CORRESPONDENCE

Importance of epithelial mesenchymal transition (EMT) in COPD and asthma

We read with interest the recent review article by Bartis et al in Thorax and a similar one from some of the same authors in European Respiratory Review, addressing the potential importance of epithelial mesenchymal transition (EMT) in lung development and disease. We would like to take issue with the approach used, which is to emphasise ‘molecular patterns’ potentially associated with EMT, rather than starting with any empiric evidence that EMT is present as an active pathological process.

EMT has been differentiated into three different types. It is a vital process during embryogenesis (type 1 EMT), but can also be induced as a result of persistent epithelial stimulation leading to organ fibrosis (type 2 EMT). In COPD, this could be responsible for destruction of small airways. Epithelial stimulation can also lead to malignancy, through type 3 EMT, that is, EMT plus angiogenesis, which we have documented in large airway.

The major criteria for recognising EMT activity in vivo were suggested by Zeisberg et al, which emphasised especially reticular basement membrane (Rbm) fragmentation, due to transitioning epithelial cells digesting their way through to the lamina propria (LP), accompanied by expression of mesenchymal markers. Notably, such criteria are present in COPD airways. In contrast, asthmatic airways look nothing like this, that is, they have a thick Rbm but it is not fragmented (figure 1). Most of the studies reported on asthma in relation to EMT are based on stimulation of epithelial cells in vitro, without any core empiric evidence in vivo. However, there are published micrographs from asthmatic children where EMT could be present, which should be followed up.

EMT-type molecular changes can be induced even in epithelial cell cultures and have been described as a transient phenotype called ‘reversible scatter’, where withdrawal of the inducer allows the epithelium to return to its original state.

We suggest that a monothemic focus on ‘molecules’ in cell culture in isolation has done no favours to EMT research in airway disease. Actual tissue showing EMT characteristics in patients should be the starting point, and then can be informed further by manipulating appropriate tissue culture and using detailed molecular methods to understand processes more deeply, but that is second-order research, which has been elevated to a gold standard. Look first for a fragmentation and hypercellular (±hypervascular) Rbm.

Sukhwinder Singh Sohal,1 Chris Ward,2 Eugene Haydn Walters3

1NHMRC Centre of Research Excellence for Chronic Respiratory Disease, School of Medicine, University of Tasmania, Hobart, Tasmania, Australia
2Institute of Cellular Medicine, Newcastle University, Newcastle, UK
3Correspondence to Dr Eugene Haydn Walters, NHMRC Centre for Research Excellence in Chronic Respiratory Disease and School of Medicine, MS1, 17 Liverpool Street, Private Bag 23, Hobart, TAS 7000, Australia; sssohal@utas.edu.au

Contributors SSS: design of study, literature search, figures, performed the histological analyses, data collection, data interpretation and writing.

CW: contributed to writing of the manuscript.
EHW: design of study, clinical assessments, overview of all analyses, data interpretation and writing.

Competing interests None.

Ethics approval The Human Research Ethics Committee (Tasmania) Network.

Provenance and peer review Not commissioned; internally peer reviewed.


REFERENCES

1 Bartis D, Mise N, Mahida RY, et al. Epithelial--mesenchymal transition in lung development and disease: does it exist and is it important? Thorax 2013;2013:204608
4 Soltani A, Muller HK, Sohal SS, et al. Distinctive characteristics of bronchial reticular basement membrane and vessel remodelling in chronic obstructive pulmonary disease (COPD) and in asthma: they are not the same disease. Histopathology 2012;60:964–70.

Figure 1 Bronchial biopsies (A) from an asthmatic subject, with black arrows indicating thick and homogenous reticular basement membrane (Rbm) with no sign of fragmentation or hypercellularity; (B) from a typical COPD subject, with black arrows indicating Rbm fragmentation and hypercellularity, the core hallmark of active epithelial mesenchymal transition.