Inhibition of human allergic T-cell responses by IL-10–treated dendritic cells: Differences from hydrocortisone-treated dendritic cells

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Background: Dendritic cells (DCs) are able to induce human allergic T_H1 responses as well as T_H2 responses.
Objective: In this study, we examined the effect of anti-inflammatory agents such as IL-10 and hydrocortisone (HC) on the accessory function of DCs and the resulting T-cell response, especially that of T_H2 cells.
Methods: Naive and memory $CD4^+$ T cells from atopic donors were stimulated with autologous allergen-pulsed DCs generated from $CD14^+$ monocytes by culture with GM-CSF/IL-4 and fully matured with IL-1β, TNF-α, and PGE_2 in the presence or absence of IL-10 or HC.
Results: IL-10–treated DCs and, to a lesser extent, HC-treated DCs showed a decreased expression of MHC II molecules, the costimulatory molecule CD86, and the DC-specific marker CD83, as well as a strongly reduced IL-12 secretion. Consequently, T-cell proliferation was reduced after stimulation with IL-10– or HC-treated DCs alike. However, pretreatment of DCs with IL-10 inhibited the production of T_H1 and T_H2 cytokines by T cells, whereas HC-treated DCs inhibited production of IFN-γ but induced an increased release of IL-4 and no change in IL-5. Both effects were long-lasting; cytokine production remained low (which was due not to enhanced apoptosis but to functional hyporesponsiveness) or even increased after restimulation with fully matured DCs.
Conclusion: These data indicate that IL-10– or HC-treated DCs differ in their ability to influence human allergic T-cell responses. This has major implications for therapeutic strategies aiming at the downregulation of proallergic T_H2 responses. (J Allergy Clin Immunol 2001;108:242-9.)

Key words: *Dendritic cells, IL-10, hydrocortisone, T_H1/T_H2, allergy*

Dendritic cells (DCs) are the most potent antigen-presenting cells (APCs) in vitro and in vivo, endowed with the ability to initiate new immune responses because of their capacity to activate naive T lymphocytes for T_H1-type cytokine (IL-2, IFN-γ) or T_H2-type cytokine (IL-4, IL-5, IL-10, IL-13) production.[1-4] Today, DCs can be generated in large numbers from $CD14^+$ monocytes in the peripheral blood by culturing with GM-CSF and IL-4. The resulting immature DCs differentiate into mature DCs in the presence of proinflammatory cytokines (TNF-α, IL-1β, and IL-6), PGE_2, LPS, or CD40 ligand).[5-8] A number of studies have shown that DCs favor the induction of T_H1-mediated immune responses because of their production of IL-12.[9,10] However, there are some publications, including a recent report by us, demonstrating that DCs are also able to promote T_H2 cells and that DCs are required for the development of allergic inflammation in response to inhaled allergen.[11-14] In this respect, it has been suggested that DCs can be classified into distinct lineages, called *DC1* and *DC2*, according to the type of immune response initiated by them.[15,16] The polarization in DC1 or DC2 is further influenced by the microenvironment, especially the presence of IFN-γ during activation of immature DCs, which promotes the development of DC1 with a capability for high IL-12 production; in contrast, PGE_2 promotes low IL-12 production and a T_H2-driving capacity (DC2).[17] However, in our hands, DCs stimulated in the absence of PGE_2 show an immature phenotype and an impaired T_H1- as well as T_H2-inducing capacity.[14]

Abbreviations used
APC: Antigen-presenting cell
DC: Dendritic cell
GC: Glucocorticoid
HC: Hydrocortisone

Glucocorticoids (GCs) and IL-10 are potent anti-inflammatory and immunoregulatory agents.[18,19] Both inhibit cytokine secretion of T_H1 and T_H2 cells and suppress the accessory cell function of monocytes/macro-phages via downregulation of the expression of MHC class II costimulatory and adhesion molecules as well as of many proinflammatory cytokines.[20-23] Inhibition of APC function of DCs by IL-10 or GCs has been described only in experimental systems in which alloantigen-specific or superantigen-driven T-cell stimulation was used.[24-28] The influence of IL-10– or GC-treated DCs on T_H2 cell functions has not yet been investigated, especially not in an allergen-specific setting, which is of particular relevance to atopic diseases.

The aim of the present study was to investigate the effects of IL-10 and hydrocortisone (HC) on the differentiation, maturation, and T cell–stimulatory capacity of DCs derived from $CD14^+$ monocytes from atopic individuals, with special attention to their influence on T_H2 responses.

