

STATE OF THE ART REVIEW

Allergic asthma: a tale of many T cells

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Clinical and
Experimental
Allergy

Summary

Asthma is a common immune-mediated disorder characterized by reversible airway inflammation, mucus production, and variable airflow obstruction with airways hyperresponsiveness (AHR). In most cases the airway inflammation characteristic of asthma is thought to result from an allergic-type reaction to an inhaled substance from the environment (so-called allergic asthma). In allergic asthma, allergen exposure stimulates eosinophilic inflammation of the airways associated with infiltration of T cells. Although the recruitment of eosinophils into the airways is an important component in the pathogenesis of asthma, the trafficking of T lymphocytes into the airways is now believed to establish and orchestrate the asthmatic inflammatory response. This review explores the roles of various T cell subsets in the pathogenesis of allergic airway inflammation and highlights the contributions of these cells in regulating asthma.

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Asthma pathogenesis

One of the earliest steps in the establishment of allergic sensitization is the generation of an antigen-specific T cell response to an allergen. This results from engagement of T cells by allergen-loaded antigen presenting dendritic cells [1]. A network of dendritic cells is located under the airway epithelium where they can survey the airway for invading pathogens and inhaled antigens [2, 3]. It is thought that adjuvant signals from airway epithelium, generated in response to inhaled stimuli, influence the migration and maturation state of dendritic cells and T cells, and helps determine whether a particular antigen will trigger a T cell-mediated inflammatory response [2, 4–7]. When properly stimulated, airway dendritic cells will migrate to the draining lymph node where they present antigen and stimulatory signals to cognate T cells leading to their activation [8]. These activated T lymphocytes then migrate into the airways where they secrete cytokines and other mediators, which direct the late asthmatic response (LAR) in the lungs. In addition, long-lived memory T cells are generated, which continue to survey the airways for specific inhaled antigens.

After the initial sensitization to an allergen, re-exposure to it results in a rapid exacerbation of allergic airway inflammation. Inhaled allergen binds to preformed IgE

and IgG in the airways and stimulates mast cells and macrophages to release mediators, such as histamine, as well as the production and release of such mediators as leukotrienes, TNF, and various chemokines and T helper 2 (Th2) cytokines. Release of these mediators, associated with the early-phase of an asthmatic reaction, results in mucus production, bronchoconstriction, vascular leak, and the initial recruitment of T cells into the airways. The early-phase of an asthmatic reaction is initiated within minutes, and is subsequently followed several hours later by a late-phase reaction distinguished by an influx of eosinophils and activated T cells into the airways.

Experimental evidence suggests that T cells are the primary mediators of the asthmatic inflammatory response, in particular, the Th2-type cell subset seems to be critically important [9]. In support of this central role of Th2 cells, an increase in Th2 lymphocytes and their cytokines was observed in the airways of human asthma patients [10–13]. In addition, studies done in murine models of allergic airway inflammation have demonstrated that Th2 cells and their secreted cytokines are essential for the development of eosinophilia and airway hyperresponsiveness (AHR) [14–18], supporting a role for Th2 cells and their cytokines in the pathogenesis of asthma. Based on this, it has been proposed that a therapeutic strategy targeting Th2 cell trafficking into

