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Differentiation of dendritic cells from different human circulating progenitors and effect of PPAR-gamma stimulation

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Dendritic cells (DCs) of the immune system include - among others - Langerhans cells ($CD1a^+$, langerin/$CD207^+$) and connective tissue DCs (DC-SIGN/$CD209^+$). These cells can be generated in vitro from different precursors, but the results have been inconsistent and the differentiation of specific subtypes has been hard to achieve. Although DCs express PPAR-gamma, the expression of this receptor by DC precursors and the effect of its stimulation on DC differentiation are poorly known. This study has addressed the differentiation potential into DCs of different precursors collected from peripheral blood of healthy adult human donors and the effect of rosiglitazone, an agonist of PPAR-gamma, on that differentiation. Upon immunomagnetic separation, $CD14^+$ monocytes and $CD34^+$ and $CD133^+$ progenitors were cultured with cytokines for 8 d ($CD14^+$) or 18 d ($CD34^+$ and $CD133^+$); rosiglitazone (1 μmol/l) was added in some experiments. All precursors generated HLA-DR^+(high) DCs; those from $CD34^+$ and $CD133^+$ precursors were in part large and more rich in organelles, in part medium-sized and less rich in organelles. A proportion of cells, varying with the precursors ($CD14^+$<$CD34^+$<$CD133^+$), were $CD1a^+$ and $CD207^+$; in cells derived from $CD34^+$ and $CD133^+$ progenitors they were among the large ones. Many cells from any culture expressed CD209, also together with CD207. Rudimentary Birbeck granules were observed in few DCs from any precursor. Variable percentages of DCs, highest among those from $CD133^+$ precursors, expressed CD80, CD83 and CD86. Rosiglitazone led to significant increase in $CD207^+$ DCs among cells generated from $CD133^+$ precursors; DCs derived from $CD133^+$ precursors stimulated the proliferation of $CD4^+$ lymphocytes much more than that of $CD8^+$ ones and such proliferation was significantly reduced if DCs had been generated in the presence of rosiglitazone. Freshly isolated CD133+ cells showed a number of copies of mRNA for PPAR-γ higher than $CD14^+$ and $CD34^+$ cells. The results indicate that: the differentiation potential of hematopoietic cells into DCs with different phenotypes depends on the step reached by the precursors in vivo; the orientation towards Langerhans cells can begin very early; the differentiation in vitro does not mimic entirely that in vivo; the most immature progenitors, $CD133^+$ cells, express PPAR-gamma; stimulation of these receptors may play a role in modulating DC differentiation.