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Steps and control mechanisms of human dendritic cell differentiation

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Among immune system dendritic cells (DCs), Langerhans cells (LCs) - found in stratified squamous epithelia - express langerin/CD207 and CD1a and contain Birbeck granules, while connective tissue DCs express DC-SIGN intensely. DCs may be generated in vitro from monocytes and from immature haematopoietic precursors; PPAR (peroxisome proliferator activated receptor)-gamma stimulation can direct CD133+ precursors to generate DCs with a LC phenotype [1]. In order to achieve deeper knowledge on human DC subtypes differentiation, circulating CD14+ monocytes have been isolated by immunomagnetic separation and cultured with GM-CSF, IL-4, and TGF-beta for 7 days. Maturation was induced by further culture for 48 h with TNF-alpha, IL-1 beta and IL-6 [2]. Rosiglitazone was used to stimulate PPAR-gamma. The cells were analysed by phase contrast and electron microscopy and by immunofluorescence. Both with and without rosiglitazone, cells with a dendritic shape were generated together with non-dendritic, elongated cells with the aspect of anti-inflammatory (M2) macrophages. All the generated, mature cells expressed MHC-II intensely. DCs grown with rosiglitazone were CD207-, while those grown without rosiglitazone appeared CD207+; in neither conditions did cells contain Birbeck granules, while in both conditions DCs expressed DC-SIGN, more intensely with than without rosiglitazone. Elongated non-dendritic cells expressed CD14 more intensely than DCs, and CD80, CD83 and CD86 as intensely as DCs. The results indicate that upon addiction of rosiglitazone the differentiation of cultured monocytes to LCs is hampered, at variance with what happens with cultures of CD133+ precursors. They also indicate that the generation of non-dendritic elongated cells, possibly M2 macrophages, can occur in association with that of dendritic cells.

References

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Keywords

Cell culture, electron microscopy, immunofluorescence, Langerhans cells, monocytes, PPAR-gamma.