candidate will be enrolled in the Paris-Saclay University PhD program beginning next fall (September/October 2020).

We are looking for highly motivated MSC candidate with an excellent academic record who are interested in an ambitious multidisciplinary project on oncogenic G protein-coupled receptors (GPCRs). The purpose of our project is related to the CXCR4-ACKR3 (patho)physiological roles in Human papillomavirus (HPV) oncogenesis: controlling the shift from commensalism to pathogenesis **(see below)**.

Candidates should have: i) a MSc degree in Life Sciences or obtain a MSc degree by October 2020; ii) completed a research internship with relevant expertise; ii) obtained high grades during his/her studies and they should be fluent in English.

Candidates should fulfill the eligibility criteria for Marie Curie Innovative Training Networks: i) They must be, at the time of recruitment by the host organization, in the first four years (full-time equivalent) of their research careers and have not yet been awarded a doctoral degree. This is measured from the date when they obtained the MSc degree which would formally entitle them to embark on a doctorate and ii) Eligible candidates may be of any nationality but must not, at the time of recruitment have resided or carried out their main activity (work, studies, etc) in France for more than 12 months in the 3 last years immediately prior to the reference date.

Please send the following information (as one pdf file) to the email address (nadine.belzic@inserm.fr) including:

- Detailed CV (include information on your BSc and MSc studies, languages, achievements, expertise)
- Motivation letter, explaining your motivation why you apply with us.
- Provide contact details of at least 2 references (names, addresses, emails).
- Reference letter from one of the enlisted references
- Copies of your key educational certificates
- Transcript of Records (i.e. documents enlisting your performance as BSc and MSc student over time by listing the course units or modules taken, credits gained and the grades awarded). If you have not completed your MSc degree yet include all grades obtained so far.
- If applicable provide a language certificate

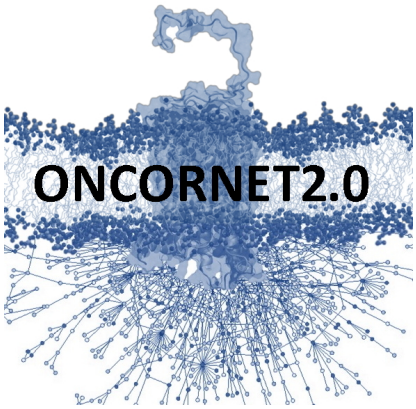
Application are open until June 2020.

Next EU Training Network ONCORNET2.0 on oncogenic GPCR networks

ONCORNET2.0 builds on the success of ONCORNET (Oncogenic GPCR Network of Excellence and Training), a first-in-kind ITN in GPCR drug discovery that has successfully delivered scientific advance and training to talented early stage researchers (ESRs) (**www.oncornet.eu**). ONCORNET2.0 will incorporate recent scientific and technological breakthroughs to understand and target two oncogenic G protein-coupled receptors (GPCRs); the chemokine receptors CXCR4 and ACKR3 (CXCR7). These are highly expressed in multiple tumours but their role in cancer progression remains poorly understood. We will develop new strategies for CXCR4/ACKR3 modulation and investigate their effects on oncogenic responses, to yield key new knowledge and potential leads for drug development.

ONCORNET2.0 will bring together the leading GPCR research groups in Europe and will educate the next generation of young researchers (15 PhD students) by a multi-disciplinary training. This programme integrates both research (e.g. drug discovery, proteomics, imaging) and transferable (e.g. entrepreneurship, academic writing, media training) skill sets through blended learning. This will ensure that the ESRs can effectively operate in today's drug discovery programs and will increase European competitiveness in the field of drug discovery.

Beneficiary partners: Academic groups: Martine Smit, Jacqueline van Muijlwijk, Rob Leurs, Iwan de Esch (Vrije Universiteit Amsterdam, NL), Steve Hill, Meritxell Canals, Steve Briddon (University of Nottingham, UK), Philippe Marin, Thierry Durroux, Sébastien Granier, Jean Philippe Pin (CNRS, FR), Martin Lohse (Max-Delbruck-Centrum für Molekulare Medizin, DE), Carsten Hoffmann (Universitätsklinikum Jena, DE), Françoise Bachelerie, Géraldine Schlecht-Louf (INSERM, FR), Federico Mayor, Petronila Penela (Universidad Autónoma de Madrid, ES), Graeme Milligan, Gerry Graham (University of Glasgow, UK) and SMEs: QVQ (Raimond Heukers, NL) and InterAx (Maria Waldhoer, CH). **Partner organizations**: Cisbio (Eric Trinquet, FR), Heptares (Chris de Graaf, UK), ALMAC (Alastair Hay, UK), Promega (Rachel Ohana, Keith Wood, US) and Learning By Simulation (LBS) (Leon Delbressine, NL).