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METHODS

Blood donors

Venous blood from atopic donors with allergic rhinoconjunctivitis or asthma to grass pollen, birch pollen, rye pollen and/or house dust mite (*Dermatophagoides pteronyssinus*) was collected. Specific sensitization was documented by positive skin prick test results to the respective allergen and detection of allergen-specific IgE in the sera (RAST class ≥ 2).

In vitro generation of monocyte-derived DC

PBMCs were isolated from heparinized blood by means of Ficoll-Paque 1.077 (Biochrom, Berlin, Germany) density centrifugation, and 1×10^7 cells per well were incubated for 45 minutes in a 6-well plate (Costar, Bodenheim, Germany) in RPMI 1640 medium supplemented with 3% autologous serum at 37°C. After the nonadherent cells were washed, the remaining monocytes (purity, >90% $CD14^+$) were incubated in 3 mL per well of X-VIVO 15 (Bio-Whittaker, Walkersville, Md) supplemented with 1% heat-inactivated autologous serum, 1000 U/mL IL-4 (Strathmann Biotech GmbH, Hannover, Germany), and 800 U/mL GM-CSF (Leucomax, Sandoz AG, Nürnberg, Germany). On day 7, the resulting immature DCs were pulsed with 10 μg/mL of grass pollen, birch pollen, rye pollen, or house dust mite allergen extracts (Alk-Scherax, Hamburg, Germany) and further stimulated with 1000 U/mL TNF-α, 2000 U/mL IL-1β (Strathmann Biotech GmbH), and 1 μg/mL PGE_2 (Minprostin E_2, Pharmacia & Upjohn GmbH, Erlangen, Germany) to induce their full maturation. At the same time, 20 ng/mL of IL-10 (DNAX, Palo Alto, Calif) or 5×10^{-6} mol/L HC (Sigma, Deisenhofen, Germany) was added to the culture. Mature DCs were harvested 48 hours after stimulation, washed twice, and used for T-cell stimulation assays.

Purification of naive and memory T cells

Autologous $CD45RA^+$ (naive) were positively selected and $CD45R0^+$ (memory) $CD4^+$ T cells negatively selected from PBMCs through use of antibody-coated paramagnetic MicroBeads (MACS, Miltenyi Biotec, Bergisch Gladbach, Germany), according to the protocol of the manufacturer. Separation was controlled by flow cytometry (purity, >98% $CD4^+$ T cells, >95% $CD45RA^+$ $CD4^+$ T cells, and >95% $CD45R0^+$ $CD4^+$ T cells).

Induction of proliferative responses and cytokine production in naive and memory $CD4^+$ T helper cells

For proliferation assays, 1×10^5 $CD45RA^+$ or $CD45R0^+$ $CD4^+$ T cells were cocultured in 96-well plates (Costar) in triplicate with titrated numbers of autologous allergen-pulsed DCs, either pretreated with IL-10 or HC or else untreated, in 200 μL X-VIVO 15. After 5 days, the cells were pulsed with 37 kBq per well of [^{3}H]TdR ([methyl-^{3}H]thymidine, ICN, Irvine, Calif) for 6 hours, and [^{3}H]TdR incorporation was evaluated in a β counter (1205 Betaplate, LKB Wallac, Turku, Finland).

For cytokine production assays, 5×10^5 $CD45RA^+$ or $CD45R0^+$ $CD4^+$ T cells were cocultured in 48-well plates with 5×10^4 autologous allergen-pulsed DCs, either pretreated with IL-10 or HC or else untreated, in 1 mL X-VIVO 15. After 1 week of culture, T cells were restimulated with newly generated allergen-pulsed DCs, IL-10– or HC-treated or untreated, and supernatants were collected 24 hours later. For some experiments, 100 U/mL IL-2 (Proleukin, Chiron GmbH, Ratingen, Germany) was added during the second stimulation.

Analysis of surface marker expression by flow cytometry

Surface phenotyping of DCs was performed by staining 5×10^4 cells with specific mouse antihuman mAbs for 20 minutes on ice. Antibodies used were CD80 (MAB104, Immunotech, Hamburg, Germany), CD83 (HB15a, Immunotech), CD86 (BU63, Camon, Wiesbaden, Germany), and rat antihuman HLA-DR (YE2/36HLK, Camon). After being washed with PBS containing 2% FCS, the cells were stained with PE-conjugated donkey antimouse IgG (Dianova, Hamburg, Germany) and fluorescein (DTAF)–conjugated goat antirat IgG (Dianova). After 20 minutes the cells were washed and analyzed in a FACSCalibur (Becton Dickinson, Mountain View, Calif) equipped with CellQuest software (Becton Dickinson).