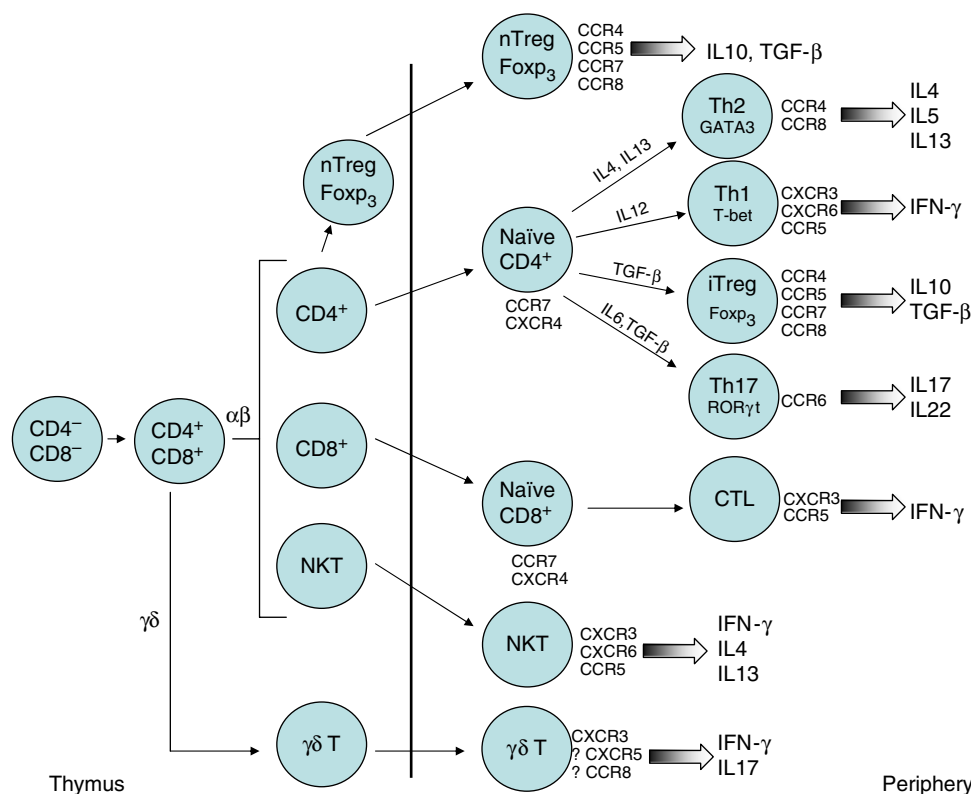


Fig. 1. Development of T cell subsets. $CD4^- CD8^-$ double negative T cells develop into $CD4^+$, $CD8^+$, NKT, and $\gamma\delta$ T cell subsets in the thymus. A subpopulation of $CD4^+$ cells develops into natural Tregs in the thymus. After emigrating from the thymus, upon antigen presentation and activation, naïve $CD4^+$ cells further differentiate into effector subsets, such as Th1, Th2, adaptive Tregs, or Th17 in secondary lymphoid organs depending on the cytokine milieu. Encounter with antigen-loaded dendritic cells in secondary lymphoid organs and peripheral tissue also stimulates naïve $CD8^+$ cells to proliferate and differentiate into cytotoxic T cells. Activation of different T cell subsets results in the migration of the cells via chemokine receptors and subsequent production of the indicated cytokines.

the lung could be ideal for reducing airway inflammation in asthma and controlling disease [19]. However, while most data suggest that Th2 cells are central to the pathogenesis of asthma, some studies suggest that other T cell subsets, including Th1 cells [20, 21], natural killer T (NKT) cells [22–24], and Th17 cells [25–30], accumulate in the airway of asthmatics and may also play a role in its pathogenesis. Furthermore, studies in humans and mouse models of asthma suggest that Foxp3⁺ regulatory T cells (Tregs) in the airways can modulate allergic airway inflammation [31–34]. These data suggest that the immune mechanisms in asthma are highly complex, and thus it may not be possible to fully suppress inflammation by targeting a single T cell subset. In this review, we describe the current knowledge on the role of different T cell subsets in the pathogenesis of allergic asthma as well as the mechanisms that control their accumulation in the airways.

T cell development

T lymphocytes, like all immune cells, originate from haematopoietic stem cells in the bone marrow. However,

whereas the majority of blood lineages complete the development process within the bone marrow, most T cells undergo partial development within the thymus. T cells begin the development process in the thymus as double negative (DN) T cells, lacking both CD4 and CD8 co-receptors (Fig. 1). As thymocytes, they continue the development process and express both CD4 and CD8 co-receptors, and are called double positive (DP) T cells. They then become committed to express either $\alpha\beta$ or $\gamma\delta$ T cell receptor chains after which they proceed through a complicated and well-regulated process of positive and negative selection, and then further develop into $CD4$ or $CD8$ single positive (SP) T lymphocytes [35, 36]. These mature T cells then migrate from the thymus into the periphery as naïve T cells [37]. Upon encounter with cognate antigens in the periphery, naïve T lymphocytes then differentiate into effector cells such as cytotoxic and helper T cells, as well as Tregs [38].

