

Vitiligo, P.N.E.I. and Low Dose Cytokines and Growth Factors

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Vitiligo is a skin disorder characterized by a progressive depigmentation which is caused by the loss of melanocytes at the cutaneous level. The causes of melanocyte loss are still unclear, but a relevant number of observations lead researchers to ascribe cellular immunity as having an important role in vitiligo pathogenesis. In vitiligo, the observed imbalance in cytokine expression at cutaneous lesions level both on the border of affected area with healthy skin and in the center of the spot, is probably due to a shift of the immune system with a prevalence of Th1/Th17 (high IL-1 and IL-17 levels) response instead of a Tregs/Th2 one (low IL-4 level) and may be part of etiology of this autoimmune disease [1-3]. TNF- α also has a pivotal role in oxidative stress-mediated cytotoxicity directed against melanocytes and keratinocytes and sustained by T-cells and B-cells activation [4,5].

Apoptosis of keratinocytes is a key event in Vitiligo onset. Keratinocytes produce a number of growth factors that support the viability of the melanocytes through paracrine action [6]. Among these factors, the basic fibroblast growth factor (bFGF or FGF2) is a potent regulator of melanocytes proliferation, differentiation and function; there is an inverse correlation between the levels of TNF- α and bFGF in the presence of vitiligo and low levels of bFGF are responsible of melanocytes death and, finally, of skin lesion depigmentation [7]. TNF- α is, therefore, a key player of cell-mediated autoimmune response and inflammation, responsible of the keratinocytes apoptosis [8].

It is therefore arguable that the inflammatory phenomenon supported by this cytokine and the breaking down of the paracrine crosstalk between keratinocytes and melanocytes are central events in inducing and sustaining vitiligo and thus represents one of the key targets within a therapeutic strategy based on deep knowledge of the etiology of the disease.

Low-Dose Medicine starts from the innovative therapeutic concept of restoring physiology through activated low dose communicating (messenger-signaling) molecules such as hormones, neuropeptides, interleukins, and growth factors. The availability of low-dose medicines containing highly diluted and Sequentially Kinetic-Activated (SKA) cytokines and growth factors represents a unique opportunity for the study of an innovative immunological therapeutic approach for vitiligo treatment.

The therapeutic use of SKA low dose bFGF (Guna S.p.a. – Italy) is aimed at improving the stimulation of the residual population of melanocytes (via up-regulation of trans-membrane receptors) mimicking the paracrine signaling exerted, in physiological conditions, by keratinocytes. The effect of bFGF is improved if in association

with the pool of anti-inflammatory cytokines that acts reducing the apoptotic phenomena and the cytotoxicity mediated by TNF- α .

The anti-inflammatory SKS low dose molecules pool is composed by Anti-IL-1; IL-4; IL-10 and β -endorphin.

Anti-IL-1 is useful in the reduction of IL-1-mediated acute inflammation, present in perilesional region; IL-4 exerts an effective control against autoimmune triggers, reducing cell-mediated cytotoxicity; IL-10 is the opposing cytokine of both IL-1 and TNF- α and is effective in chronic inflammation control; β -endorphin, as β -endorphin oxidation reduces melanin synthesis (high level of oxidative stress is typical in vitiligo) [9].

The use SKA low dose bFGF and specific SKA low dose anti-inflammatory cytokines pool represents a new therapeutic approach for vitiligo strictly based on disease etiology and aimed both to stop the disease progression, through opposing chronic inflammation, and to induce skin repigmentation by direct stimulation of melanocytes.

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