Introduction*
Asthma in the New Millennium
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The 45th Annual Thomas L. Petty Aspen Lung Conference was held June 5 to 8, 2002. The title the conference was “Asthma in the New Millennium.” In planning this meeting, the organizers realized that the “explosion” of new information in regard to the pathophysiology and therapy for asthma would bring cutting edge scientific exchange throughout the sessions. This Aspen Lung Conference was planned with an emphasis on the basic and translational sciences, but also included new and novel therapies for asthma. The conference attendance reached another all-time high, which included scientists from 13 different countries. This, indeed, led to the excellent exchange of ideas and new information at an exceptionally high level.

The state-of-the-art asthma presentations focused on the biology of inflammation, the distal lung, functional consequences of airway structural changes, genetics/genomics, the epithelium, infection and asthma, airway smooth muscle, nocturnal asthma, severe asthma, bronchial hyperresponsiveness, airway remodeling, pediatric aspects, and new and exploratory therapies. There were a large number of high-quality poster presentations and 19 oral abstract presentations covering a variety of novel and late-breaking research. Always stressed at the Aspen Lung Conference are the discussion sessions after the state-of-the-art and abstract presentations. The interactions were always lively and challenging. The conference summarizer, Jeffrey M. Drazen, MD, eloquently put all this information together and challenged all of us to define asthma phenotypes and genotypes for better future therapies.

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Transgenic Modeling of Interleukin-13 in the Lung*
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Interleukin (IL)-13 is a key cytokine in asthma pathogenesis. We used constitutive and inducible overexpression transgenic mice to characterize the mechanisms by which IL-13 causes phenotypic alterations in the lung. These studies demonstrated that chemokine receptor-2, transforming growth factor-β1, and IL-11 play an important role in the regulation of inflammation and remodeling in the IL-13-treated lung. The study results also demonstrated that IL-13 induces vascular endothelial growth factor, which causes bronchial circulation neovascularization in the murine airway. Last, it was demonstrated that IL-13 induces adenosine accumulation and that adenosine in turn stimulates IL-13 elaboration. These approaches validated in vitro genetic targets against which therapies can be directed to selectively regulate aspects of the IL-13 phenotype.

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Key words: adenosine; airway remodeling; interleukin-11; interleukin-13; transforming growth factor-β1; vascular endothelial growth factor

Abbreviations: ADA = adenosine deaminase; AR = adenosine receptor; CC10 = Clara cell-10-kd; CCR = chemokine receptor; CMV = cytomegalovirus; dox = doxycycline; hGH = human growth hormone; IL = interleukin; MCP = monocyte chemotactic protein; MIP = macrophage inflammatory protein; MMP = matrix metalloproteinase; MUC = mucin; Re = receptor α; rtTA = reverse tetracycline transactivator; tet-O = tetracycline operator; TGF = transforming growth factor; Th = T helper; tTS = tetracycline-controlled transcripational suppressor; VEGF = vascular endothelial growth factor

Asthmatic airways dysfunction used to be considered largely in terms of the contraction of airways smooth muscle (bronchospasm). However, numerous studies have prompted an appreciation of the central role of inflammation in this disorder. These studies also have demonstrated that T helper (Th) type 2 cells and their cytokine mediators likely play a central role in this disorder via the initiation and maintenance of airway inflammation, the regulation of B-cell and eosinophil function, the induction of mucus responses, and the stimulation of airway remodeling.1

In addition to inflammation, structural alterations (variously referred to as airway remodeling) exist in the asthmatic airway. These alterations are thought to be caused by asthmatic inflammation and have been demonstrated, in modeling studies, to be able to contribute to the symptoms and physiologic dysregulation characteristic of...