32nd IFSCC Congress
London 19-22 September 2022

Establishment of an in vitro model to study the effect of psychological stress on human skin stem cells

Poster ID 272

Kappler, Katharina[1]; Wandrey, Franziska[1]; Cuddapah, Chennakesava[2]; Salvi, Roberto[2]; Zülli, Fred[1]
[1] Mibelle Biochemistry, Buchs, Switzerland; [2] Curio Biotech SA, Visp, Switzerland

Introduction:

One of the major **stress response systems** in vertebrates is the **hypothalamus-pituitary-adrenal (HPA) axis** that connects the central nervous system with the endocrine system and regulates the secretion of glucocorticoids. Interestingly, the **human skin expresses major elements of the HPA axis** including corticotropin releasing factor (CRF), CRF receptors and glucocorticoids, such as cortisol (1). **Stress also involves the sympathetic nervous system** and the **release of catecholamine neurotransmitters, such as epinephrine and norepinephrine**. These neurotransmitters as well as the adrenergic receptors they bind to are also present in the skin (2). Whereas the effect of stress on keratinocytes is partially known (3, 4), the function of **psychological stress on skin stem cells is largely unexplored.** Thus, we aimed to develop an ***in vitro* model using skin stem cells and a psychological stress inducer** along with an appropriate end point, which can be used for efficacy screening to identify modulators of chronic psychological stress in the skin.

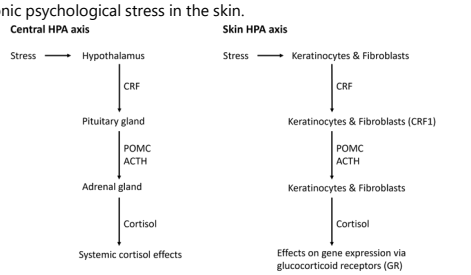

Figure 1: The central HPA axis and the elements of the HPA axis expressed in skin cells.

Materials & Methods:

The assay was established in human epidermal progenitor/stem cells (HEPSCs), treated with different stress inducers for 6 hours or for 2 and 4 days to simulate acute and chronic psychological stress. Supernatants were harvested and analyzed for IL-1β, IL-8 and IL-6 by ELISA to assess potential biomarkers. In a last step, using this model, four plant stem cell extracts were tested for their potential to protect HEPSCs from psychological stress.

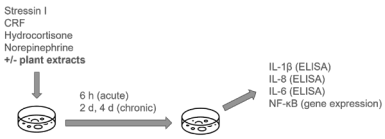

Figure 2: Schematic diagram of the experimental design.

Results & Discussion:

Whereas the secretion of IL-8 and IL-1β was less pronounced and consistent, **IL-6 was identified as a reliable biomarker** in this model. **Chronic stress induced by treatment with norepinephrine or stressin I, a CRF1 agonist**, led to a significant and reproducible increase of IL-6 secretion.

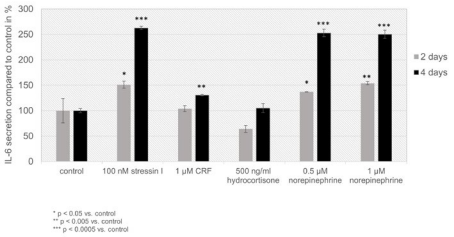

Figure 3: Release of IL-6 from HEPSCs treated with different stress inducers.

Using this model, **plant stem cell extracts with protective potential** against psychological stress were identified.

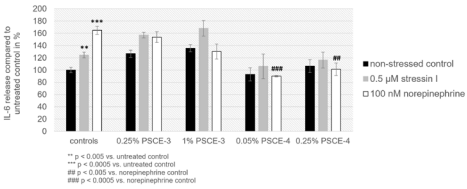

Figure 4: Release of IL-6 from stress-induced HEPSCs after treatment with exemplary plant stem cell extracts PSCE-3 and PSCE-4.

Conclusions:

The established *in vitro* model can help to **elucidate the consequences of chronic psychological stress on the self-renewal capacity of the skin** and can be used for efficacy screening of molecules to **identify modulators of chronic psychological stress in the skin**, which is important for the development of a new generation of **neurocosmetic active ingredients**.

Acknowledgements:

The authors thank the R&D laboratory team of Mibelle Biochemistry for the preparation of the test samples.

References:

1. Slominski, A., et al., *Differential expression of HPA axis homolog in the skin.* Mol Cell Endocrinol., 2007. 265-266: p. 143-149.
2. Slominski A., et al., *Sensing the environment: Regulation of local and global homeostasis by the skin neuroendocrine system.* Adv Anat Embryol Cell Biol. 2012; 212: v–115.
3. Zbytek, B., et al., *Corticotropin-releasing hormone affects cytokine production in human HaCaT keratinocytes.* Life Sciences, 2002. 70: p. 1013-1021.
4. Zbytek, B., L.M. Pfeffer, and A.T. Slominski, *Corticotropin-releasing hormone stimulates NF-κB in human epidermal keratinocytes.* J Endocrinol., 2004. 181(3): p. R1-R7