$CD4^+$ T cells

Antigen stimulation of $CD4^+$ T cells results in activation and differentiation of these cells into several different

functional subsets. Th1 cells are defined by the production of IFN- γ and orchestrate protection from intracellular pathogens; Th2 cells are characterized by the production of IL-4, IL-5, and IL-13 and mediate protection from extracellular parasites [39, 40]. A third subset of Th cells, called Th17 cells, has been characterized. These cells are distinguished by their production of IL-17 and IL-22 and are believed to be involved in the clearance of extracellular bacteria and fungi [41, 42]. Recent advancements in T cell biology have discovered a subset of CD4⁺ T cells that constitutively express the α chain of the IL-2 receptor (CD25) and the forkhead transcription factor FoxP3. These CD4⁺CD25⁺ cells are characterized by the expression of IL-10 and TGF- β and are involved in regulating and suppressing inflammation. Thus, these CD4⁺ cells are denoted Tregs [43–47].

T helper 2 cells

There is considerable experimental evidence from both human and animal studies suggesting that Th2 cells and their cytokines mediate allergic airway inflammation. Human studies have shown that Th2-type cytokines were found to be elevated at baseline in the airways of asthmatic subjects [10, 12, 48], and the levels increase after segmental allergen challenge [11, 49–53]. Consistent with these findings, additional studies have demonstrated an increase in Th2 cytokine production in CD4⁺ T cells in the lungs of asthmatic individuals [12, 54–57]. In addition, high levels of the Th2 cell transcription factors STAT6 and GATA3 were detected in bronchial-biopsies of asthmatic patients [58, 59]. Because GATA3 and STAT6 are transcription factors that are important for both the differentiation of naïve T cells into Th2 cells and for the secretion of Th2 cytokines [60–63], high levels of these transcription factors suggests an increased population of Th2 cells.

The Th2 cytokine IL-13 appears to be associated with asthma. IL-13 was found to be over-expressed in the sputum of mild asthmatic subjects [64, 65], and IL-13 mRNA expression was increased in bronchial biopsy samples from mild asthmatics [66, 67]. A recent study by Saha et al. provides further data supporting a correlation between IL-13 production and asthma inflammation by showing that not only is IL-13 expression increased in the sputum and in bronchial biopsy samples from individuals with severe asthma, but its expression is related to the degree of eosinophilic inflammation [13]. Thus, these studies support the hypothesis that Th2 cells are playing an important role in asthma pathogenesis.

Mouse studies also support the concept that Th2 cells play a central role in allergic airway inflammation. Consistent with the findings from human studies, investigators have demonstrated that the Th2-type cytokine IL-13 is critical for allergen-induced eosinophil recruitment and

AHR in a murine model of allergic airway inflammation [14, 15]. Furthermore, depletion of Th2 cells from a mouse model prevented the development of AHR and eosinophilic inflammation [68]. Finally, adoptive transfer of antigen-specific Th2 cells into naïve mice followed by aerosol challenge with antigen leads to eosinophilic airway inflammation, mucus hyper-secretion, and AHR [69–71].

Despite the large amount of data suggesting a central role for Th2 cells in the pathogenesis of asthma, some groups have reported that Th2 cells are not the only T cell subset involved in asthma pathogenesis [23, 48, 72, 73]. Our laboratory has shown that there is not a preferential enrichment of Th2 cells or Th2-associated chemokine receptors observed in the bronchoalveolar lavage (BAL) of human asthmatics before and 24 h following segmental allergen challenge [23]. Another study has demonstrated that although the total number of IL-4-producing T cells was increased following segmental allergen challenge, the percentage of these cells was not different from pre-challenge levels [30]. Thus, the current data regarding Th2 cells leaves open the possibility that other T cell subsets are also recruited into the asthmatic lung following antigen challenge.

