Authors' response: Epithelial-mesenchymal Transition (EMT) is a common molecular programme in epithelial cells which can be triggered by injury

We thank Sohal *et al*[1] for commenting on our recent paper.[2] The authors argue in their commentary that morphological/histological signs of epithelial-mesenchymal transition (EMT) in patients' samples, for example, reticular basement membrane fragmentation, are more relevant in detecting EMT than looking for typical EMT-associated molecular patterns in the first place.

EMT is defined as the gradual differentiation of epithelial cells into mesenchymal cells involving intermediate phenotypes. Different types of EMT seem to be quite universally present in organ development and repair of epithelial injury. We would like to highlight that tissue repair is increasingly viewed as the partial recapitulation of the developmental programme[3] and accentuate the classic view that 'tumours are wounds that do not heal'.[4]

The common attribute of chronic lung diseases where EMT is thought to be involved in the pathogenesis is sustained epithelial damage from noxious endogenous or exogenous agents. Fibrotic changes of various patterns are ubiquitous in these accompanied with tissue remodelling.[5] The EMT phenotype of epithelial cells—namely, downregulation of cell surface E-cadherin and tight junction proteins, nuclear translocation of β-catenin, activation of canonical Wnt pathway and SNAI family transcription factors—seems to be commonly present in tissue remodelling and fibrotic lung diseases and in malignancies.

We argue that EMT should be viewed as a more general molecular programme of epithelial cells which is a part of phenotypic plasticity and an adaptation tool to cellular stress facilitating repair or —in case of an unfavourable outcome—fibrosis or malignant transformation. Epithelial cells of intermediate phenotype (ie, expressing several mesenchymal markers) are present in COPD asthma and pulmonary fibrosis—as we outlined in our recent review article.[2]

The important question is whether epithelial cells in vivo differentiate beyond the intermediate phenotype in large numbers in fibrosis; that is, is there a 'full-blown' EMT which triggers the full transition to properly differentiated mesenchymal cells? Or are these just transient phenotypic changes? Recent experimental results on this issue are controversial in both animal models as well as in human histology samples as we have discussed in detail in our recent paper.[2] Whether epithelial-derived mesenchymal cells are important in the development of fibrotic tissue and what the clinical importance of EMT in pulmonary diseases with fibrosis is remain to be understood in the future.

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