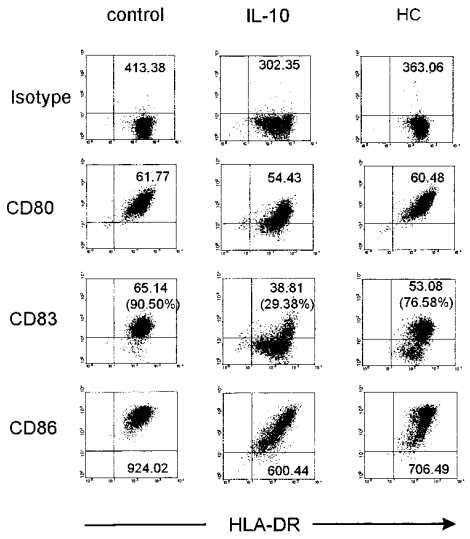

FIG 1. Modulation of surface marker expression of allergen-pulsed DCs by IL-10 and HC. DCs were matured without (*control*) or with the addition of IL-10 or HC on day 7 of culture. After 48 hours, cells were double-stained for HLA-DR and additional marker, as indicated. The figure shows 1 representative example, including the mean fluorescence intensity and the percentage of positive cells (for CD83), of 15 separate experiments.

Quantification of cytokine production by ELISA

Human IL-12p70 was measured by means of an ELISA Kit (Diaclone Research, Besançon, France) according to the manufacturer's instructions (detection limit, <3 pg/mL). Human IL-4, IL-5, IL-10, IL-12p40, IFN-γ (BD PharMingen, San Diego, Calif), and IL-6 (R&D Systems, Wiesbaden, Germany) were measured by ELISA according to the instructions of the distributors of the pairs of antibodies used, as described previously.[14] The detection limit was 8 pg/mL for IL-4, 16 pg/mL for IL-10, and 32 pg/mL for all other cytokines.

Statistics

The Student *t* test was used to test the statistical significance of the results; $P \leq .05$ was considered significant.

RESULTS

Effect of IL-10 or HC on the phenotype and cytokine production of monocyte-derived allergen-pulsed DCs from atopic individuals

We investigated the influence of the 2 anti-inflammatory agents IL-10 and HC on the phenotype of monocyte-derived, allergen-pulsed DCs from atopic donors that were matured in the presence or absence of IL-10 or HC. Preliminary experiments had shown that the

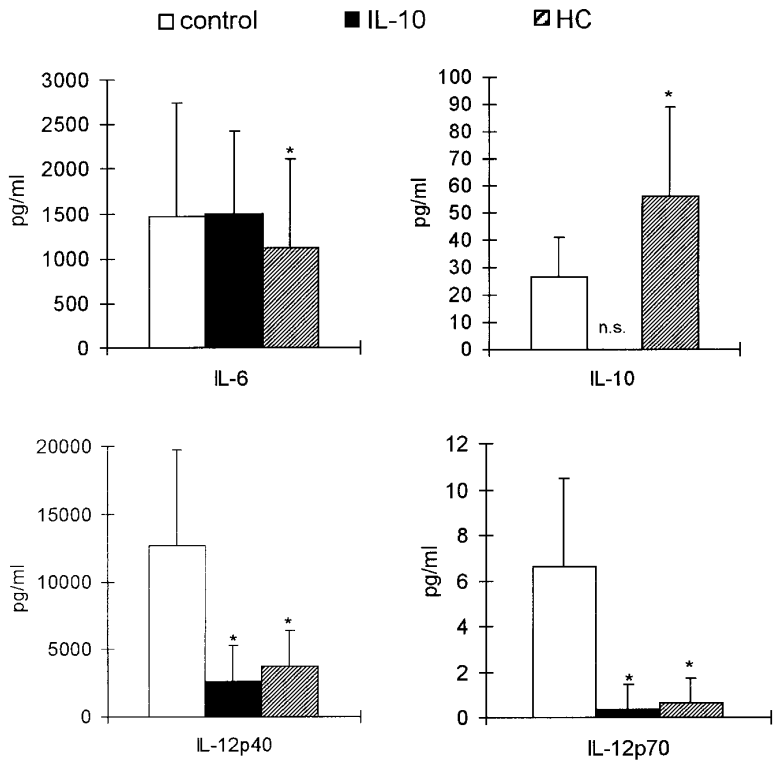

FIG 2. Inhibition of cytokine production of allergen-pulsed mature DCs by treatment with IL-10 and HC. DCs were matured without (*control*) or with the addition of IL-10 or HC on day 7 of culture. Supernatants were harvested 24 hours later for assessment of IL-12p40 and IL-12p70 (n = 11) production and after 48 hours for analysis of IL-6 (n = 11) and IL-10 (n = 9) production by ELISA. The results represent the means ± SDs. *Asterisks* indicate statistically significant differences ($P \leq .05$) between untreated and IL-10– or HC-treated DCs. *n.s.,* Not shown.

