CORRESPONDENCE

Epithelial mesenchymal transition (EMT) in small airways of COPD patients

We congratulate Milara et al for getting a paper suggesting that epithelial mesenchymal transition (EMT) is important in the pathogenesis of chronic obstructive pulmonary disease (COPD) into a top respiratory journal. This is quite a breakthrough.

In the discussion, Milara et al were somewhat dismissive of our findings on EMT markers in large airways of COPD patients; commenting that our study was limited by the mesenchymal protein expressions analysed (MMP-9, S100A4, vimentin) being potentially expressed by inflammatory cells. In a follow-up paper we excluded such confounding. Further, our study illustrated that cells in the basal epithelium, and reticular basement membrane (Rbm) in smokers/COPD double-stain for cytokeratin(s) and the ‘EMT marker’ S100A4, confirming a likely epithelial origin of these cells. Notably, Milara et al also stained their tissue with vimentin.

The authors also queried the relevance of our findings on larger airways EMT to COPD. A major feature of COPD, in addition to small airway destruction, is its association with lung (airway) cancer. We have found large airways EMT to be associated with increased angiogenesis; this is a process reminiscent of EMT-type 3, a pro-cancer stroma in contrast with the more specifically profibrotic EMT-type-2 which lacks angiogenesis.\(^4\) Active EMT-type-3 in large airways might be the link between COPD and lung cancer development.

For adherens proteins E-cadherin and ZO-1, the authors reported no staining in the smokers/COPD patients’ epithelium, suggesting their expression is lost as the part of EMT. It is true that E-cadherin and ZO-1 epithelial expression does decrease during EMT, but if disappeared completely the epithelium would fall apart. Their protein analysis and immunofluorescence data on primary human bronchiobronchial epithelial cells shows E-cadherin and ZO-1 expression, albeit decreased. We have also been looking at small airways in smokers and see a lot of E-cadherin staining but also N-cadherin expression, as another likely expression of EMT (figure 1).

Rbm fragmentation\(^2\) which is a vital part of the EMT process\(^5\) is evident in the small airway tissue sections shown in the Milara et al paper, as is hypercellularity of the Rbm. However, neither important structural hallmark of EMT is commented upon. The arrows pointing out α-SMA staining, which is below the Rbm, seem to be in the wrong place.

In spite of our reservations, this study highlights the potential importance of EMT in COPD, which might change the way we think about this disease process and its nasty clinical consequences.

Sukhwinder Singh Sohal, Eugene Haydn Walters
NHMRC Centre for Research Excellence for Chronic Respiratory Disease, School of Medicine, University of Tasmania, Hobart, Australia

Correspondence to Professor Eugene Haydn Walters, NHMRC Centre for Research Excellence in Chronic Respiratory Disease and School of Medicine, 17 Liverpool Street, Private Bag 23, Hobart, Tasmania 7000, Australia; haydn.walters@utas.edu.au, sssosal@utas.edu.au

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

Figure 1 Small airways in surgically resected lung sections from smokers undergoing thoracotomy: (A) black arrows indicating E-cadherin expression in the epithelium; (B) black arrows indicating N-cadherin expression in the epithelium.

REFERENCES
5 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.
Epithelial mesenchymal transition (EMT) in small airways of COPD patients

Sukhwinder Singh Sohal and Eugene Haydn Walters

Thorax published online March 14, 2013

Updated information and services can be found at:
http://thorax.bmj.com/content/early/2013/03/13/thoraxjnl-2013-203373

These include:

References
This article cites 5 articles, 0 of which you can access for free at:
http://thorax.bmj.com/content/early/2013/03/13/thoraxjnl-2013-203373#BIBL

Open Access
This is an open-access article distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non-commercial and is otherwise in compliance with the license. See: http://creativecommons.org/licenses/by-nc/3.0/ and http://creativecommons.org/licenses/by-nc/3.0/legalcode

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

Open access (245)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/