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Role of the microenvironment in the imbalance between Th1/Th17 and Th2 cytokines of Mesenchymal stem Cells derived from psoriatic skin

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Psoriasis is an inflammatory and immuno-mediated disease [1] characterized by the over-expression of several Th1-Th17 cytokines, which are able to maintain a low-grade inflammatory status. The expression and secretion of Th1, Th2 and Th17 cytokines has been extensively evaluated in differentiated skin cells of psoriatic patients, while little is known about their production by MSCs in psoriatic skin. Indeed, it is known that the psoriatic microenvironment influences the MSCs phenotypic profile [2]. This works aims to evaluate the immunobiology of psoriatic MSCs (PsO-MSCs) and the potential paracrine effect that can be exerted by Healthy MSCs (H-MSCs) on PsO-MSCs.

To assess these questions, MSCs were isolated from skin of psoriatic and healthy subjects. Subsequently, indirect co-culture of H-MSCs with PsO-MSCs was performed; effects on proliferation and expression of cytokines linked to Th1/Th17 and Th2 pathways were assayed before and after co-culture.

The results show that before co-culture, proliferation of PsO-MSCs was significantly higher than H-MSCs ($p<0.05$) and the levels of secreted cytokines confirmed the imbalance of Th1/17 versus Th2 axis.

After co-culture of H-MSCs with PsO-MSCs, healthy MSCs seem to exert a "positive" influence on PsO-MSCs driving the inflammatory phenotypic profile of PsO-MSCs towards a physiological pattern. The proliferation rate decreased, towards values nearer to those observed in H-MSCs and the secretion of the cytokines that mostly identified the inflammatory microenvironment that characterized psoriasis, such as IL6, IL12, IL13, IL17A, TNFα, and GCSF, is significantly lower in co-cultured PsO-MSCs than in individually cultured PSO-MSCs (p at least <0.05).

In conclusions, our preliminary results seem to provide an intriguing molecular explanation for the ever increasing evidence of therapeutic efficacy of allogeneic MSCs infusion in psoriatic patients.

References

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Key words

Mesenchymal stem cells (MSCs), psoriasis, inflammation.