Handbook of Experimental Pharmacology
“Dendritic Cells”

The Use of Dexamethasone in the Induction of Tolerogenic DCs

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Abstract Dendritic cells (DCs) have a central role in immune regulation, ranging from tolerance induction to the induction of specific immune responses. DCs serve as an essential link between innate and adaptive immunity. This broad range of powerful immune stimulatory as well as regulatory functions has made DCs as targets for vaccine development strategies. One approach to promote the tolerogenicity of...
DCs is to suppress their maturation by pharmacological agents, including glucocorticoids (GCs). In the present chapter we will review GCs used in vitro with cultured DCs, applied in vivo, or used to generate tolerogenic DCs for cellular therapy.

1 Introduction

Dendritic cells (DCs) are bone marrow-derived cells that populate all lymphoid and nonlymphoid organs. They have a central role in immune regulation, ranging from tolerance induction and the prevention of autoimmunity to the induction of antitumor immunity and the protection against infectious agents. Although DCs are a heterogeneous group of cells that represent differences in origin, anatomic location, cell surface phenotype, and function, they all have potent antigen presenting capacity for stimulating naive, memory, effector and/or regulatory T cells. Therefore, DCs serve as an essential link between innate and adaptive immune responses (Banchereau and Steinman 1998; Steinman and Banchereau 2007).

This broad range of powerful immune stimulatory and regulatory functions has made DCs targets for vaccine development strategies. This includes cellular vaccination for treatment of cancer or infectious diseases, as well as “negative vaccination” for the treatment of autoimmune diseases and prevention of allograft rejections. The latter can be accomplished by inhibiting the immunostimulatory capacity of DCs, or more importantly, exploiting tolerogenic DCs to specifically silence immune responses. One approach to promote the tolerogenicity of DCs is to suppress their maturation using antiinflammatory cytokines or pharmacological agents or genetically engineered DCs expressing immunosuppressive molecules, as recently reviewed by several groups (Hackstein and Thomson 2004; Woltman and van Kooten 2003; Adorini et al. 2004; Morelli and Thomson 2007). One class of agents that have shown promising effects on prevention of DC maturation, and widely applicable are glucocorticoids (GC). In the present chapter we will specifically focus on the use of GC, either in vitro in cell cultures or applied in vivo, or used to generate tolerogenic DCs for cellular therapy.

2 Glucocorticoids

Glucocorticoids (GC) are among the most potent immunosuppressive and anti-inflammatory drugs currently available and are efficacious in the treatment of both Th-1 and Th-2 associated inflammatory diseases, including allograft rejection, rheumatoid arthritis and asthma (Wilckens and De Rijk 1997). The therapeutic effects of GC were initially ascribed to the strong inhibitory effect on T cells. At the moment, however, it is obvious that also antigen presenting cells (APC) are strongly affected by GC. It has been demonstrated that GC downregulates the production of proinflammatory cytokines by monocytes and macrophages and also affect DC function; the subject of the present review. Various derivatives of GC are used in clinical practice and, as far as we know, there are no differences in the functional effects