optimal concentrations were 20 ng/mL for IL-10 and 5×10^{-6} mol/L for HC (data not shown). The pretreatment of DCs with IL-10 inhibited their maturation; this was characterized by a significantly decreased expression (mean fluorescence intensity and percentage) of the MHC class II molecule HLA-DR, the costimulatory molecules CD80 and (especially) CD86, and the DC-specific marker CD83 (Fig 1). However, expression of CD83 and CD86 was only slightly (but still significantly) downregulated after treatment of DCs with HC, whereas expression of CD80 and HLA-DR was not affected at all (Fig 1).

Because the production of DC-derived proinflammatory and immunoregulatory cytokines plays an important role during T-cell differentiation, we investigated the influence of IL-10 and HC pretreatment on IL-6, IL-10, and IL-12 production of DCs from atopic donors. As shown in Fig 2, maturation of DCs in the presence of IL-10 or HC strongly inhibited the production of IL-12p40 and the biologically active IL-12p70 molecule in comparison with control DCs. The proinflammatory cytokine IL-6, however, was inhibited only by HC-treated DCs; IL-10–treated DCs did not change their IL-6 production significantly (Fig 2). Although IL-10 production by mature untreated DCs was very low and sometimes even not detectable, it was significantly upregulated by pretreatment of DCs with HC (Fig 2); IL-10 production by DC cultures that were additionally treated with IL-10 was not shown.

Effect of IL-10 and HC on the T cell–stimulatory capacity of allergen-pulsed DCs from atopic individuals

To analyze the influence of IL-10 or HC on the DC-induced T-cell proliferation, naive ($CD45RA^+$) and memory ($CD45R0^+$) $CD4^+$ T cells from atopic donors were stimulated with autologous allergen-pulsed DCs and [^{3}H]TdR incorporation was measured after 5 days of culture. As shown in Fig 3, IL-10– or HC-treated DCs markedly inhibited allergen-induced T-cell proliferation of autologous naive and memory T helper cells. In line with the observation that the phenotype of mature DCs was affected more strongly after pretreatment of DCs with IL-10 than after pretreatment with HC, IL-10–treated DCs inhibited allergen-induced T-cell proliferation more efficiently than HC-treated DCs (Fig 3). When unpulsed DCs were used as controls, no T-cell proliferation was observed.

IL-10– or HC-pretreatment of allergen-pulsed DCs differentially modulates the cytokine production of naive and memory $CD4^+$ T cells from atopic individuals

To investigate how the described different effects of IL-10 and HC on the phenotype and accessory function of DCs would influence the cytokine profile by T helper cells from

atopic individuals stimulated by these different DCs, allergen-pulsed DCs that were matured in the presence or absence of IL-10 or HC were cocultured with autologous naive or memory CD4+ T cells. The use of IL-10–treated DCs as APCs strongly inhibited the production of the type 1 cytokine IFN-γ by naive and memory CD4+ T cells from atopic donors but also inhibited the production of the type 2 cytokines IL-4 and IL-5. Because naive T helper cells, even ones from atopic donors, produced only small amounts of IL-4, a further inhibition of the production of this cytokine could not be demonstrated in this subset (Fig 4).

The use of HC-treated DCs as APCs inhibited IFN-γ production only by naive T helper cells (and to a lesser extent by memory T helper cells); in contrast, production of IL-4 by naive and memory T helper cells was even increased (Fig 4). Production of IL-5 was not significantly affected. In every experiment, when unpulsed DCs were used as a control, production of all cytokines was very low or even not detectable (data not shown).

Stability of the different effects of IL-10–treated and HC-treated DCs on the cytokine production of allergen-specific T helper cells from atopic individuals

To test whether these different effects of IL-10– and HC-treated DCs on T_H1 and T_H2 cytokine production by T cells were long-lasting, naive and memory CD4+ T cells from atopic donors were cocultured with IL-10– or HC-treated DCs during primary stimulation. The second stimulation was performed with untreated, fully mature DCs. Naive and memory CD4+ T cells that were cultured with IL-10–treated DCs during the primary coculture still showed decreased proliferative responses (data not shown) and decreased production of the T_H1 cytokine IFN-γ after secondary stimulation (Fig 5). In contrast, production of the T_H2 cytokines IL-4 and IL-5 remained decreased only among naive T helper cells, whereas preactivated (memory) T cells produced amounts of T_H2 cytokines comparable to those produced by T cells stimulated with fully matured DCs (Fig 5).