Early stage researcher 14 (ESR14) project: CXCR4-ACKR3 (patho)physiological roles in Human papillomavirus (HPV) oncogenesis: controlling the shift from commensalism to pathogenesis.

Supervision: Dr. Francoise Bachelerie, Dr. Géraldine Schlecht (**http://umr996.inserm.fr/)**

I - Project proposal:

Background:

Our team has a long-standing interest in studying the interplay between viruses and their host both at the virus-specific target and immune cell levels. Chemokines and their receptors are central in this interplay considering their broad expression among cells and tissues and their control over many homeostatic processes (*e.g.* cell survival, proliferation, or trafficking) with the corollary being their implication in several types of disorders (*e.g.* infectious and immune diseases, cancers). Our interest mainly focuses on the CXCL12/CXCR4-ACKR3 trio, which was reported being hijacked by some viruses and notably Human Papillomavirus (HPV).

Objectives:

1. Cross-talk between leukocytes and HPV-target cells at the skin and mucosal epithelial barriers with a focus on candidates identified in the ONCORNET1.0 program (*i.e.* proteomics and transcriptomics results).
2. Importance of the circadian clock and its control by CXCR4/ ACKR3 in host surveillance toward viral-driven oncogenesis.
3. Assessing the impact of modulating the identified pathways using tools generated by the ONCORNET2.0 consortium (*e.g.* photoactivatible ligands).

Expected Results:

By analyzing HPV life cycle as a prototypical example of a commensal virus (virome) with oncogenic potential, we hope identifying more generally host factors that control the shift from commensalism to pathogenesis at epithelial barriers. This will be done by combining in house expertise (mouse models including humanized mice) with tools previously generated in frame of the ONCORNET1.0 consortium (*e.g.* nanobodies, CRISPR-Cas9 gene editing technology).

Methodology:

3D-epithelial cell cultures – CRISPR-Cas9 - RNA-Scope – Histology –Flow cytometry - HTRF/BRET-based assays

Planned secondments:

CNRS – Evaluate the existence and localization of CXCR4 and ACKR3 oligomers in tissues [m12];

Vrije Universiteit Amsterdam – Phosphorylation barcoding of CXCR4 and ACKR3 and photoswitchatible ligands in developed (patho)physiological cell models [m24].

II - Requirement candidate:

Required diploma: MSc degree in molecular/biomedical Life Sciences, Microbiology/immunology Sciences or related Life Sciences degree.

Required expertise: Biochemistry, Molecular biology, Cell biology.

Recommended expertise: HTRF/BRET-based assays, imaging, viral-particle-related assays, Flow-cytometry, mice model practice.

Key publications:

- Koenen J, Balabanian K, Bachelerie F, Schlecht-Louf G, Gallego C. Atypical chemokine receptor 3 (ACKR3): a comprehensive overview of its expression and potential roles in the immune system. Molecular Pharmacology. 2019 April 30. doi: 10.1124/mol.118.115329. Mini-Review.
- de Wit RH, Heukers R, Brink HJ, Arsova A, Maussang D, Cutolo P, Strubbe B, Vischer HF, Bachelerie F, Smit MJ. CXCR4-Specific Nanobodies as Potential

Therapeutics for WHIM syndrome. J Pharmacol Exp Ther. 2017 Oct;363(1):35-44. doi: 10.1124/jpet.117.242735.
- Meuris F, Carthagena L, Jaracz-Ros A, Gaudin F, Cutolo P, Deback C, Xue Y, Thierry F, Doorbar J, Bachelerie F. The CXCL12/CXCR4 Signaling Pathway: A New Susceptibility Factor in Human Papillomavirus Pathogenesis. PLoS Pathog. 2016 Dec 5;12(12):e1006039. doi: 10.1371/journal.ppat.1006039. eCollection 2016 Dec.
- Calmette J, Bertrand M, Vétillard M, Ellouze M, Flint S, Nicolas V, Biola-Vidamment A, Pallardy M, Morand E, Bachelerie F, Godot V, Schlecht-Louf G. Glucocorticoid-Induced Leucine Zipper protein controls macropinocytosis by dendritic cells. The Journal of Immunology. 2016 Dec 1;197(11):4247-4256.
- Bachelerie F, Graham GJ, Locati M, Mantovani A, Murphy PM, Nibbs R, Rot A, Sozzani S, Thelen M. (2014) New nomenclature for atypical chemokine receptors. Nat Immunol. 2014 15:207-8. doi: 10.1038/ni.2812.

For more information:

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Dr. Géraldine Schlecht - geraldine.schlecht-louf@universite-paris-saclay.fr

Application:
Please send your application to nadine.belzic@inserm.fr