# MASTER 2 BIOLOGIE DE LA PEAU
# ANNEE 2019-20 (STAGE DU 6 JANVIER AU 19 JUIN 2020)

**Titre du sujet de stage : IL-36 signaling in psoriatic inflammation**

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**Sujet de stage** (une dizaine de ligne) **:**

Psoriasis is one of the most common skin inflammatory diseases worldwide. The vitamin D3 analog calcipotriol has been used alone or in combination with corticosteroids in treating psoriasis, but how it suppresses psoriatic inflammation remained elusive. Combining experimental mouse psoriasis model, genetic tools, ex vivo and in vitro cultures, as well as human psoriasis biopsies, our recent study (JCI

Insight. 2019 PMID:30674716) revealed that in contrast to what was previously believed, calcipotriol acts on its receptor VDR on keratinocytes to suppress the production of cytokine IL-36 (psoriasis signature molecules), and subsequently reduces the production of IL-23/IL-17 in psoriasis. Moreover, we uncovered that calcipotriol/corticosteroid therapy effectively disrupts the IL-36-IL-23/IL-17 positive feedback loop at two key nodes: in keratinocytes (IL-36) by the action of calcipotriol and in immune cells (IL-23/IL-17) by the action of corticosteroid. To explore further the cellular and molecular network of IL-36 signaling in psoriatic inflammation, the M2 research will aim at investigating the functional study of IL-36α/γ in psoriasis pathogenesis, and exploring the downstream pathway. To this aim, we will use our newly generated mouse genetic tools (knockout and fluorescent reporter), combined with a cutting-edge laser-microporation technology for cytokine delivery into mouse skin, immunological approaches, and cellular/molecular biological analyses, to delineate the specific pathological role for IL-36α and IL-36γ. Studies are expected to contribute to identify and develop novel therapeutic strategies for pathologies implicating IL-36 signaling, including psoriasis and beyond.

**Technologies utilisées :** Various techniques will be crucial for the project, including in vivo studies with mouse genetic tools and experimental protocols, immunological approaches (flow cytometry: surface marker staining and intracellular cytokine staining; cell sorting; adoptive cell transfer), cellular and molecular methods (e.g. qRT-PCR, RNAseq, in vitro or ex vivo cell/tissue culture, immunostaining, confocal microscopy).

**Mots clés : Skin; Inflammation; Immunity; Cytokine**

**Publications d'intérêt si possible (5 maxi) :**

German, B., Wei, R., Hener, P., Martins, C, Ye, T., Gottwick, C, Yang, J, Seneschal, J., Boniface, K and Li, M. **2019**. Disrupting IL-36 and IL-23/IL-17 loop underlies the efficacy of calcipotriol and corticosteroid therapy for psoriasis. ***JCI Insight*** PMID: 30674716