2025 SymbNET PhD Summer School on Host- Microbe Symbioses

Interplay of Bioactive Peptides and the Gut-Skin Axis: A Novel Perspective on Psoriasis Therapy

Isa Silva[1,2], Jo L.W. Lambert[2,3], Manuela Pintado[1] and Ezequiel R. Coscueta[1]

[1]Universidade Católica Portuguesa, CBQF - Centro de Biotecnologia e Química Fina – Laboratório Associado, Escola Superior de Biotecnologia, Rua Diogo Botelho 1327, 4169-005 Porto, Portugal
[2] Department of Head and Skin, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium
[3] Department of Dermatology, Ghent University Hospital, Ghent, Belgium

ABSTRACT

Psoriasis is a chronic immune-mediated inflammatory skin disease characterized by keratinocyte hyperproliferation and immune dysregulation, involving the activation of Th1/Th17 cells and elevated levels of cytokines such as TNF-α, IL-17, and IL-23. Although current treatments range from topical corticosteroids to systemic biologics, recent studies highlight the importance of the gut–skin axis in psoriasis pathogenesis, where gut dysbiosis and increased intestinal permeability contribute to systemic inflammation. This emerging link underscores the need for therapeutic strategies that address both gut and skin homeostasis.

We developed a PhD project hypothesizing that bioactive peptides (BPeps) derived from natural dietary sources can modulate inflammation and epithelial barrier integrity in both the gut and skin, offering a novel therapeutic avenue for psoriasis based on host–microbe interactions and personalised nutraceuticals.

Selected using bioinformatics and machine learning tools, 4 BPeps were synthesized and will be screened in intestinal cell models to evaluate their immunomodulatory effects in gut dysbiosis and psoriasis. This includes profiling cytokine expression and analyzing NF-κB and JAK-STAT signaling pathways. Promising peptides will undergo simulated gastrointestinal digestion, and their colonic fractions will be tested in gut fermentation models to assess effects on microbiota composition, short-chain fatty acid production, and barrier function.

Absorbed peptide fractions and microbiota-derived metabolites will then be applied to *in vitro* and *ex vivo* 3D psoriatic skin models to assess their influence on inflammation, tissue regeneration, and skin barrier restoration. In parallel, intact BPeps will be directly tested on psoriatic skin to evaluate local activity. This approach enables a comparative evaluation of peptide effects in both gut and skin systems and the gut-skin axis.

By bridging immunonutrition, microbiome science, and dermatology, this research advances novel peptide-based therapies and deepens our understanding of host–microbe symbioses in chronic inflammatory diseases.