The trafficking of T cells into the airways is thought to orchestrate the asthmatic response, and it has been of interest to investigators to determine the mechanisms behind T cell recruitment into the inflamed airways. Prior studies have demonstrated that chemokine receptors expressed on Th2 cells are responsible for the migration of these cells when stimulated with their respective chemokine ligands [74–76]. In support of a role for chemokine receptors in T cell trafficking in asthma, we found that G protein-coupled chemoattractant receptors are mediating the trafficking of Th2 cells into the airway before and after allergen challenge [77]. Specifically, expression of the chemokine receptors CCR4 and CCR8 on Th2 cells [75, 76] have led researchers to hypothesize a role for these specific receptors in the trafficking of Th2 cells to the asthmatic lung. Data in support of this hypothesis include reports implicating CCR4 in mediating T cell recruitment to the airways in response to allergen [78–81] and, notably, a study demonstrating that T cells expressing CCR4 are found in the lungs of asthmatic patients [78]. Additionally, Schuh et al. assessed that CCR4-deficient mice developed less airway inflammation [82], and CCR4 ligands were found to be up-regulated in asthmatic airways after allergen challenge [83]. However, despite these data demonstrating a role for CCR4 in the development of Th2 responses to allergen, some contradictory reports dispute the significance of CCR4 in the trafficking of Th2 cells to inflamed airways. One study using mice deficient in CCR4 demonstrated that the absence of CCR4 did not protect these mice from airway inflammation or AHR [84]. Additional research done in guinea pigs has shown that blocking CCR4 with a specific antibody does not

significantly affect CCR4⁺ T cells in the BAL or the recruitment of T cells to the lungs, further indicating alternative pathways in the recruitment of T cells to the inflamed airways [85].

CCR8 is another chemokine receptor that has been associated with a Th2 cell phenotype; however, the significance of CCR8 in asthma is less certain. Panina-Bordignon et al. have shown that T cells expressing CCR8 are found in the airways of asthmatic patients, but the level of CCR8 expression was not up-regulated to the same extent as CCR4 [78]. It has also been shown that the CCR8 ligand CCL1 was not increased after allergen challenge in humans [83], further suggesting that CCR8 may not be playing a significant role in the recruitment of T cells to the allergic lung. There are also difficulties interpreting data regarding studies done in mouse models of asthma. It has been reported that TCA-3, the murine ligand of CCR8, was elevated in inflamed airways [86]. However, conflicting results show that the absence of CCR8 does not affect Th2 cytokine responses or airway inflammation [87]. Therefore, the role of CCR8 remains an unanswered question and, although the current data demonstrate a role for chemokine receptors in the recruitment of Th2 cells to the asthmatic lung, further study is needed to understand the mechanisms by which they are exerting their activity.

T helper 1 cells

Th1 cells are also recruited into the asthmatic lung, but their role in the asthmatic response remains unclear [88–90]. In contrast to the levels of Th2 cytokines, the number of cells expressing mRNA for IFN- γ , a Th1-type cytokine, was reported to be similar in both normal and asthmatic patients [56]. Additionally, expression of T-bet, a transcription factor important in IFN- γ production, was decreased in T cells isolated from the airways of asthmatic patients compared with non-asthmatic individuals [91]. Other groups have demonstrated that the percentage of IFN- γ Th1 cells decreases in comparison with pre-challenge levels [23, 48], suggesting that although Th1 cells migrate to the allergic lung, they may not be the preferential cell type that is recruited. In contrast to these findings, however, some groups have reported that there are increased IFN- γ -producing cells in human BAL fluid after administration of segmental allergen challenge [20, 73]. The question remains, therefore, whether Th1 cells augment or regulate the asthmatic response.

In support of the hypothesis that Th1 cells enhance the asthmatic response and aid in the recruitment of Th2 cells to the airways, Randolph et al. [89] demonstrated in a mouse model of asthma that the adoptive transfer of antigen-specific Th1 cells and subsequent antigen challenge resulted in the recruitment of Th1 cells into the airway and Th1-type inflammation of the lung. In con-

trast, adoptive transfer of antigen-specific Th2 cells in the same model resulted in mild Th2 cell recruitment and airway inflammation. However, adoptive transfer of both Th1 and Th2 cells into the same host followed by antigen challenge resulted in the recruitment of both T cell subsets into the airways and eosinophilic inflammation. In further support of a role for Th1 cells in allergic airway inflammation, the administration of antigen and IL-18 (a cytokine that promotes the production of IFN- γ) to naïve mice recruited adoptively transferred memory Th1 cells to the airways and induced airway inflammation and hyper-responsiveness [92], and the administration of anti-IFN- γ Ab into sensitized mice resulted in a marked reduction in AHR [93].

