PROTECTION OF CUTANEOUS NEURONS BY A NEW PEPTIDOMIMETIC ENDOWED WITH NEUROTROPHIC AND ANTI-APOPTOTIC PROPERTIES

I. Imbert[1], and J-F. Nicolaÿ[1]

[1]*Exsymol SAM, MC98000, Monaco*

The cutaneous network of unmyelinated nerve fibers is extremely dense, and closely interacts with the many cell types present in dermis and epidermis, including keratinocytes, fibroblasts, Langerhans cells, and melanocytes. Cell communication involves various neuroendocrine factors, with cell differentiating and proliferative activities, or inflammatory properties. Thus, nervous cells in the skin not only create a sensory system connected to the central nervous system, but also mediate many of the biological activities of the skin.
Environmental challenges, that are of particular importance since the nervous network reaches the most superficial layers of the skin, and the aging process induce a loss of neurons or metabolic function impairements. This results in an decline in sensory nerve function, a poor wound repair, inflammatory disturbances of great relevance for pigmentary disorders and pathological pigmentations, a depressed immune response, and finally a global alteration of the barrier function.

Preservation of the sensory network of the skin, e.g. definition of "neuroprotective agents", thus appears as a major challenge that requires specific protective strategies.

We have investigated the properties of an innovative protective agent, using the PC12 cell line, a commonly accepted model of peripheral neurons.
NGF-treated PC12 cells with neuron-like morphology were stressed in two separate experimental designs by UVB or growth factor deprivation, and protection was assessed qualitatively (microscopical monitoring of cell morphology) and quantitatively (dosage of LDH activity in the culture medium).
In both experiments, sub-millimolar concentrations of the peptidomimetic can greatly improve cell survival and differentiation. This compound can prevent cells from entering in the apoptotic program which is, as a particular feature of nervous cells, involved in many neurodegenerative diseases and aging.
Mechanisms of action were also investigated. Strong antioxidant properties demonstrated with chemical and biochemical tests, partly account for efficacy. In addition a cytokine-like effect, referred as a "neurotrophic effect", was shown to participate in the protection, improving neuronal differentiation and extending average lifespan.

Altogether these data demonstrate the original neuroprotective and anti-neurodegenerescence properties of a promising agent for the preservation of the neurocutaneous network, bringing benefits in many physiopathological mechanisms involving cutaneous innervation, such as age-related sensitivity loss and pigmentation disorders.