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Human dendritic cell differentiation from monocytes

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Dendritic cells (DCs) induce, sustain, and regulate immune responses and are essential mediators of immunity and tolerance. These cells are specialized to capture antigens, process and present them to T cells to initiate immune responses towards pathogens and tumours. DCs are heterogeneous for origin, anatomical localization, phenotype and function. They differentiate from haematopoietic stem cells-derived precursors, migrate from sites of antigen uptake to lymphoid organs, mature and interact with lymphocytes. Langerhans cells (LCs) are immature DCs, are located in stratified squamous epithelia of the epidermis and mucosae. LCs express CD1a, langerin/CD207, E-cadherin and have intracytoplasmic Birbeck granules. We wonder if the PPAR (peroxisome proliferator activated receptor)-gamma stimulation can give rise to LCs in vitro starting from CD14+ monocytes, as occurs with CD133+ haematopoietic precursors (1). Circulating CD14+ monocytes have been isolated by immunomagnetic separation and cultured with GM-CSF, IL-4, TNF-α and TGF-β for 7 days. The complete maturation was induced by further culture for 48 h with the same cytokines, but the concentration of the TGF-β was increased (2). Rosiglitazone was used to stimulate PPAR-γ from the start of the culture. The cells were analysed by phase contrast, electron microscopy, immunofluorescence, flow cytometry and mixed lymphocyte reaction. All cultures generated mature cells that expressed MHC-II intensely, both with and without rosiglitazone, and had lymphocyte stimulating activity. The obtained DCs express the DC-SIGN, such as connective tissue DCs, more intensely with than without rosiglitazone. Some of these cells were CD1a+ and among them a small part was CD207+, *i.e.* they were LC-like, however they never contained Birbeck granules. The percentages of cells CD1a+ and CD207+ were slightly higher without rosiglitazone. The results indicate that upon addition of rosiglitazone the *in vitro* differentiation of monocytes to LCs is hampered, at variance with what happens with cultures of CD133+ precursors. For this reason, experiments have been planned with CD34+ haematopoietic stem cells, because the generation of different types of DCs is a necessary step to gain control on these cells for medical purposes.

References

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Keywords

Cell culture; monocytes; Langerhans cells; PPAR-gamma; electron microscopy; immunofluorescence; flow cytometry.