

Opening therapeutic options for lung disease

Spicing up a cystic fibrosis solution

The spice turmeric and the enzyme lipoxin might not have much in common at first sight, but both are providing possible new therapeutic avenues for the management of cystic fibrosis (CF).

CF is caused by mutations in the CFTR gene that encodes the all-important chloride ion channel. But attempts to cure CF by gene therapy continue to be dogged by the failure to find safe and effective ways of transporting genes to cells.

Researchers are puzzling over how this mutation can lead to lung disease. 'While the direct chloride channel properties of CFTR seem adequate to explain other CF-associated phenomena [extra-salty sweat and pancreas dysfunction], the link between mutant CFTR and

disease pathogenesis in the lung has not been clear,' says Chris Karp of the University of Cincinnati, Ohio, US.

Karp's interest centres on lipoxins, found at comparatively low concentrations in the lung secretions of CF patients. His group tested the effects of a stable lipoxin analogue in mice whose lungs were infected with a bacterium known to impair CF lung function. Not only were the mice able to reduce bacteria numbers faster, but the disease was less severe than in control mice¹. Some of lipoxin's activities are the opposite of the limiting side effects of other modulators of the eicosanoid pathway (eg aspirin), suggesting that lipoxins may be safe and



Turmeric may help to treat cystic fibrosis

effective for treatment, says Karp.

Also at an early stage in the pipeline is an ingredient of the spice turmeric. US research suggests that curcumin can correct the most common CFTR mutation, $\Delta F508$, which accounts for over two-thirds of all CF cases². In this mutation, the chloride channel is initially intact, but gets trapped by the cell's 'quality control' machinery and is unable to reach the cell surface to carry out its function. 'If it corrects the $\Delta F508$ trafficking defect [in people] it could have a very positive effect, but it is far too early to speculate,' says Michael Caplan of Yale University School of Medicine, one of the group of US and Canadian researchers involved in the study. *Cath O'Driscoll*

References

1 D Takai *et al*, *Nature Immunol.*, 2004, **5**, 388
2 M E Egan *et al*, *Science*, 2004, **304**, 600