REFERENCES

1. **Maher TM,** Wells AU, Laurent GJ. Idiopathic pulmonary fibrosis: multiple causes and multiple mechanisms? *Eur Respir J* 2007;**30**:835—9.
2. **Scotton CJ,** Chambers RC. Molecular targets in pulmonary fibrosis: the myofibroblast in focus. *Chest* 2007;**132**:1311—21.
3. **Serini G,** Bochaton-Piallat ML, Ropraz P, *et al*. The fibronectin domain ED-A is crucial for myofibroblastic phenotype induction by transforming growth factor-beta1. *J Cell Biol* 1998;**142**:873—81.
4. **Kono Y,** Nishiuma T, Nishimura Y, *et al*. Sphingosine kinase 1 regulates differentiation of human and mouse lung fibroblasts mediated by TGF-beta1. *Am J Respir Cell Mol Biol* 2007;**37**:395—404.
5. **Ammit AJ,** Hastie AT, Edsall LC, *et al*. Sphingosine 1-phosphate modulates human airway smooth muscle cell functions that promote inflammation and airway remodeling in asthma. *FASEB J* 2001;**15**:1212—14.
6. **Dhami R,** He X, Schuchman EH. Acid sphingomyelinase deficiency attenuates bleomycin-induced lung inflammation and fibrosis in mice. *Cell Physiol Biochem* 2010;**26**:749—60.
7. **Pyne S,** Pyne NJ. Sphingosine 1-phosphate signalling in mammalian cells. *Biochem J* 2000;**349**:385—402.
8. **American Thoracic Society.** Idiopathic pulmonary fibrosis: diagnosis and treatment. International consensus statement. American Thoracic Society (ATS), and the European Respiratory Society (ERS). *Am J Respir Crit Care Med* 2000;**161**:646—64.
9. **Hoet PH,** Lewis CP, Dinsdale D, *et al*. Putrescine uptake in hamster lung slices and primary cultures of type II pneumocytes. *Am J Physiol* 1995;**269**:L681—9.
10. **Milara J,** Mata M, Mauricio MD, *et al*. Sphingosine-1-phosphate increases human alveolar epithelial IL-8 secretion, proliferation and neutrophil chemotaxis. *Eur J Pharmacol* 2009;**609**:132—9.
11. **Milara J,** Ortiz JL, Juan G, *et al*. Cigarette smoke exposure up-regulates endothelin receptor B in human pulmonary artery endothelial cells: molecular and functional consequences. *Br J Pharmacol* 2010;**161**:1599—615.
12. **van Oostrum J,** Calonder C, Rechsteiner D, *et al*. Tracing pathway activities with kinase inhibitors and reverse phase protein arrays. *Proteomics Clin Appl* 2009;**3**:412—22.
13. **Xin C,** Ren S, Kleuser B, *et al*. Sphingosine 1-phosphate cross-activates the Smad signaling cascade and mimics transforming growth factor-beta-induced cell responses. *J Biol Chem* 2004;**279**:35255—62.
14. **Willis BC,** Borok Z. TGF-beta-induced EMT: mechanisms and implications for fibrotic lung disease. *Am J Physiol Lung Cell Mol Physiol* 2007;**293**:L525—34.
15. **Frippiat C,** Chen QM, Zdanov S, *et al*. Subcytotoxic H2O2 stress triggers a release of transforming growth factor-beta 1, which induces biomarkers of cellular senescence of human diploid fibroblasts. *J Biol Chem* 2001;**276**:2531—7.
16. **Samadi N,** Bekele R, Capatos D, *et al*. Regulation of lysophosphatidate signaling by autotaxin and lipid phosphate phosphatases with respect to tumor progression, angiogenesis, metastasis and chemo-resistance. *Biochimie* 2011;**93**:61—70.
17. **Keller CD,** Rivera Gil P, Tolle M, *et al*. Immunomodulator FTY720 induces myofibroblast differentiation via the lysophospholipid receptor S1P3 and Smad3 signaling. *Am J Pathol* 2007;**170**:281—92.
18. **Ruwisch L,** Schafer-Korting M, Kleuser B. An improved high-performance liquid chromatographic method for the determination of sphingosine-1-phosphate in complex biological materials. *Naunyn Schmiedebergs Arch Pharmacol* 2001;**363**:358—63.
19. **Shea BS,** Brooks SF, Fontaine BA, *et al*. Prolonged exposure to sphingosine 1-phosphate receptor-1 agonists exacerbates vascular leak, fibrosis, and mortality after lung injury. *Am J Respir Cell Mol Biol* 2010;**43**:662—73.
20. **Huang L,** Fu P, Ma W, *et al*. Sphingosine kinase 1 deficiency protects bleomycin induced mouse lung fibrosis. *Am J Respir Crit Care Med* 2011;**183**:A2152.
21. **Thomeer M,** Grutters JC, Wuyts WA, *et al*. Clinical use of biomarkers of survival in pulmonary fibrosis. *Respir Res* 2010;**11**:89.
22. **Swaney JS,** Moreno KM, Gentile AM, *et al*. Sphingosine-1-phosphate (S1P) is a novel fibrotic mediator in the eye. *Exp Eye Res* 2008;**87**:367—75.
23. **Marwick JA,** Kirkham P, Gilmour PS, *et al*. Cigarette smoke-induced oxidative stress and TGF-beta1 increase p21waf1/cip1 expression in alveolar epithelial cells. *Ann N Y Acad Sci* 2002;**973**:278—83.
24. **Kim DS,** Kim SY, Kleuser B, *et al*. Sphingosine-1-phosphate inhibits human keratinocyte proliferation via Akt/protein kinase B inactivation. *Cell Signal* 2004;**16**:89—95.
25. **Bocchino M,** Agnese S, Fagone E, *et al*. Reactive oxygen species are required for maintenance and differentiation of primary lung fibroblasts in idiopathic pulmonary fibrosis. *PLoS One* 2010;**5**:e14003.

Journal club

Environmental micro-organisms and childhood asthma: the more the merrier?

Epidemiological studies have shown that children who grow up on traditional farms are protected from atopic conditions, including asthma. However, how this protection arises is not clearly understood. It has been postulated that immunological responses to an increased microbial exposure in early childhood is important. This study investigates, specifically, whether it is the *variety* of microbial exposure that is protective.

Two cross-sectional studies are described (PARSIFAL n=489 and GABRIELA n=444) in which the prevalence of asthma and atopy in children who live on farms are compared with a control group. Samples of dust were collected from children's bedrooms and analysed for bacteria and fungi. Results showed that the farm-dwelling children were exposed to a greater diversity of micro-organisms, even in an indoor environment. Furthermore, the prevalence of asthma was inversely related to the greater diversity of microbial exposure, independent of whether the children lived on a farm or not. Neither study showed a significant inverse correlation with atopy.

The finding that microbial diversity protects children against asthma is an important but potentially misleading one. The study discusses the dangers of accepting this hypothesis, as the number of receptors that trigger the innate immune system are limited and easily saturated. The study was only able to identify families of species of microbes, but it has taken the first step towards finding individual micro-organisms that may contribute to the protection that farms confer to their inhabitants and therefore a potential live vaccine against asthma.

► **Ege MJ,** Mayer M, Normand AC, *et al*. Exposure to environmental microorganisms and childhood asthma. *N Engl J Med* 2011;**364**:701—9.

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Published Online First 23 May 2011

Thorax 2012;**67**:156. doi:10.1136/thoraxjnl-2011-200404