



Tackling Steroid Resistance in IBD therapy

29th April 2009, St Albans, Herts. Scientists at The Universities of Liverpool and Edinburgh are investigating whether a recently discovered gene could play a role in predicting “steroid resistance” in patients suffering from inflammatory bowel disease (IBD).

The study could eventually lead to the improved individualisation of treatment for patients with ulcerative colitis and Crohn’s disease and avoid the need for exposure to high doses of steroids and their unwanted side effects (osteoporosis, cataracts, etc).

Funded with a £119,942 grant from the National Association for Colitis and Crohn’s Disease (NACC), the two-year project is being led by Professor Munir Pirmohamed in the University’s Department of Pharmacology.

Prof Alastair Watson, a Gastroenterologist in Liverpool, who is a co-applicant states, “In clinical practice, steroids (corticosteroids) such as prednisolone are widely used in the treatment of both ulcerative colitis and Crohn’s disease to bring the inflammation in the patient’s bowel under control. However, some patients do not respond to steroids and we do not understand why.”

Professor Pirmohamed explains, “Recent studies performed by Dr Gwo-Tzer Ho and Prof Jack Satsangi at the Gastroenterology Unit, University of Edinburgh, with whom we are collaborating on this study, have shown that steroid resistance may be related to a key drug transport gene from the ABC-superfamily of genes. This was discovered following detailed genetic analysis of steroid response in newly diagnosed patients with inflammatory bowel disease over the last 10 years in Scotland. This novel finding provides us with an important avenue for further research”.

Professor Pirmohamed added, “Our study will evaluate the interaction of various steroids with this new gene and assess its capacity to pump out steroids including prednisolone, hydrocortisone, methylprednisolone, dexamethasone and budesonide from the cells. By the end of the study, we will know the gene’s role in the gut wall and lymphocytes and whether levels vary between, individuals and whether steroids can increase the activity of this pump. Taken together, this knowledge will contribute to an understanding of the phenomenon of ‘steroid resistance’.

IBD affects around one in 400 people in the UK. Common symptoms include inflammation and ulceration of the intestine and colon, pain, severe diarrhoea, tiredness and weight loss. The

cause of the disease is yet to be definitively identified, although scientists believe it could be due to a combination of genetic predisposition and environmental factors. Currently, there is no cure and patients manage their condition with a mixture of lifestyle changes, anti-inflammatory drugs including steroids and, in severe cases, surgery.

The CEO of NACC Richard Driscoll, explains, "Since 1984, NACC members have raised over £4.5 million and more than 100 research awards have been made to hospitals and universities throughout the United Kingdom. This year, our Medical Research Committee selected three

studies to receive NACC research awards which we hope will contribute to finding improved treatments and ultimately a cure for IBD.

"We welcome Professor Pirmohamed's work and hope that his study will eventually improve the individualisation of therapy so that patients identified as steroid resistant can be given different drugs rather than the current 'trial and error' approach." **ENDS**

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