There have also been several reports that suggest Th1 cells are playing more of a regulatory role in allergic asthma. One study demonstrated that although antigen-specific Th1 cells were not capable of hindering Th2 cell or eosinophilic recruitment into the lung, they could suppress overall Th2-mediated airway inflammation [90]. Other studies have shown that Th1 cells could inhibit the asthmatic response through IFN- γ [94, 95]. Finally, administration of IL-16, a cytokine with preferential chemotactant activity for Th1 cells, has been shown to result in a marked decrease in both inflammation and AHR [96], suggesting that Th1 cells are being recruited to the allergic lung via IL-16 and suppressing inflammation. Thus, these data collectively support the hypothesis that Th1 cells display a regulatory function in asthma.

One mechanism behind Th1 cell recruitment to the lung could be that Th1 cells are recruited to the allergic lung through the expression of CXCR3. Work done in our laboratory has demonstrated that CXCR3 was significantly reduced on human CD4⁺ BAL T cells, while its ligands were markedly increased after allergen challenge [23], suggesting that this chemokine receptor pathway is playing a role in the recruitment of T cells into the asthmatic lung. In support of a role for CXCR3 in asthma, expression of CXCL10, a CXCR3 ligand, was shown to be increased in human asthma [95]. Additionally, Pilette et al. found that CXCL10 is significantly up-regulated in atopic asthmatics following allergen challenge [83]. Finally, CXCL10 expression is increased in the airways in a mouse model of asthma [97]. Thus, the CXCR3 pathway may be involved in asthma, but its role and relevance remains a subject of investigation.

T helper 17 cells

Although relatively little is known about the contribution of Th17 cells in asthma, several recent studies suggest that Th17 cells may be involved in the asthmatic response. One recent study has shown that mRNA of the predominant product of Th17 cells, IL-17, is expressed in the sputum of asthmatics [26]. Consistent with this finding, IL-17 protein

is increased in individuals with allergic asthma [30]. Additional data showed that not only was human IL-17 production increased in allergic asthmatic subjects, but its production was further enhanced in the presence of allergic stimuli [25, 27, 29]. Furthermore, it has been demonstrated that IL-17 expression was decreased by oral corticosteroids in asthmatic patients [98], further suggesting that IL-17 and, by inference, Th17 cells are playing a role in augmenting asthma.

Consistent with human data, mice that were sensitized by epicutaneous antigen exposure demonstrated a robust Th17 response and airway inflammation [28], suggesting that IL-17 is important for the development of lung inflammation. Mice deficient in IL-17 did not develop airway inflammation when challenged with antigen [99]. Additional work has shown that IL-17 production is increased in an animal model of allergic asthma [100]; however, this study also found that IL-17 production negatively regulated established asthma.

It has recently been shown that human and mouse Th17 cells express the chemokine receptor CCR6 [101, 102], although the expression of other chemokine receptors, such as CCR4, have been reported as well [103]. These findings suggest that Th17 cells could migrate into the asthmatic airway through the induction of CCL20 as we have found in the human airway following antigen challenge [23, 104]. Taken together, these studies lend support to the idea that Th17 cells may be involved in the asthmatic response, but the contribution of this T cell subset is only beginning to be studied.