T cells primarily stimulated with HC-treated DCs still produced higher amounts of IL-4 after restimulation with fully matured DCs than did T cells primarily stimulated with fully matured DCs, and they produced comparable amounts of IL-5. The production of the T_H1 cytokine IFN-γ was decreased after restimulation with fully matured DCs only among naive T helper cells, whereas preactivated (memory) T helper cells showed no more reduced IFN-γ production after restimulation with fully matured DCs (Fig 5).

The long-lasting inhibitory effects of IL-10– or HC-treated DCs on the cytokine production of T helper cells are due not to induction of apoptosis but to induction of functional hyporesponsiveness

In the following experiments, we analyzed whether the reduced production of T_H1 and/or T_H2 cytokines after

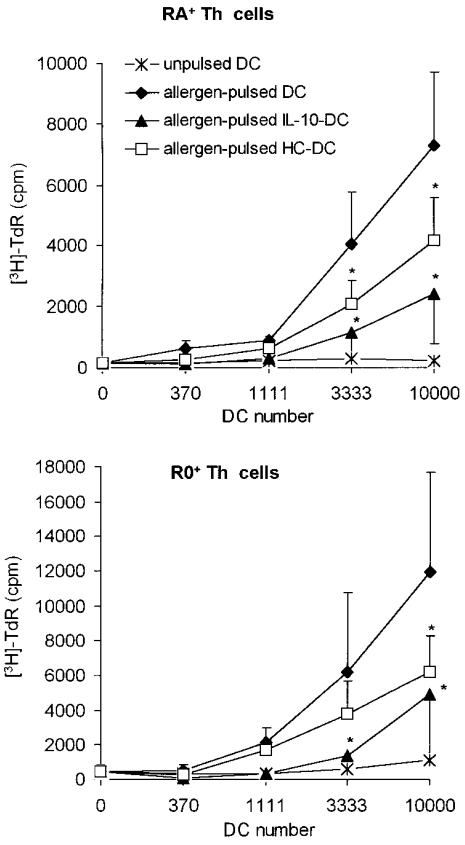

FIG 3. Inhibition of the T cell–stimulatory capacity of allergen-pulsed DCs by IL-10 and HC. 1×10^5 CD45RA+ or CD45R0+ CD4+ T cells were stimulated with titrated numbers of autologous allergen-pulsed DCs, either pretreated with IL-10 or HC or else untreated. After 5 days, the cells were pulsed with 1 μCi of [3H]TdR for 6 hours before harvesting. The data represent the means ± SDs from 8 independent experiments. *Asterisks* indicate statistically significant differences ($P \leq .05$) between untreated and IL-10– or HC-treated DCs.

stimulation of naive and memory T helper cells with IL-10– or HC-treated DCs was due to enhanced apoptosis of these T helper cells. However, determination of cell death by annexin V and propidium iodide revealed that induction of apoptosis was even inhibited after stimulation of naive and memory T helper cells with IL-10– or HC-treated allergen-pulsed DCs in comparison with untreated DCs (data not shown).

To investigate whether IL-2, a cytokine that has been described as overcoming the state of anergy in the context of T_H1 or Tc1 cells,[24,29] could also reverse the long-lasting inhibited production of the T_H2-cytokines IL-4 and IL-5 by naive T helper cells after stimulation with IL-10–treated DCs and the decreased production of IFN-γ after stimulation with HC-treated DCs, naive T helper cells cultured with IL-10– or HC-treated DCs during the first coculture were restimulated with fully matured DCs during the second coculture in the presence of 100 U/mL IL-2. In all cases, as shown in Fig 6, production of T_H1 and T_H2 cytokines was almost fully restored by the addition of IL-2, indicating that the hyporesponsive cells were functionally inhibited.

