

**Professor Subrata Ghosh - Imperial College London**

**Grant awarded £42,500 (2 years)**

***A prospective study of the intestinal expression of vanilloid receptor 1 in and other novel afferent receptors in symptomatic Crohn's disease patients and relationship to objective markers of inflammation, CDAI score and pro-inflammatory cytokine expression.***

Crohn's disease significantly impairs quality of life due to abdominal pain, diarrhoea and urgency of bowel motions. Most symptoms are a direct consequence of inflamed intestine, but in a significant minority, symptoms continue even after the inflammation has subsided due to treatment. Understanding of such pain has advanced due to recognition of key receptors on nerve ending such as vanilloid receptor 1 (VR1). However, whether over-expression of such receptors underlies symptoms in Crohn's disease patients who remain symptomatic despite improvement of inflammation remains uncertain and this will be explored in the proposed research project. This is an ill-understood and under-researched area in the management of inflammatory bowel disease.

Receptors such as VR1 offer a potential treatment target in Crohn's disease patients suffering from pain and other rectal symptoms, especially if they continue to have symptoms even after effective anti-inflammatory therapy. VR1 inhibitors and other nerve ending receptor inhibitors may expand the therapeutic armamentarium to treat symptoms in Crohn's disease, provided the rationale of such therapy can be established.

We are in a favourable position to investigate this area by having both international expertise in study of these receptors as well study of inflammatory mediators on site, as well as a large number of patients and a well equipped gastrointestinal physiology laboratory. We propose to study a group of well-characterised Crohn's disease patients before and after effective therapy (steroids, infliximab, azathioprine.) This will show the relationship between inflammation and expression of VR1 receptor, as well as short-term changes induced by therapy and relationship to symptoms. More established changes would be studied in a well-characterised group of patients who have symptoms, but no obvious evidence of active inflammation. This latter group will be compared with a control group of patients whose symptoms as well as inflammation have subsided. Such a study will determine the contribution of over-expression of VR1 or other nerve ending receptors to the symptoms of pain and urgency of bowel motions in patients with Crohn's disease having varying severity of inflammation.

Currently the treatment of Crohn's disease patients who suffer from longstanding chronic pain and other bowel disturbances remains unsatisfactory. Many such patients may end up dependent on opioids for pain relief, and the poor quality of life may lead to depression and even suicidal tendencies. In any case, opioids such as morphine provide poor pain relief in such visceral pain with a high degree of side effects and dependence. New understanding of the triggering of such pain may provide alternative therapies. Our proposed research should provide novel information of scientific and practical importance, and such research is likely to be internationally competitive.