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Capacity of CD34+ progenitor-derived dendritic cells to distinguish between sensitizers and irritants

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Abstract

In an attempt to develop an in vitro test to identify contact sensitizers, mostly dendritic cells (DCs) derived from monocytes (Mo-DC) have been used. Less is known about the potency of DC derived from CD34+ progenitors (CD34-DC) for in vitro allergen testing.

CD34+ progenitor derived DC were exposed to nine well-known allergens (one weak, three moderate and five strong allergens) and two irritants. Surface marker expression (CD86, CD83 and HLA-DR) and cytokine production (IL-6, IL-12 and TNF-α) were analyzed after 24 h exposure to these chemicals. All allergens tested induced a significant increase in at least one of the DC surface markers. In contrast, none of the irritants tested were able to significantly upregulate membrane marker expression in exposed DC. The level of upregulation of CD86, CD83 and HLA-DR was dependent on the nature and concentration of the chemical, but not on the classification of the allergen. Changes in cytokine production (IL-6, IL-12 and TNF-α) were not consistently related to exposure to an allergen. Based on these results, we conclude that the in vitro test using CD34-DC has the capacity to distinguish between allergens and irritants based on altered phenotypic characteristics.
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Keywords: Dendritic cells; CD34+ progenitor cells; Allergens; Phenotype markers; Cytokines

Abbreviations: BC, benzalkonium chloride; CD34-DC, dendritic cells derived from CD34+ cord blood cells; CIN, alpha-hexylcinnamaldehyde; DC, dendritic cells; DNBS, dinitrobenzenesulfonic acid; DNCB, dinitrochlorobenzene; DNFB, dinitrofluorobenzene; EUG, eugenol; IL-6, interleukin-6; IL-12, interleukin-12; Mo-DC, dendritic cells derived from CD14+ monocytes; Ni, nickel; OXA, oxazolone; PD, potassium dichromate; rh-TNF-α, recombinant human tumor necrosis factor-α; SDS, sodium dodecyl sulfate; SI, stimulation index; TNBS, 2,4,6-trinitrobenzene sulfonic acid

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1. Introduction

Small molecular weight chemicals can induce skin sensitization and as a consequence lead to allergic contact dermatitis. To analyze the allergic potential of new chemicals, several in vivo animal tests (e.g. guinea pig test, mouse ear swelling test, local lymph node assay) are currently used (Gerberick et al., 1992; Kligman and Basketter, 1995). To reduce the number of animals needed for contact sensitization testing, a lot of efforts have been undertaken to establish in vitro systems (Ryan et al., 2001).

Dendritic cells (DCs) that are localised in the skin (Langerhans cells) play a major role in the development of an allergic reaction (Hart, 1997). These professional antigen-presenting cells (APCs) are able to take up and proteolytically process the allergen. During this process DC become activated when they are provided with adequate chemokine and cytokine signals (Sallusto et al., 1995). The activated cells show a significant increase in (1) the surface expression of the class II major histocomptability complex antigen (MHC II), (2) the surface expression of CD83 (a mature DC marker) and (3) the surface expression of several costimulatory molecules (e.g. CD80, CD86) (Aiba and Katz, 1990), which play an important role in the interaction between the T cell and the APC. Once activated, DC also produce certain cytokines (e.g. interleukin-6 (IL-6), interleukin-12 (IL-12), tumor necrosis factor-α (TNF-α) (Enk and Katz, 1992; Hope et al., 1995). IL-6 together with IL-1β are known to act as important costimulatory cytokines for T-cell activation in vivo (mice), whereas TNF-α is thought to be necessary for the migration of DC to the regional lymph nodes. After exposure to contact allergens in vivo, DC are known to produce IL-12, which directs the T-cell proliferation towards T-helper 1 (Th1) differentiation (Heufler et al., 1996). Contact sensitization is known to be a Th1 response. DC activation and maturation is necessary in order to present the modified allergen to naïve T-lymphocytes in the draining lymph node. Subsequently, T-cells are activated (sensitized) and start to proliferate (Hart, 1997; Banchereau and Steinman, 1998).

In contrast to sensitization, irritation is a non-immunological inflammatory reaction. Irritants cause damage to all cells that come into contact with these toxic compounds and as a consequence inflammatory effectors are attracted to the exposure site.

Several attempts have been undertaken to develop an in vitro screening assay based on human DC to identify potential contact allergens. The in vitro test based on DC derived from human monocytes (Mo-DC), is the most frequently used (Romani et al., 1994; Sallusto and Lanzavecchio, 1994), whereas less is known about the model based on DC derived from CD34+ progenitors (CD34-DC) from human cord blood (Strunk et al., 1996).

Previous research indicated that in vitro cultured CD34-DC were able to discriminate between the model allergen nickel (Ni) and the model irritant sodium dodecyl sulfate (SDS) by phenotypic changes (CD86, CD83 and HLA-DR) and the production of IL-6 (De Smedt et al., 2001). Comparative analysis of the phenotype of Mo-DC and CD34-DC after exposure to a limited number of allergens showed no major differences in the discriminating capacity of both DC populations (De Smedt et al., 2002). However, whereas the yield of Mo-DC was less than the number of monocytes initially plated, the yield of the CD34-DC was 10–15 times the starting cell number (De Smedt et al., 2002). As a consequence, this enables us to test several chemicals simultaneously with cells obtained from one donor. Therefore, in this study we further evaluated the sensitivity and specificity of the in vitro CD34-DC system by exposing the cells to nine allergens and two irritants. Phenotypic changes as well as cytokine production of the CD34-DC were evaluated.

2. Materials and methods

2.1. Source of cells

Cord blood samples were collected from the umbilical vessel of placentas immediately after delivery of normal full-term infants. Collection of the blood was done by lifting the placenta and allowing the blood to flow into heparinized tubes, containing Iscove's Modified Dulbecco's Medium (IMDM), supplemented with 10% foetal bovine serum (FBS) and sodium heparin (Sigma, Bornem, Belgium) at a final concentration of 200 U/ml. Cord blood samples were stored at room temperature and handled within 24 h after collection. The ethical commission of the hospital approved collection of cord blood samples and oral informed

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