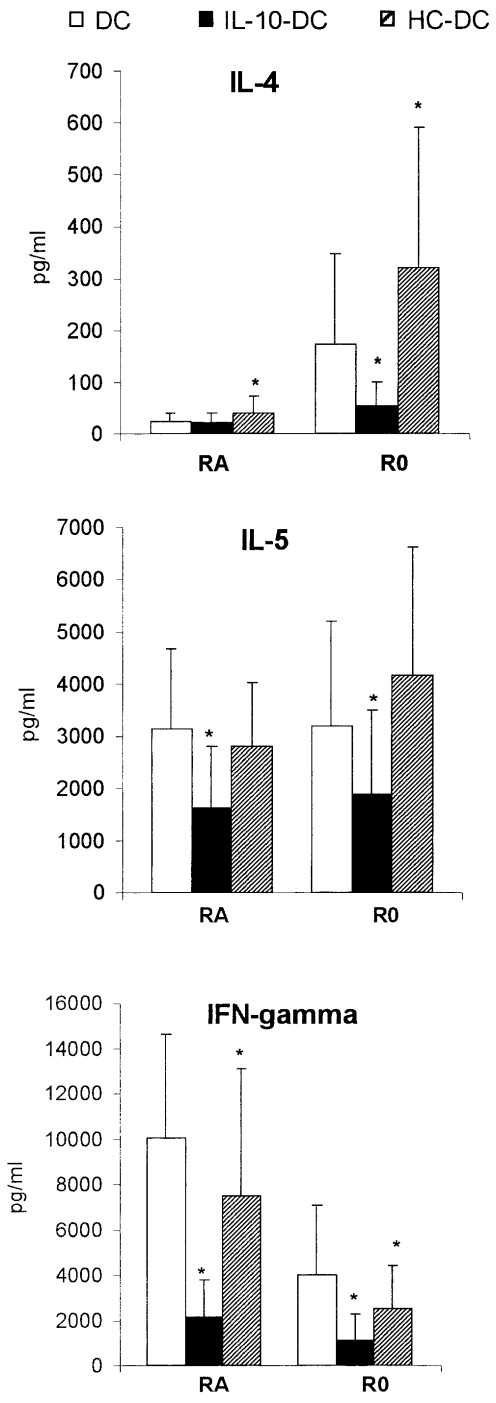

FIG 4. IL-10– or HC-treated DCs differentially modulate cytokine production of naive and memory T helper cells from atopic donors. 5×10^5 CD45RA+ or CD45R0+ CD4+ T cells were stimulated with 5×10^4 autologous allergen-pulsed DCs, either pretreated with IL-10 or HC or else untreated. After 1 week of culture, T cells were restimulated with 5×10^4 newly generated DCs or with IL-10– or HC-treated DCs of the same donor. Supernatants were collected 24 hours later and analyzed for IL-4, IL-5, and IFN-γ content by ELISA. Shown are the means ± SDs from 19 (for IL-10–treated DCs) and 16 (for HC-treated DCs) independent experiments. *Asterisks* indicate statistically significant differences ($P \leq .05$) between untreated and IL-10– or HC-treated DCs.

DISCUSSION

In the present study we demonstrated that exposure of DCs to the anti-inflammatory agents IL-10 or HC differentially influences human allergic immune responses. The use of IL-10–treated allergen-pulsed DCs for T-cell stimulation resulted in decreased production of T_H1 (IFN-γ) cytokines as well as T_H2 (IL-4, IL-5) cytokines by naive and memory CD4+ T cells from atopic individuals, whereas HC-treated DCs inhibited only T_H1 production, enhancing IL-4 production (Fig 7). In accord with the induction of decreased IFN-γ production by T cells, IL-10– or HC-treated DCs themselves produced lower levels of IL-12p40 and IL-12p70 than fully matured DCs. However, phenotype and APC function of mature DCs were affected more efficiently after pretreatment of DCs with IL-10 than after pretreatment with HC, which probably explains the strong inhibitory effect of IL-10–treated DCs on T_H1 and T_H2 cells.

Concerning the effect of IL-10 on DCs, our results are in line with those of recent studies showing that IL-10–treated human DCs induce an alloantigen- or peptide-specific anergy in T_H1 cells producing lower levels of IL-2 and IFN-γ.[24] In the murine system, it was reported that DCs generated in vitro in the presence of IL-10 have an impaired capacity to induce a T_H1-type response in vivo, leading to an enhanced development of T_H2 lymphocytes.[30,31] In our study, however, we report for the first time that pretreatment of human DCs with IL-10 results not only in a reduced proliferation and IFN-γ production of naive and memory T helper cells but also in a reduced production of the type 2 cytokines IL-4 and IL-5. This discrepancy might result from the fact that in the murine system IL-10 is produced only by T_H2 cells, whereas in human beings T_H1 as well as T_H2 cells are able to secrete IL-10.[32] In this respect, it was demonstrated that IL-10 not only inhibits inflammatory processes mediated by T_H1 cells (because of a direct inhibitory effect on CD4+ T cells[33] and because of downregulating the APC function of monocytes/macrophages[20]) but also might be useful in inhibiting allergic immune responses induced by T_H2 cells.[18,32]

