Tissue remodelling and fibrostenosis in Crohn’s disease – a study of molecular signals and biomarkers.

A Multicentre Study

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IBD- incidence

- IBD is now a global disease with increasing incidence in newly industrialised countries

- Two main conditions- ulcerative colitis and Crohn’s disease

- Incidence is stabilising in western countries

- Prevalence is about 0.3%

Ng, Shi et al. Lancet 2018
Global Incidence of IBD

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Crohn’s disease and ulcerative colitis

Crohn’s disease

Ulcerative colitis

Ileum (33%)

Ileo-colon (45%)

Colon (20%)
Complications of Crohn’s disease

• Poor nutritional status due to lack of absorption (due to inflammation)

• Strictures or fibrosis (narrowing of bowel lumen)

• Fistula formation

• Abscess formation (infected collections)
Strictures and treatment
Fibrogenesis in stricturing Crohn’s disease
Pathogenesis of fibrosis in CD

Quiescent Gut

- ECM homeostasis
- Wound healing
- Production of structural proteins

Activated Gut

- Cell injury amplification
- Inflammatory signalling
- ECM turnover
- Proliferation
- Fibrogenesis

Gut Fibroblast

Healthy

Crohns

UC
TRAFIC study

• We wanted to understand the pathology of strictures better

• Deep study of histology from samples of patients undergoing surgery

• Application of new techniques in lab to the samples obtained

• Compare findings with patients who do not have strictures

• To follow-up the clinical course of patients for a period of 24 months to record complications like stenosis, fistulisation and record events such as steroid use, hospitalisation and surgery.

• Study for potential targets of therapy to prevent or reverse fibrosis in high risk patients
Study Design

• Non-interventional exploratory prospective cohort study collecting blood and tissue samples in the following cohorts of patients with IBD
  
  • Patients undergoing surgery for fibrostenosing Crohn’s disease (core group)

Comparators
• Inception patients (new diagnosis of IBD)
• Patients not exposed to biologics
• Patients on anti-TNFα therapy (pre and post therapy)
• Patients who have discontinued biological therapy
• Patients on ustekinumab (pre and post therapy)
• Patients on vedolizumab (pre and post therapy)
• Patients who have had a resection in the past
• Patients with diagnosis of irritable bowel syndrome (non-diseased control)
Contd…

• Prospective study (now has HRA, Research Ethics Committee approval)

• Successfully recruited 40 patients so far

• Relevant samples collected from patients and processed in the lab

• Histology, immunohistochemistry

• Biological markers of disease and complications
Eligibility

• Patients aged between 18 and 80 years of age

• Patients must have a confirmed diagnosis of IBD at least 1 month prior to recruitment

• Able to consent
Recruitment

- **Patient cohorts**
  - Identified by members of the clinical care team from clinic and endoscopy lists prior to their routine outpatient clinic or endoscopy appointment.

  - Patients approached to give blood samples during their routine clinic appointment will be given a copy of the Patient Information Sheet.

  - Interested patients will sign a consent form.

  - Samples will be taken at appropriate times at their clinic visit.

  - Blood samples & biopsies that are taken for research will be additional to what is taken for standard care.

  - The total volume of blood at one sitting will not exceed 50mls (approximately 25mls to 30mls for research).

  - The blood samples obtained are then given a unique reference number and transported to the laboratory.
Data

• RedCap (online research database)

• Anonymised data; patient identified with unique study code

• Database created by UoB team

• Follow up data for 24 months at least for all patients
Any questions?

**Study Contacts**
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