ABSTRACT

Dendritic cells (DCs) are a heterogeneous population of cells with different origin, phenotype and function that share the crucial role of inducing, coordinating and maintaining adaptive immune responses. Most of the knowledge on human DCs relies on experiments performed with DCs differentiated *in vitro* from monocytes treated with diverse cocktails of recombinant cytokines; in particular it is well established that human monocytes differentiate into DCs when cultured with granulocyte-macrophage colony-stimulating factor and interleukin (IL)-4. However, the possibility that monocytes represent precursors for tissue human DCs under physiological conditions remains controversial. Moreover, it is not completely established which cell population synthesizes the cytokines required for monocyte differentiation *in vitro* and how their secretion is regulated *in vivo*.

In this thesis is shown that, on specific activation, T lymphocytes are capable of secreting cytokines, which in turn induce the differentiation into DCs of antigen-presenting and bystander monocytes. Depending on the functional polarization of the activated T lymphocytes, monocytes differentiate into DCs with diverse phenotype and functionality.

Monocytes exposed to cytokines released by T helper (Th)1 and Th0 lymphocytes differentiate into DCs with a reduced antigen uptake and antigen presentation capacity. Moreover, these DCs show a limited capacity to induce Th1 polarization of naive T cells but are capable of priming IL-10-secreting T cells, thus displaying tolerogenic potential. Conversely, DCs derived from monocytes sensing cytokines released by Th2 lymphocytes are antigen-presenting-cells (APCs) endowed with a marked Th1 polarization capacity.

Starting from the point that monocytes are co-recruited with lymphocytes in chronic inflammation sites, the results obtained in this work suggest that functionally different DCs can be generated in environments characterized by the prevalent release of Th1-, Th0-, or Th2-associated cytokines. Because the APCs capacities of these DCs showed opposite functional consequences, it has been proposed an *in vitro* model that can reproduce a contribution in the regulation of the ongoing human immune response by monocyte-derived inflammatory DCs.

***Key words**: antigen presentation – cytokines – cell differentiation – chronic inflammation – T lymphocytes – human monocytes*