Editoriais / Editorials

Plasticity of dendritic cells during differentiation and maturation

A plasticidade das células dentríticas durante a diferenciação e a maturação

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In general, there are two major immunotherapeutic strategies for the induction of the immunological response: 1) active immunotherapy based on the use of dendritic cells (DCs) for the activation of the immunological system and 2) passive immunotherapy based on the use of antigen-specific T lymphocytes or of components of the immunological system such as anti-tumor antibodies.

In contrast to standard vaccines used for disease prevention, vaccines based on DCs used for anti-tumor treatment or against infectious agents are developed exclusively in order to induce the immunological system to react vigorously against diseases already installed.[1,2]

Studies using animal models have investigated different aspects regarding the use of DCs in anti-tumor immunotherapy and have observed that DCs generated *ex-vivo* and activated with specific tumor antigens may trigger the cell immune response in some situations and the humoral response in others. Furthermore, other studies in which classical therapy was combined with DCs have resulted in a better prognosis for the disease. Taken together, these results have led to the development of different clinical protocols for the determination of DC efficacy in the treatment of different types of cancer or of infectious diseases.

Despite the growing number of clinical protocols involving the use of DCs, to date there is no consensus about the effect of different cultures and isolation conditions on the morphological characteristics and the immuno-phenotypic profile of the major surface markers of DCs. Another problem faced in DC culture is the need to obtain an initial monocyte population of high purity, an essential step for obtaining a homogeneous DC population.

The article by Fontes *et al.* in this issue deals with these two points. The authors suggest a modification of the standard protocol for the isolation of a monocyte population from mononuclear cells. This protocol involves a second Percoll gradient after the Ficoll gradient, resulting in the derivation of a monocyte population of high purity (> 90%). In their study, the authors also showed that TNF-α or PGE_1 *per se* induce an increased expression of the DC1a+ molecule to levels similar to those obtained after induction with TNF-α + PGE_1 or LPS. Lipopolysaccharide [LPS] can trigger a potent stimulatory action on DC maturation, but cannot be used in clinical assays due to its high toxicity.

In addition, regarding the expression of co-stimulatory molecules (DC80, DC40 and DC83), the authors showed that the combination of TNF-α + PGE_1 is more efficient when compared to each of these agents alone. These results can be explained by the fact that TNF-α, PGE_1 and LPS induce DC maturation by different mechanisms. Our group has recently compared the protein profile of immature and mature DCs with literature data, reaching the conclusion that the proteomic profile depends on the stimulus used.[3] Taken together, these data show the complexity of the mechanism of DC maturation and suggest that different stimuli can modulate the plasticity of these cells *in vitro* or *ex-vivo*.

References

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