The enhancing effect of HC on the capacity of DCs to induce T_H2 cytokine production is in accord with the results in a recent study by Vieira et al,[26] who found that GC-treated DCs secrete lower amounts of bioactive IL-12 and induce less IFN-γ but more IL-5 and IL-10 in superantigen-stimulated CD4+ T helper cells. Despite the preferential activation of T_H2-like cells, GCs are useful for the therapy of allergic diseases, probably because in addition to the anti-inflammatory effects, allergen-specific IgE production is inhibited as a result of inhibition of the activation of allergen-specific T helper cells; in contrast, production of total IgE is eventually enhanced because of increased IL-4 levels—a result of decreased IL-4 usage by APCs.[34] Our data concerning the effect of HC on DC function support findings in earlier studies demonstrating that GC pretreatment inhibits the maturation of DCs, as indicated by decreased expression of costimulatory molecules and CD83 as well as by

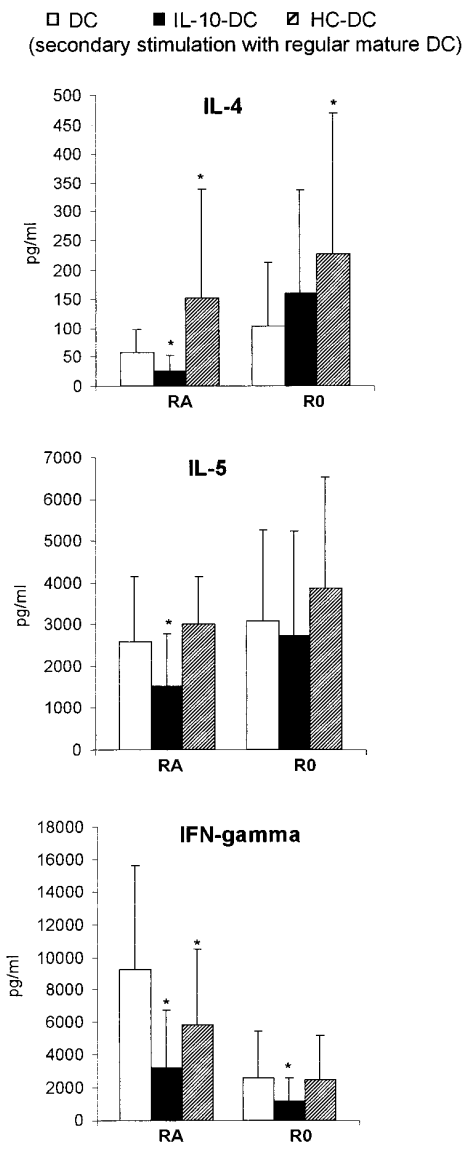

FIG 5. Long-lasting and stable effect of IL-10– or HC-pretreatment of DCs on cytokine production by T cells. 5×10^5 CD45RA+ or CD45R0+ CD4+ T cells were primarily stimulated with 5×10^4 autologous allergen-pulsed DCs, either pretreated with IL-10 or HC or else untreated. After 1 week of culture, T cells were restimulated with 5×10^4 newly generated, fully mature, allergen-pulsed DCs of the same donor. Supernatants were collected 24 hours later and analyzed for IL-4, IL-5, and IFN-γ content by ELISA. Shown are the means ± SDs from 26 (for IL-10–treated DCs) and 24 (for HC-treated DCs) independent experiments. *Asterisks* indicate statistically significant differences ($P \leq .05$) between untreated and IL-10– or HC-treated DCs.