Regulatory T cells

Foxp3⁺ Tregs are the major regulators of autoimmunity and are critical for control of antigen-specific inflammation [105, 106]. Thus, it is possible that the recruitment of Tregs into the airways could suppress allergic airway inflammation [107]. Recently, one study has shown that atopic asthmatics had a higher frequency of allergen-specific IL-4-producing peripheral blood T cells, whereas normal subjects had a higher frequency of IL-10-producing peripheral blood T cells [31]. Because Tregs regulate T cell inflammation through the production of IL-10, the decrease in IL-10-producing cells in asthmatic patients suggests a decrease in Treg activity in these individuals. Consistent with these data, a study examining paediatric asthmatic patients found a lower percentage of CD4⁺CD25^{hi} T cells (Tregs) in the BAL as compared with healthy children or children treated with corticosteroids [32]. Additional studies in animal models of allergic airway inflammation have provided more insight into the role of Tregs in asthma. The adoptive transfer of CD4⁺CD25⁺ draining lymph node cells (73% Foxp3⁺) into sensitized mice before challenge resulted in an abrogation of AHR [107]. Additionally, when CD4⁺CD25^{hi}

Tregs were depleted in a mouse model that is normally resistant to airway inflammation, these mice exhibited an increase in Th2 cytokines and eosinophilia in the airways after sensitization with allergen [34]. Furthermore, adoptive transfer of antigen-specific Tregs into allergen-sensitized mice prevented allergic airway inflammation and AHR [108]. Finally, a recent study by Curotto de Lafaille et al. shows that Foxp3⁺ Tregs are important for regulating chronic allergic inflammation in mice and are essential cells for establishing tolerance in the respiratory mucosa [109]. These data collectively suggest that Tregs are playing an important role in the regulation of allergic asthma but the mechanism remains unanswered.

One question of importance has been the location in which the Tregs are exerting their regulatory function and the mechanisms that localize these cells to their functional location. It has been postulated that the chemokine receptors expressed on Tregs, such as CCR4, CCR5, CCR7, and CCR8, could play a role in recruiting these regulatory cells to either the allergic lung or the lymph node [110–114]. Localization of Tregs remains of interest and further study is required to determine the mechanism and tissue localization of Tregs in allergic asthma.

Natural killer T cells

Recent reports suggest a role for CD1d-restricted NKT cells in allergic asthma, although the magnitude of their contribution to the asthma phenotype remains controversial. Akbari et al. reported that NKT cells comprise the majority (> 60%) of T cells in the BAL of asthmatic patients [22]. However, our laboratory has shown that although there were more NKT cells in the BAL as compared with blood of asthmatics, the percentage of NKT cells was < 2.5% of the total lymphocyte population [115], suggesting that the NKT cell population was not the predominant T cell subset. Furthermore, we have found that the percentage of BAL NKT cells was the same before and after segmental allergen challenge [23]. In accordance with our findings, Vijayanand et al. and others also found < 1% of T cells in the BAL of asthma patients were NKT cells [24, 116–119], providing further support that although NKT cells are enriched in the BAL as compared with blood, NKT cells are not the predominant T cell in an asthmatic response. Work done in murine asthma models also support the hypothesis that although CD1d-restricted NKT cells play a role in generating the allergic airway response [120, 121], NKT cells are not sufficient to induce allergic airway inflammation [122].

CD1d-restricted NKT cells have been shown to express high levels of CXCR3, CCR5 and CCR6, and intermediate levels of CCR4 [123], and it is likely that these receptors regulate the recruitment of NKT cells to the asthmatic lung. Taken together, these data suggest that although

CD1d-restricted NKT cells contribute to allergic airway inflammation, conventional T cells are the predominant and likely to be the more important T cell population in asthma.

CD8⁺ T cells

Studies have tried to delineate the role of CD8⁺ T cells in the asthmatic response. It has previously been reported that production of IFN- γ by sputum CD8⁺ T cells was increased in subjects with asthma when compared with normal subjects [57], suggesting a role for CD8⁺ T cells in allergic inflammation. Another group has implicated a role for these T cells in asthma by showing that activated memory CD8⁺ T cells are important effector cells in allergic airway inflammation [124]. This study demonstrated that the transfer of CD3⁺CD8⁺ effector T cells into CD8⁺-deficient mice restored allergic airway inflammation. In accordance with this result, Hamelmann et al. have shown that depletion of CD8⁺ T cells in a naïve mouse prevented airway inflammation and AHR upon sensitization and challenge of the mice [125], further suggesting a role for CD8⁺ T cells in asthma pathogenesis. In contrast to these studies, however, several groups have reported that CD8⁺ cells play a minimal role in allergic airway inflammation. One study demonstrated that there is a very small number of CD8⁺ cells in the lungs and airways in allergic airway inflammation [126]. Providing further complexity in defining the role CD8⁺ T cells play in allergic asthma, additional studies have shown that the number of CD8⁺ T cells in the lung and airways are not changed after allergen challenge [127, 128]. Consistent with these data, Das et al. demonstrated that activated CD8⁺ T cells are not sufficient to mediate an asthmatic response in the absence of CD4⁺ T cells [122]. Thus, although it is unclear how much CD8⁺ T cells contribute to allergic asthma, they are not likely to be a predominant T cell subtype in promoting the allergic asthmatic response.

