2016-02

IC-**3i** International PhD Program

PhD thesis project

2017 Call for application

Characterization and Modulation of a New Pigment Reservoir

General information

Call	2017
Reference	2016-02-DELEVOYE
Keyword(s)	Skin pigmentation, Melanocytes and Keratinocytes, Organelles, Intracellular Trafficking, Imaging

Director(s) and team

Thesis director(s)	Cédric Delevoye
Research team	Team Raposo ; Structure and Membrane Compartments
Research department	UMR 144 - Subcellular Structure and Cellular Dynamics

Description of the PhD thesis project

The team Structure and Membrane Compartments explores the inter- and intracellular mechanisms of pigmentation. Over the past years, the team has made seminal contributions to novel concepts in fundamental cell biology (roles of exosomes secreted by keratinocytes, model for melanosome and recycling endosome biogenesis) that led to the elucidation of cellular and molecular mechanisms of the pigmentation in health and disease, including genetic diseases characterized by subtypes of albinism. The team has international recognized expertise in different electron microscopical methods, as well as in subcellular organization and molecular mechanisms of trafficking.
Skin color plays critical photoprotective functions against harmful solar radiations. Thus, disorders affecting pigmentation impact well-being, quality of life and increase the risk of skin cancers. In epidermis, keratinocytes receive melanin pigment produced by melanocytes. However and despite their crucial roles, very little is known about how keratinocytes control their pigmentation.

The proposed project aims at a better understanding of the fate of melanin pigments in epidermal keratinocytes. Based on recent studies from the lab, we will address the intracellular pathways and mechanisms as well as extracellular signals allowing keratinocytes to maintain or degrade melanin pigments. Altogether, we aim to unravel new mechanisms within an integrated context. This study will not only open new avenues in the field of cell biology and pigmentation, but also pinpoint new targets allowing to design relevant models to test active compounds to treat pigmentation disorders.

International, interdisciplinary & intersectoral aspects of the project

This project will benefit from already established collaborations with internationally recognized groups located in Europe and USA. This will allow the applicants to visit, discuss and pursue experiments abroad. The project will greatly benefit from a recent Research and Development collaboration with an industrial partner that will be maintained over the time of this study. This largely intersectoral project will foster the development of new and relevant skin models by the industrial partner. Besides using a large variety of experimental approaches, with a strong emphasis on state-of-the-art imaging methods from light to electron microscopies, the applicant will be constantly exposed to inherent interdisciplinarity of the 12 units of Institut Curie.

Recent publications

1. **Delevoye C**, Heiligenstein X, Ripoll L, Gilles-Marsens F, Dennis MK, Linares RA, Derman L, Gokhale A, Morel E, Faundez V, Marks MS, **Raposo G**.
BLOC-1 Brings Together the Actin and Microtubule Cytoskeletons to Generate Recycling Endosomes.
Curr Biol. 2016 Jan 11;26(1):1-13. doi: 10.1016/j.cub.2015.11.020.

2. Dennis MK, **Delevoye C**, Acosta-Ruiz A, Hurbain I, Romao M, Hesketh GG, Goff PS, Sviderskaya EV, Bennett DC, Luzio JP, Galli T, Owen DJ, **Raposo G**, Marks MS.
BLOC-1 and BLOC-3 regulate VAMP7 cycling to and from melanosomes via distinct tubular transport carriers.
J Cell Biol. 2016 Aug 1;214(3):293-308. doi: 10.1083/jcb.201605090.

3. Lo Cicero A, **Delevoye C**, Gilles-Marsens F, Loew D, Dingli F, Guéré C, André N, Vié K, van Niel G, **Raposo G**.
Exosomes released by keratinocytes modulate melanocyte pigmentation.
Nat Commun. 2015 Jun 24;6:7506. doi: 10.1038/ncomms8506.

4 van Niel G, Bergam P, Di Cicco A, Hurbain I, Lo Cicero A, Dingli F, Palmulli R, Fort C, Potier MC, Schurgers LJ, Loew D, Levy D, **Raposo G**.
Apolipoprotein E Regulates Amyloid Formation within Endosomes of Pigment Cells.
Cell Rep. 2015 Oct 6;13(1):43-51. doi: 10.1016/j.celrep.2015.08.057.

5. **Delevoye C**, Miserey-Lenkei S, Montagnac G, Gilles-Marsens F, Paul-Gilloteaux P, Giordano F, Waharte F, Marks MS, Goud B, **Raposo G.**
Recycling endosome tubule morphogenesis from sorting endosomes requires the kinesin motor KIF13A.
Cell Rep. 2014 Feb 13;6(3):445-54. doi: 10.1016/j.celrep.2014.01.002.

Expected profile of the candidate

Applicants should be creative, hard-working, self-motivated and collaborative. Background in cell biology is strongly recommended. Applicants should have either experience or strong motivation to learn state-of-the-art imaging approaches (immunofluorescence, live cell imaging and electron microscopy). Other complementary methods will be used including primary human cell culture and conventional cell and molecular biological techniques. Most of the project relies on cells cultured in vitro and 3D tissues, but *in/ ex vivo* approaches can be envisaged.