Airway epithelial cells as guardians of immune homeostasis?

We read with interest the paper by Wang et al and accompanying editorial by Smyth showing that healthy murine airway epithelial cells (AECs) are potent inhibitors of dendritic cell (DC)-induced T cell activation. Several AECs infected with respiratory syncytial virus (RSV) lost this regulatory function, allowing activation of T cell responses and airway inflammation. These in vitro observations match with the high concentrations of pro-inflammatory mediators and cells found clinically in the bronchoalveolar lavage fluid of infants with RSV bronchiolitis.

The paper by Wang et al adds to a growing body of evidence that AECs are involved in maintaining airway immune homeostasis. Mayer et al previously showed that primary murine and immortalised human AECs induce an anti-inflammatory microenvironment inhibiting DC maturation and reducing T cell proliferation through constitutive secretion of transforming growth factor-β. Wang et al comment that further studies in human primary AECs are required to validate the findings in a clinical setting. Smyth also highlights the importance of research to investigate the function of AECs in health.

Primary AECs cultured from protocol bronchoscopic brushings taken from clinically stable lung allograft recipients free from chronic allograft dysfunction represent a useful model to study AEC function in a healthy, steady state, albeit alloimmune environment. In a recent paper we have shown that epithelial cell-conditioned medium from stable lung allografts drives the production of macrophage-like cells from monocytes rather than DCs. It is unclear whether this effect only occurs in the airway of lung transplant recipients or if it reflects a general role for AECs in the homeostasis of DC populations in the lung. Nonetheless, our findings provide complementary human evidence to the murine observations of Wang et al and indicate that, in a steady state, AECs may be important in local immune homeostasis and promote an anti-inflammatory and pro-phagocytic airway milieu.

An emerging hypothesis that encompasses these observations is therefore that, in the healthy state, AECs regulate local immune homeostasis in the epithelium and promote anti-inflammatory conditions in the airway. In response to epithelial damage such as RSV infection, danger signals are released into the microenvironment by AECs which drive the production and maturation of professional antigen-presenting DCs, promoting T cell activation and airway inflammation.

To explore this hypothesis more fully we suggest that future studies should include primary human tissue in both health and disease, and that this strategy can complement and extend animal studies.

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was plated on 7H11 Middlebrook agar made selective with antibiotic tablets (Mycobacteria Selectatabs (Kirchner), MS24 series (Mast Diagnostics, UK)) and the viable colony count was calculated. The patients were divided into three groups:

- **Group 1**: four patients who produced sputum spontaneously throughout treatment (3 men; median age 47.5 years (range 35–72)); 3 Caucasian, 1 Asian; 1 HIV-positive; all sensitive to first-line TB treatment. Three patients with isoniazid-resistant TB underwent IS when this ceased (7 men; median age 31 years (range 17–47); 5 Black African, 2 Caucasian, 1 Asian; 1 HIV-positive; 6 sensitive to first-line TB treatment).
- **Group 2**: four patients who never produced sputum and had induced sputum (IS) samples collected throughout (3 men; median age 38.5 years (range 23–51); 2 Black African, 1 Caucasian, 1 Jamaican; 1 HIV-positive; 3 sensitive to first-line TB treatment).
- **Group 3**: eight patients who initially produced spontaneous sputum but underwent IS when this ceased (7 men; median age 31 years (range 17–47); 5 Black African, 2 Caucasian, 1 Asian; 1 HIV-positive; 6 sensitive to first-line TB treatment).

Patients with fully susceptible TB (n = 13) were treated with standard 6-month chemotherapy. FMRP was part funded by a research fellowship from Tibotec and Bayer for clinical trials. FMRP was part funded by a research fellowship from Tibotec and EDCITP, neither had any involvement in the study.

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