

alveolar cell traffic, that Porter highlights, may not be readily made in mice. In sharp contrast to humans, mice lack a bronchial circulation. The dominance of the pulmonary circulation is reflected in the work carried out by Corry *et al.* These authors repeatedly emphasise that their studies concern parenchymal leucocytes. When egression is inhibited, leucocytes accumulate in pulmonary parenchymal tissues 'causing' severely impeded gas exchange.<sup>4</sup> Oxygen is an effective remedy in these lethally affected mice.<sup>3</sup> Corry *et al.*<sup>3</sup> particularly underscore that 'differences in smooth muscle or other contractile cell function cannot explain the increased mortality observed.' Hence, Porter's statement that death in this model is by 'bronchoconstriction' is puzzling. Then Porter discusses data suggesting that mouse lung injury evoked by intratracheal bleomycin is caused by transepithelial neutrophil egression. We are not equally convinced. For example, n-formyl-neoleucyl-leucyl-phenylalanine (nFNLP) may not be used as a specific inducer of neutrophil egression, as quoted by Porter. nFNLP-like peptides are multipotent agents and avidly induce neutrophil toxicity as well.

Nearly 130 years have passed since Julius Cohnheim held classic lectures on inflammation.<sup>5</sup> He discussed the resolution of inflammatory infiltrates in mucosally lined organs, specifically noting the advantageous outward transport available to bronchi and lung alveoli. Cohnheim's contemporary and perpetual authority, Henry Hyde Salter, observed cell-rich sputum production at resolution of severe asthma. Salter intriguingly analysed how the most peripheral airways could be cleared of cellular exudates since coughing would have little impact here.<sup>6</sup> It seems overdue to fill in the large gaps in our knowledge concerning clearance of cells from the human bronchiolar-alveolar lumen.

Carl G Persson,<sup>1</sup> Lena Uller<sup>2</sup>

<sup>1</sup>Department of Clinical Pharmacology, Laboratory Medicine, Lund University Hospital, Lund, Sweden;

<sup>2</sup>Department of Experimental Medical Science, Lund University, Lund, Sweden

**Correspondence to** Professor Carl G Persson, Department of Clinical Pharmacology, Laboratory Medicine, Lund University Hospital, Lund, Sweden; carl.persson@med.lu.se

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## Can cells other than Th17 lymphocytes be important sources of IL-17 in the lungs?

We read with interest the recent paper by Facco *et al* which showed that Th17 cells are present in blood, bronchoalveolar lavage (BAL) and lung tissue from people with sarcoidosis. The authors conclude that Th17 cells are involved in the pathogenesis of sarcoidosis as a multisystem disorder.<sup>1</sup>

Interestingly, the paper mentions expression of interleukin (IL)-17 protein by macrophages. Currently, a strong emphasis exists in the literature on the role of Th17 lymphocytes in the production of IL-17 in the lungs. However, Th17 cells are not the only source of IL-17 identified.<sup>2</sup> IL-17 is also known to be produced by  $\gamma\delta$  and natural killer T cells.<sup>3–4</sup> It has also been suggested that in human alcoholic liver disease, atherosclerosis and rodent models of lipopolysaccharide-induced airway inflammation IL-17 can be localised to neutrophils.<sup>5–7</sup> Furthermore, we have recently demonstrated that IL-17 protein expression is raised in the lower airway of people with advanced cystic fibrosis lung disease.<sup>8</sup> This IL-17 protein expression was immunolocalised to both neutrophils and mononuclear cells.<sup>8</sup>

It is known that granulocytes may be part of the inflammatory process in sarcoidosis.<sup>9–10</sup> The BAL method used by Facco *et al* was referenced, via the online supplement, to an original paper that used a 200 ml lavage. A differential cell count seems to have been produced from a cytospin, but in the table listing differential BAL data the percentage of neutrophils was not stated.

It would therefore be of interest if the authors could clarify the methodology used for the BAL and differential cell counts, whether any neutrophils were detected in BAL from people with sarcoidosis, and if so, did neutrophils demonstrate IL-17 immunolocalisation? Such data may support a paradigm indicating that IL-17 expression may involve cells in addition to Th17 lymphocytes in sarcoidosis. This may also be relevant to other lung pathologies where IL-17 is implicated.

Malcolm Brodrie,<sup>1,2</sup> James Lordan,<sup>1,3</sup> Christopher Ward<sup>1</sup>

<sup>1</sup>Institute of Cellular Medicine, Newcastle University, Newcastle upon Tyne, UK; <sup>2</sup>Department of Respiratory Paediatrics, Great North Children's Hospital, Newcastle upon Tyne, UK; <sup>3</sup>Cardiopulmonary Transplantation Unit, Freeman Hospital, Newcastle upon Tyne, UK

**Correspondence to** Dr Malcolm Brodrie, c/o Paediatric Respiratory Secretaries, Old Children's Outpatients Department, Royal Victoria Infirmary, Newcastle upon Tyne NE1 4LP, UK; m.j.brodrie@ncl.ac.uk

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## Authors' response

We thank Dr Brodrie and coworkers for their letter<sup>1</sup> and fully agree on the necessity to evaluate whether cells other than lymphocytes and macrophages are involved in IL-17 release in sarcoid lungs. The main manifestation of sarcoidosis is an accumulation of mononuclear inflammatory cells, mostly CD4<sup>+</sup> T cells and monocytes/macrophages in involved organs, including the lungs.<sup>2</sup> As specified in our 'Materials and methods' section, we evaluated cells obtained by filtering bronchoalveolar lavage (BAL) fluid through gauze. A standard morphological and immunological analysis of BAL cellular components was performed. The analysis included cell recovery and differential count of macrophages, lymphocytes, neutrophils