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Modulation of aromatic hydrocarbon receptor (AhR) activity in the skin**Raphaël Coatmeur***Aix-Marseille Université, France*

Since 2016, the World Health Organisation has classified air environmental pollution as a major public health problem. The skin is the body's first line of defense against aggressions such as pathogens, toxins and harmful pollutants. The aryl hydrocarbon receptor (AhR) is a transcription factor playing a crucial role in skin defense. Indeed, AhR was initially described as a key chemo-sensor to environmental pollutants, as it regulates xenobiotic metabolism enzymes expression. It also plays an important role in the regulation of several genes involved in inflammation and immune response. However, prolonged activation of AhR by exogenous chemicals, such as Polycyclic Aromatic Hydrocarbons or dioxins, can lead to its deregulation and potentially to the development of skin diseases (atopic dermatitis, psoriasis and skin cancers). The aim of this project is to modulate AhR activity in the skin in order to develop innovative treatments using our non-competitive antagonist, MM107, synthesized by the PROTAC technique. In primary human keratinocytes, after AhR stimulation by an agonist, we observed by qRT-PCR that MM107 inhibited the induction of AhR target genes expression. These results were confirmed, at the protein level, for AhR itself and NF- κ B. In addition, the catalytic activities of CYP1A1&1B1 and MMP1&13 were significantly decreased. MM107, in presence of an AhR agonist, also decreased the production of the pro-inflammatory cytokines TNF- α , IL-1 β and IL-8; while increasing the anti inflammatory cytokine TGF- β level. MM107, our proprietary molecule designed to specifically target AhR, could improve treatments of inflammatory skin diseases in which AhR has been involved.

Biography

Raphaël Coatmeur has obtained with honours two research Masters in Pharmacokinetics and Cosmetic Formulation. He is currently completing his PhD at the Mediterranean Institute of Marine and Continental Biology at the Faculty of pharmacy in Marseille in partnership with the biotech company Alphenyx (CIFRE grant) and should defend his PhD by the end of 2021. His thesis director and co director are Pr. Philippe Piccerelle, director of bio-ingeneering department of faculty of pharmacy and Dr. Laetitia Rapetti- Vachieri, science director of Alphenyx.

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