Editorial

Asthmatic airway remodeling: long overlooked but too important to ignore

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Structural changes within the asthmatic airway were first described 100 years ago by Huber and Koessler in cases of fatal asthma (1). The term "airway remodelling" emerged later as a collective term to describe a variety of airway structural changes including increased airway smooth muscle (ASM) mass, subepithelial fibrosis, epithelial metaplasia and increased vascularisation. Together these changes lead to a thickened and stiffer airway wall over time, which drives fixed airflow obstruction in asthmatic patients with important implications for symptoms and management (2,3). Airway remodelling and fixed airflow obstruction are associated with increased asthma severity and accelerated decline in lung function in asthma patients (3,4). It is clear, therefore, that attempts to halt or reduce airway remodelling could have a hugely beneficial impact on patients living with asthma, particularly those living with the severest forms of the disease.

Despite fixed airflow obstruction (also known as irreversibility of airflow obstruction) being described as far back as 1977 (5) by Professor Turner-Warwick, it has remained an understudied and often overlooked pathological feature of asthma, as evidenced by the fact that we still have no effective treatments that halt or reverse airway remodelling. In this issue of *Annals of Translational Medicine* Huang and Qiu provide an in depth narrative review of recent advances in asthmatic airway remodelling (6), an article that is timely if we are to push forward our understanding of the mechanisms driving this critical but often ignored pathological feature of asthma. Only through better understanding will we collectively be able to develop novel therapies that halt or reverse asthmatic airway remodelling.

The underlying pathological mechanisms driving airway remodeling in asthma are complex and incompletely understood but as Huang and Qiu highlight, the fact that airway remodeling develops despite the use of anti-inflammatory drugs suggests that it occurs in conjunction with airway inflammation rather than being driven by it (6). This is supported by the observations that airway remodeling has been observed in preschool wheezers, which do not correlate with airway inflammation and predate an asthma diagnosis (2,7,8). In 2011, Grainge *et al.* demonstrated a potential role for bronchoconstriction as a driver of airway remodeling (9), which has since been supported by numerous studies (2,10,11). A direct biomechanical link between airway contraction and the development of airway remodeling could help to explain why worse airway remodeling is associated with more severe, difficult to treat and/or poorly controlled forms of asthma. Conversely, however, it is possible that the presence

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of airway remodeling creates an asthma phenotype that is inherently difficult to treat. Huang and Qiu make the case that airway remodeling contributes to glucocorticoid resistance in asthma, which is a major component of difficult to treat asthma (6). Whether airway remodeling is the result of or a driver of severe, difficult to treat asthma is still largely unclear and an area that warrants further study.

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