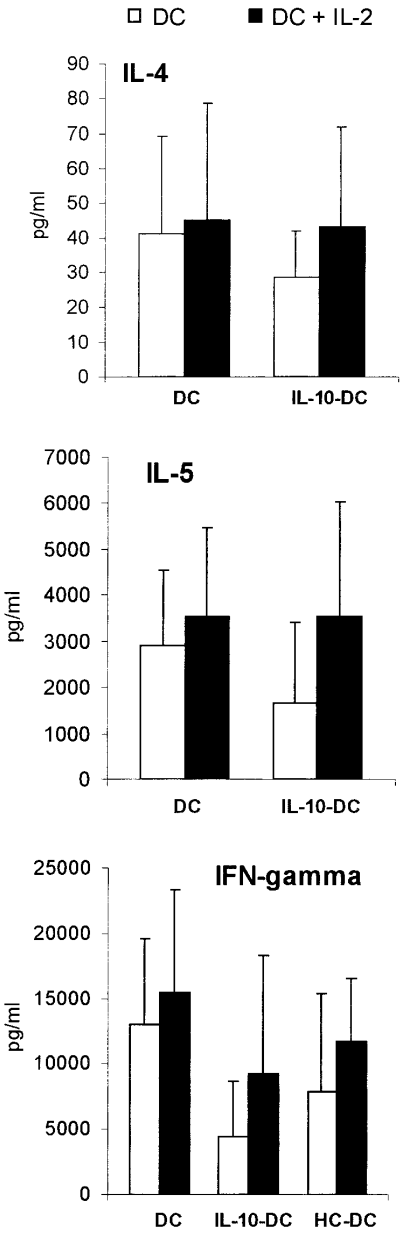

FIG 6. IL-2 restores the cytokine response to cells previously inhibited by coculture with IL-10– or HC-treated DCs. 5×10^5 CD45RA+ CD4+ T cells were primarily stimulated with 5×10^4 autologous allergen-pulsed DCs, either pretreated with IL-10 or HC or else untreated. After 1 week of culture, T cells were restimulated with 5×10^4 newly generated, mature, allergen-pulsed DCs of the same donor without or with the addition of 100 U/mL IL-2. Supernatants were collected 24 hours later and analyzed for IL-4, IL-5, and IFN-γ content by ELISA. Shown are the means ± SDs from 8 independent experiments.

a lower T cell–stimulatory potential.[27,28] Our findings are further in line with 2 recent reports showing that IL-10 production of human monocytes is enhanced, whereas IL-12 production is inhibited, by GC.[35,36]

The effects of IL-10 and HC were long-lasting and stable, especially in naive T helper cells; proliferation as well as cytokine production of T_H1 and T_H2 cells remained decreased or increased after restimulation with untreated fully matured DCs. However, memory T helper cells that were primarily stimulated with IL-10–treated DCs showed no more reduced T_H2 cytokine production after restimulation with fully matured DCs. This difference between naive and memory T helper cells indicates that the cytokine production of naive T helper cells can

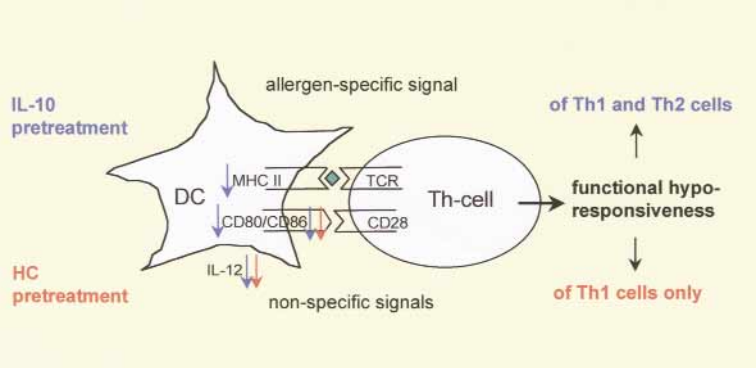

FIG 7. IL-10– and HC-pretreated DCs differentially modulate allergen-specific T-cell responses. Whereas pretreatment of allergen-pulsed DCs with IL-10 induces functional hyporesponsiveness of allergen-specific T_H1 and T_H2 cells, HC-pretreated DCs inhibit T_H1 but not T_H2 cells.

be influenced more easily with long-lasting effects. The long-lasting inhibitory effect of IL-10–treated DCs on T_H2 cytokine production by naive T helper cells and on T_H1 cytokine production by both T helper cell populations, as well as the stable low levels of IFN-γ by naive T helper cells after stimulation with HC-treated DCs, is not due to enhanced cell death, because apoptosis of allergen-specific T cells was even inhibited after stimulation with IL-10– or HC-treated DCs. Although all long-lasting diminished cytokine levels could be reversed by the addition of IL-2 and although induction of anergy by IL-10–pretreated DCs has already been described in different experimental settings,[24] the fact that memory T cells still respond to normal DCs after exposure to IL-10– or HC-treated DCs argues against anergy; instead, it favors a state of hyporesponsiveness in these T cells, perhaps because of the presence of regulatory T cells.[37] Further experiments are needed to analyze this possibility.

Taken together, DCs matured in the presence of IL-10 or HC inhibit T_H1-mediated immune responses but differentially influence allergen-specific T_H2-responses (Fig 7), which is of importance for the design of new forms of immunotherapy for allergic diseases, inasmuch as in vitro cultured DCs are already used in clinical trials to stimulate cellular immune responses against cancer.[38,39] In this respect, IL-10–treated DCs might be useful for the antigen-specific downregulation of allergic immune responses in atopic individuals.

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