INFRAFRONTIER Complex *In Vitro* Models:

Advanced 3D Skin Models as Innovative Platforms for Biomedical Testing and Research

How is the model generated?

1. Human induced pluripotent stem cells (iPSCs) under feeder-free conditions are first induced into ectodermal lineage commitment by dual SMAD inhibition to promote surface ectoderm fate.
2. Cells are subsequently guided toward epidermal and dermal progenitors using a timed combination of growth factors such as FGF and WNT modulators, followed by aggregation into 3D spheroids in low-adhesion conditions.
3. These aggregates are embedded in an extracellular matrix (Matrigel) and cultured long-term in differentiation media that supports the development of layered epidermis and dermis-like structures.
4. Over several weeks, the organoids mature with keratinocyte differentiation, fibroblast emergence, and in hair follicle-like structures, making them suitable for downstream biomedical testing applications.

Potential applications:

Skin organoids will be derived at CCP from human iPSCs, pre-characterized and provided by the requestor. The organoids will serve as a versatile in vitro platform for functional testing across multiple applications: to evaluate (1) the effects of small-molecule compounds on skin differentiation and maturation, (2) the affinity, uptake, and structural stability of organoids during antisense oligonucleotide therapy, and (3) the biological impact of chemical modulators such as retinoids on skin development and homeostasis. Together, these studies will enable controlled, human-relevant assessment of pharmacological and molecular interventions in a physiologically representative 3D skin system.

Who provides this model?

Czech Centre for Phenogenomics

The Czech Centre for Phenogenomics (CCP) is a leading European research infrastructure for functional genomics and preclinical model development, operated by the Institute of Molecular Genetics of the Czech Academy of Sciences. CCP provides an integrated pipeline covering advanced genome engineering, generation of transgenic and disease models, and comprehensive in vivo phenotyping under specific pathogen-free (SPF) conditions. Within CIVM, CCP provides expertise in the generation of human iPSC-derived 3D skin organoids as complex cellular models that recapitulate key aspects of human epidermal differentiation, development and patophysiology. Such models are designed for studying rare genetic skin disorders, functional genomics, and therapeutic testing in a controlled human-relevant context. To ensure robustness and translational relevance, CCP integrates these in vitro models with complementary validation pipelines. This combined approach enables mechanistic insight, predictive modelling, and preclinical validation within a single infrastructure, while supporting the transition toward reduced animal use.

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References:

1. Gopallawa, I. et al. Applications of Organoids in Advancing Drug Discovery and Development, Journal of Pharmaceutical Sciences, Volume 113, Issue 9, 2024, Pages 2659-2667

2. Garriga-Cerda L, et al. IPSC-derived organoid-sourced skin cells enable functional 3D skin modeling of recessive dystrophic epidermolysis bullosa. J Tissue Eng. 2025 Dec 1;16: 20417314251397594.

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