Title of the PhD project
Understanding the mechanisms of dysregulated collagen turnover in skin wound healing pathologies

Disciplines: Biochemistry, cell biology, proteomics
Laboratory (lab. name, director name and when applicable, research team name)**:**
Group Metalloproteinases and Tissue Remodeling (C. Moali)
Tissue Biology and Therapeutic Engineering Laboratory (LBTI) directed by B. Verrier
Doctoral school: Interdisciplinary Doctoral program in health-sciences (EDISS) - ED 205

Description
Scientific background and rationale: Skin wound healing is a complex and tightly regulated process which aims at restoring skin structural and mechanical integrity. This process can be defective in a number of pathological contexts linked to ageing, genetic or acquired diseases and lead to non-healing or fibrotic wounds[1]. Among the numerous pathways which contribute to wound healing pathologies, the imbalance between the synthesis and degradation of fibrillar collagens is known to play a crucial role.

Aim: The main objective of the PhD project is to analyze the molecular mechanisms controlling collagen assembly and degradation in normal and defective skin wound healing.

Description of the project methodology: Skin biopsies and skin cells originating from mouse models and patients material will be analyzed using a large variety of techniques (biochemistry, shotgun and targeted proteomics, imaging techniques, molecular biology, western blots). The rare genetic disease dystrophic epidermolysis bullosa (DEB) will be used as a model of defective skin wound healing involving clear signs of dysregulated collagen turnover[2] in collaboration with A. Nyström (University of Freiburg, Germany). The first step will be to characterize the main features of the collagen network in normal and disease samples. Then, the expression and activity of the main proteins involved in the regulation of collagen assembly and degradation[3,4] will be analyzed to identify potential targets for therapeutic intervention.

Expected results: The results from this study will provide important information on the mechanisms which are dysregulated in DEB and in the large number of diseases which also display alterations of collagen turnover.

Perspectives: The main perspectives are to identify new biomarkers of DEB progression and to design novel evidence-based therapeutic approaches of DEB which could also be extended to other skin wound healing pathologies.

Skills required: High motivation and interest for science; training in biochemistry or cell biology; knowledge of skin physiopathology, extracellular matrix and/or proteomic approaches would be an advantage; fluency in English is absolutely required.

Bibliography:

1. Gurtner et al. Nature 453:314-21, 2008.
2. Nyström et al. EMBO Mol. Med. 7:1211-28, 2015.
3. Vadon-Le Goff et al. Matrix Biol. 2015, 44-46, 14-23.
4. Bekhouche et al. FASEB J. 2016, 30, 1741-56.
5. Delolme et al. Cell. Mol. Life Sci. 2015, 72, 1009-27.

Keywords: wound healing, skin, collagen, proteinases, fibrosis, epidermolysis bullosa

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Application should include: CV, application letter, Names and addresses of two references.
The application file should be sent before May 1, 2018 to: c.moali@ibcp.fr.
The open competitive recruitment process is in two steps: 1. Internal laboratory procedure. 2. Interdisciplinary jury of EDISS.