

STudent REseArch Mobility Programme (STREAM) Project proposal

Host University:

University Paris-Saclay

Field (drop-down list):

Health and welfare

Specified field, subject:

Toxicology and Immunology

Research project title:

Skin allergy: roles of Nrf2 in the mechanisms of keratinocytes activation and resolution of inflammation

Possible starting month(s):

Sep	Oct	Nov	Dec	Jan	Fev	Mar	Apr	May	Jun	Jul	Aug
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Possible duration in months:

1	2	3	4	5	6	7	8	9	10	11	12
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Exact starting and end dates will be discussed between the supervisor and the student

Date of validity: from DD/MM/YY till DD/MM/YY

Suitable for students in: ☐ Bachelor level ☒ Master level

Prerequisites: cell biology, interest in immunology and toxicology

Restrictions: -

Description (maximum 2,000 characters):

Several studies have provided evidence for an important role of the transcription factor nuclear-related factor 2 (Nrf2) in skin homeostasis and disease. In basal conditions, Nrf2, bound to Keap1, is targeted to proteasomal degradation. Under oxidative stress, the Nrf2-Keap1 interaction is resolved and the free and newly synthesized Nrf2 translocate to the nucleus where a series of antioxidative and cytoprotective genes are controlled, to prevent an excess of ROS accumulation and electrophilic stress in hapten-exposed cells. Nrf2, expressed ubiquitously, is described as a 'must' for the detoxification of all chemicals and a 'guard' for the inflammation reported in many pathologies. Our previous work has shown that Nrf2, described as a regulator of epidermal barrier function, regulates allergic skin inflammation in skin allergy, with an increase of expression of antioxidant genes (*HO-1*, *GCLC*, *NQO1*), a decreased of genes involved in tissue repair and inflammatory cytokines. Nrf2 activation in the skin, also controls sterile inflammation caused by chemicals, by regulating neutrophils recruitment, accumulation, and clearance and may maintain Langerhans cells in a tolerogenic status (unpublished data).

In keratinocytes, Nrf2 is central to 3 major protective processes: (1) chemical detoxification, (2) inflammation regulation, (3) tissue regeneration, which are essential to limit the accumulation of harmful molecules in the epidermis and the development of adverse effects.

Our preliminary data suggest that Nrf2 induction can prevent KC's inflammatory status, depending on the chemical allergen concentrations and the frequency of exposure. Therefore, understanding how Nrf2 maintains epidermal homeostasis, especially when individuals are chronically exposed to harmful chemicals, is a major challenge.



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The objectives of our project are to decipher Nrf2's role during exposure to chemical allergens by decoding its role in the mechanisms of KC activation and resolution of inflammation.

Research laboratory:

INSERM UMR-S 996

Inflammation, Microbiome & Immunosurveillance - MI2

Equipe 2 'Allergy, immunotoxicology & immunopathology'

Université paris-Saclay - Faculté de Pharmacie

5, rue J.B. Clément

F-92296 Châtenay-Malabry

Faculty and/or Department:

Faculty of Pharmacy – University of Paris-Saclay

Contact person, including position: Saadia Kerdine-Römer, Professor

Contact email: saadia.kerdine-romer@universite-paris-saclay.fr

Deadline for nomination to reach host university: 1st December

Notification of admission given by the end of: 15th December

Additional information:-