Medical Xpress

HATS off to combat asthma

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Two University of Nottingham studies exploring the causes and treatment of asthma and Chronic Obstructive Pulmonary Disease (COPD) could lead to the development of drugs to battle these debilitating conditions.

The Division of Respiratory Medicine at the University has been awarded a total of £1.24m in grants to study respiratory disease. The Wellcome Trust has awarded Prof Alan Knox and Dr Linhua Pang £700,000 to research transcriptional control of inflammatory gene expression in asthma — allowing the team to examine the part inflammatory mediators play in the way asthma sufferers react to allergens. A second grant of £540,000 from MRC to Prof Knox and his colleagues Prof Peter Fischer and Prof David Heery will explore histone acetyl transferase (HAT) inhibitors in asthma and COPD. This study will investigate a bank of plant extracts at the University of Strathclyde, seeking compounds that could combat the intercellular processes that result in the symptoms of asthma and COPD — inflammation of the airways which can lead to coughing, breathlessness and increased chest infections.

Though they are different diseases, asthma and COPD affect the human body in a similar way. In asthma, allergens irritate the lungs, in COPD, this is done by cigarette smoke. This irritation inflames the sufferer's airways, which the muscles then close, creating a narrowing effect.

Research done at the University over the past 15 years has found that the muscle layer in the airway is more complex than has traditionally been

thought. As well as going into spasm during asthma and COPD attacks the muscle layer produces a wide range of mediators and cytokines — proteins that act as chemical signallers when it comes into contact with allergens or cigarette smoke. In asthma and COPD sufferers, these proteins are produced by stimulation of airway muscle cell walls in the lungs, releasing intracellular signalling proteins called 'transcription factors' which alter the DNA of the cell and activate messenger RNA. It is these 'transcription factors' which activate the inflammation by causing release of mediators and cytokines.

The activation status of these transcription factors is determined by the balance between two competing groups of enzymes called histone acetyl transferase (HATs) and histone deacetylases (HDACs). In asthma and COPD sufferers the balance is altered so that the HATs are activated and HDACs suppressed with the result that inflammation is switched on. The investigators at the University think that if the balance could be restored by inactivating HATs then the mediators and cytokines will be switched off and inflammation dampened down.

By exploring plant extracts that may reduce the activation of HATs within airway cells, the researchers may isolate compounds that could be used to suppress inflammation in respiratory disease. Any drug successfully synthesised from such compounds could potentially revolutionise the treatment of respiratory disease. There is also the potential to treat other inflammatory diseases, such as rheumatoid arthritis and Inflammatory Bowel Disease.

Professor Alan Knox, of the Division of Respiratory Medicine at the University, said: "The majority of people with asthma have access to reasonably good anti-inflammatory treatments that can keep their conditions under control. But up to 20 per cent of sufferers don't respond well to the treatments currently available. And when it comes to COPD, anti-inflammatory drugs aren't very effective.

“By tracking the process which triggers the inflammation and then identifying the compounds that inhibit or activate these crucial enzymes, we could put into motion the development of a drug which could have a huge impact on the lives of those suffering from respiratory and other inflammatory diseases.”

Source: University of Nottingham