$\gamma\delta$ T cells

Another T cell subtype reported to contribute to allergic asthma is $\gamma\delta$ T cells. Krug et al. found that when comparing asthmatic patients with control subjects, there was an increase in Th2 cytokines and a decrease in Th1 cytokines being produced by $\gamma\delta$ T cells after allergen challenge [73], leading investigators to hypothesize these cells may be playing a pro-inflammatory role in asthma. An additional study showed an increase in intracellular IL-4 in $\gamma\delta$ T cells isolated from the airways of asthmatic patients [129]. Moreover, IL-4- and IL-5-producing $\gamma\delta$ T cells were found to be resident in the nasal passages of asthmatics [130]. Together, these results lend support to the hypothesis that $\gamma\delta$ T cells are contributing to allergic asthma.

Studies in mouse models have also demonstrated a role for $\gamma\delta$ T cells in asthma. One group has reported that the presence of $\gamma\delta$ T cells results in enhanced allergic airway inflammation [131], providing further support for a significant role for this T cell subtype in allergic asthma. Additionally, using mice deficient in $\gamma\delta$ T cells, it was found that the absence of these cells prevented the mice from developing AHR [132]. In this study, Lahn et al. reported a deficiency in this T cell subset results in decreased eosinophils in the BAL and lung, thus suggesting that $\gamma\delta$ T cells are contributing to allergic airway inflammation. However, Isogai et al. have demonstrated that CD8⁺ $\gamma\delta$ T cells inhibit late airway responses through the release of IFN- γ [133], suggesting that CD8⁺ $\gamma\delta$ T cells are important regulators of airway inflammation. Additionally, Hamelmann et al. used a mouse model of airway inflammation to demonstrate that $\gamma\delta$ T cells affect AHR but do not have a significant role in modulating airway inflammation [125]. These conflicting results may be explained by more recent findings demonstrating that there are two subsets of $\gamma\delta$ cells that can alter AHR. The V γ 1⁺ subset, when induced, enhances AHR while induction of the V γ 4⁺ subset suppresses AHR [134–138]. Although the mechanism behind how these $\gamma\delta$ T cell subsets exert their function is unknown, it has recently been reported that the development of both V γ 1⁺ and V γ 4⁺ cells requires CD8⁺ dendritic cells [139]. Therefore, although several studies suggest that $\gamma\delta$ T cells may be contributing to asthma pathogenesis, their overall role in the development of the asthma phenotype remains uncertain.

The chemokine pathways that would direct selective recruitment of $\gamma\delta$ T cells to the allergic airways are undetermined. CXCR3 has been implicated in contributing to $\gamma\delta$ T cell recruitment [83, 140], but the role of this pathway and $\gamma\delta$ T cells in asthma has not been defined. Thus, further studies investigating the role of $\gamma\delta$ T cells is required to elucidate their importance in asthma pathogenesis.

Conclusions

Asthma is a chronic inflammatory disease of the airway that is often the result of an allergic-type reaction to inhaled antigen. This inflammation is characterized by eosinophil accumulation around the airways and is believed to be primarily directed by Th2 cells that are recruited into the airways. However, emerging data has suggested a potential role for other T cell subsets, including Th1 cells, Th17 cells, NKT cells, Tregs, CD8⁺ T cells, and $\gamma\delta$ T cells. While new research is providing more insight into the role of these other T cell subsets in allergic airway inflammation, their exact function in asthma pathogenesis remains unclear. A better understanding of

the contributions of these different T cell subsets in asthma pathogenesis may lead to new therapeutic targets.

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