

**Miss Miranda Lomer - The Rayne Institute, St Thomas' Hospital, London**

**Grant awarded £5,992 (2 months)**

***Assessment of large pore (particulate) permeability: A pilot study***

The applicant previously applied to NACC (November 2000) for 2 years funding of a project on large pore (particulate) permeability in Crohn's disease. Reviewers comments were enthusiastic but suggested a pilot study in volunteers prior to the main study. This application is to undertake the pilot study before the applicant undertakes the main project.

The gastrointestinal tract houses numerous *essential* bacteria that live in symbiosis with the host. These bacteria provide fuel for gastrointestinal cells and help to prevent the invasion of pathogenic bacteria. The cause of Crohn's disease remains unknown but much recent evidence points to an abnormal response towards these essential bacteria. In fact new data suggests that even dust particles, similar in size to these bacteria, may also provoke abnormal responses in Crohn's disease. One often stated theory for this abnormal response is an increase in permeability. In other words, bacterial and similar sized species that would normally gain entry *into* the gut tissue could be doing so in Crohn's disease.

In support of this theory are numerous investigations showing that gut permeability is slightly increased in patients with Crohn's disease and even in their relatives. The problem however, is, that the molecules used to test for permeability are about one-millionth the size of bacteria. The complex nature of permeability in the gastrointestinal tract means that one cannot assume that results derived from small probes are applicable to the very much larger bacteria. Indeed this perfectly possible that there greatly abnormal permeability to bacteria or dust as an underlying problem in patients with Crohn's disease, and that this is poorly detected with small probes.

Recently a method has become available to test this hypothesis and we have all the expertise and equipment in our laboratory to apply this to patients. In this pilot study, we will confirm this method of measuring large pore permeability in healthy control subjects by feeding them a meal containing high levels of a particles-sized food additive. We will take samples of their blood at time intervals and plot the appearance of this food additive in blood. We will, at the same time look at the permeability of typical small molecules to prove that these have different permeability profiles compared to the much larger particles.

Immediately following this preliminary work, applications will be made for a subsequent study to investigate if patients with Crohn's disease, and their relative, have grossly abnormal permeability to bacterial sized agents in the gut which could lead to (a) a simple diagnostic test and (b) a target for treatment.