Ecological approach could help cystic fibrosis sufferers, researchers find

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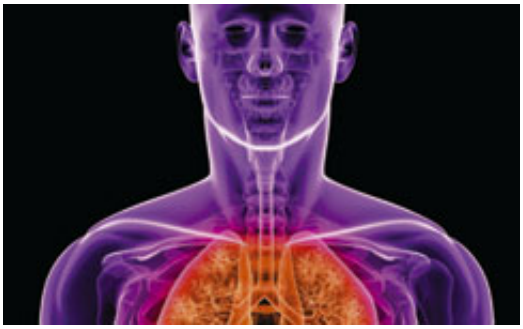

Scientists more used to studying the communities of bacteria that live in natural environments like rivers and soils are helping transform doctors' understanding of a life-threatening illness, and could ultimately shed light on many other health problems too.

Bringing the methods of microbial ecology to bear on lung infections in people with cystic fibrosis (CF) may yield insights that will radically improve their lives and help them survive longer. The idea is that we need to look at the bacteria infesting patients' lungs not as a single homogenous invading force but as a whole ecosystem of different species, interacting with each other and inhabiting diverse niches.

'Our starting point is to look at the lungs of CF patients as a functioning ecological community,' says Dr Christopher van der Gast, a microbial

ecologist at NERC's Centre for Ecology & Hydrology (CEH) who's working with medical researchers on the topic. 'We have found that a CF lung is a more diverse and complex ecosystem than previously realised, containing hundreds of unique bacterial species.' He gave a short talk about progress so far at the British Ecological Society's annual meeting in Birmingham on Tuesday.

This interdisciplinary collaboration between researchers from very different fields is already leading to exciting new findings. For example, it turns out that as a patient's lung function declines, the diversity of the microbial community in their lungs also drops. It's possible that the latter is causing the former, according to van der Gast. Ultimately this could point to ways to help patients by being able to predict worsening of disease by using the bacterial communities as marker for the state of the disease.

'We'd like to be able to monitor these microbial communities and spot changes in their diversity that give us early warning of a drop in lung function,' van der Gast adds. 'In the future, we may be able to manage these communities of microbes in the lung to benefit the patient.'

CF is a serious lung condition that affects some 9,000 people in the UK alone. The underlying problem is genetic, but it leaves sufferers vulnerable to secondary lung infections that trigger periodic turns for the worse, known as 'exacerbations'. During these, sufferers find it extremely hard to breathe and often have to be hospitalised and dosed with a cocktail of intravenous antibiotics. 95 per cent of CF patients ultimately die from a lung infection, so learning to control them more effectively could greatly prolong their lives.

Researchers already knew that the lungs of CF sufferers are often dominated by a few key species of bacteria, and have succeeded in growing these in petri dishes from samples of sputum. But this approach

has serious limitations. There are many kinds of bacteria living in the average infected lung, and each needs different conditions to flourish. Growing one kind may need warm, moist conditions with plenty of oxygen; another may depend on an oxygen-free environment.

Unless you know what's there already, it's impossible to grow every species present because you don't know what growth conditions to provide. So growing bacteria isn't a viable way of finding out what's there. Instead, the team has been using high-throughput genetic sequencing that lets them take a complete census of all the bacteria in a sputum sample, as well as getting an accurate sense of how abundant each one is.

Microbial ecologists use these to survey all the micro-organisms living in a particular environment quickly and precisely, but using them to look at the complex communities of microscopic organisms making their home in our own bodies is a new and exciting development. Combined with ecological modelling techniques, the high-throughput sequencing lets us understand these internal ecosystems in unprecedented detail.

The team has already published a paper in the *Journal of Cystic Fibrosis* investigating the impact of antibiotics given to exacerbating patients. They wondered if the drop in lung microbial diversity that they noted accompanying the reduction in lung function could be caused by all the antibiotics patients get when they are admitted to hospital. But it doesn't seem so; current findings indicate that the diversity started dropping before the antibiotics came on the scene, although van der Gast says it's possible that they are having an effect later in the process – it may be that by eliminating most of the species still present, they clear the way for the dominance of just one or two species, and that this could be harming the patient's ability to breathe.

As part of a NERC-funded project between CEH, King's College

London and the Wellcome Trust Sanger Institute, the team are currently collecting sputum samples from 1000 CF patients in the UK and US, which are being sequenced by the Sanger Institute in Cambridge. This large new study will build on the findings of their earlier work. The team will analyse samples from patients at different stages in their lives, from children to those in late middle age, to investigate how the mix of bacteria changes with age and other clinical factors. The findings should appear around the middle of 2013.

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