

# Gut microbiota in patients with Crohn's disease and their relatives

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 18/06/2010	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
<b>Last Edited</b> 27/08/2014	<b>Condition category</b> Digestive System	<input type="checkbox"/> Individual participant data

**Plain English summary of protocol**  
Not provided at time of registration

## Contact information

**Type(s)**  
Scientific

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## Additional identifiers

**Protocol serial number**  
6446

## Study information

**Scientific Title**  
Gut microbiota in patients with Crohn's disease and their relatives: a case-control study of the gut microbiota and related immunological and biochemical markers of gut inflammation in patients with quiescent Crohn's disease and the effect of a prebiotic diet

## **Study objectives**

The inflammation associated with Crohn's disease is driven by the intestinal bacteria. Patients with Crohn's disease have been shown to have an altered pattern of gut bacteria in comparison to healthy people. It is not known whether this alteration occurs early in the disease and may be a cause of Crohn's disease or is a reaction to the damage that Crohn's disease causes to the gut. A proportion of relatives of patients with Crohn's disease have some evidence of mild forms of inflammation similar to their affected relatives (leaky gut and a rise in faecal calprotectin which is a marker of inflammation) but it is not known whether they also have altered bacteria.

The aim of study one is to determine whether an altered pattern of bacteria is present in relatives of patients with Crohn's disease. The aim of study two is to find out whether following a prebiotic diet high in fructo-oligosaccharides (FOS) can increase the levels of anti-inflammatory bacteria and can reverse these mild inflammatory changes.

## **Ethics approval required**

Old ethics approval format

## **Ethics approval(s)**

Bromley Local Research Ethics Committee, 26/02/2008, ref: 07/H0805/46

## **Study design**

Multicentre non-randomised observational prevention and treatment case-controlled study

## **Primary study design**

Observational

## **Study type(s)**

Treatment

## **Health condition(s) or problem(s) studied**

Topic: Oral and Gastrointestinal; Subtopic: Oral and Gastrointestinal (all Subtopics); Disease: Gastrointestinal

## **Interventions**

Study one:

Patients, siblings and controls are compared with the following parameters:

1. Gut permeability
2. Faecal calprotectin
3. Luminal and mucosal gastrointestinal microbiota
4. Genetic predisposition to Crohn's disease
5. Peripheral lymphocyte sub-populations and expression of homing markers
6. Intestinal permeability

Study two:

Patients with Crohn's disease and their unaffected siblings who have a faecal calprotectin above the reference range are invited to undergo a 3-week dietary intervention with a supplement of fructo-oligosaccharides (FOS).

Duration of study 1: 5 hours  
Duration of study 2: 3 weeks  
Follow-up length: 3 weeks  
Study entry: registration only

## **Intervention Type**

Other

## **Phase**

Not Applicable

## **Primary outcome(s)**

1. Study one: significant difference in gut microbiota between relatives of patients with Crohn's disease and healthy controls, measured at baseline
2. Study two: significant fall in faecal calprotectin in patients and their relatives following a FOS-enriched diet, measured at 3 weeks.

## **Key secondary outcome(s)**

1. Study one: significant differences in faecal calprotectin, gut permeability, gut-homing lymphocytes in patients' relatives in comparison to patients with Crohn's disease and healthy controls. The influence of genotype on these measures will also be characterised. Measured at baseline.
2. Study two: alterations in gut microbiota, gut-homing lymphocytes and gut permeability after consuming a FOS-enriched diet for 3 weeks in patients and their relatives, measured at 3 weeks

## **Completion date**

01/08/2011

## **Eligibility**

### **Key inclusion criteria**

Inclusion criteria:

1. Aged 16 years or older, either sex
2. Diagnosis of Crohn's disease for at least 3 months defined by histology or radiology
3. Quiescent (inactive) disease as defined by a Crohn's Disease Activity Index (CDAI) below 150
4. Normal C-reactive protein (CRP) as defined by local laboratory
5. On stable Crohn's disease therapy with a total steroid dose not exceeding 10 mg prednisolone or equivalent
6. Relatives of patients:
  - 6.1. Will be aged between 16 and 35 years
  - 6.2. Will be a first degree relative of a patient as described above. Relatives older than 35 will not be recruited to maximise the chance of including some individuals who will develop Crohn's disease in the future.
7. Healthy controls will comprise age-matched patients with functional constipation or those undergoing polyp surveillance who are scheduled to undergo flexible sigmoidoscopy. A second group of controls who will not undergo sigmoidoscopy will comprise healthy volunteers.

Concomitant medication:

Patients currently taking maintenance oral 5 aminosalicylic acid (5ASA) therapy must have been on a stable dose for 4 weeks prior to study entry, and will be maintained at the same dose for

the duration of the study. No rectally administered medications (steroid or 5ASA) are allowed for the two weeks preceding entry to the study. Patients on a stable dose of oral (not exceeding 10 mg) prednisolone or equivalent for 4 weeks prior to baseline are permitted to enter the study. Patients taking azathioprine or 6 mercaptopurine must have commenced the drug at least 16 weeks prior to entry to the study and been maintained on a stable dose for at least 4 weeks prior to entry. No antibiotics, probiotics or prebiotics will be used during the study or for the preceding month. Non-steroidal anti-inflammatory drugs (NSAIDs) will not be permitted for 1 week before entry to the study. The requirement for a normal CRP is to ensure inactive disease.

For participants in study two, no changes in medication will be permitted during the study period. Participants requiring changes to their drug regime will be withdrawn from the study and continue with their usual medical care.

### **Participant type(s)**

Healthy volunteer

### **Healthy volunteers allowed**

No

### **Age group**

Adult

### **Sex**

All

### **Key exclusion criteria**

The principal exclusion criteria are standard for this type of trial in Crohn's disease.

All participants:

1. Current infection with an enteric pathogen
2. Use of antibiotics within the last month
3. Consumption of any probiotic or prebiotic within the last month
4. Change in dose of oral steroids within the last 4 weeks
5. Dose of steroids exceeding 10 mg prednisolone per day or equivalent
6. Change in dose of oral 5 ASA products within the last 4 weeks
7. Commencement of azathioprine or methotrexate within the last 4 months or change in dose of these drugs within the last 4 weeks
8. Infusion of infliximab within the last 3 months
9. Use of any alternative biological therapy within the last 3 months
10. Use of rectal 5 ASA or steroids within the last 2 weeks
11. Imminent need for surgery
12. Participant requiring hospitalisation
13. Pregnancy or lactation
14. Short bowel syndrome and previous proctocolectomy or purely anal Crohn's disease
15. Significant hepatic, renal, endocrine, respiratory, neurological or cardiovascular disease as determined by the principal investigator
16. A history of cancer with a disease-free state of less than 2 years

Patients:

17. Evidence of active Crohn's disease as defined by a CDAI of greater than 150

Relatives:

18. Previously been diagnosed with inflammatory bowel disease

Controls:

19. Previously been diagnosed with inflammatory bowel disease

20. First or second degree relative with inflammatory bowel disease

**Date of first enrolment**

02/01/2008

**Date of final enrolment**

01/08/2011

## **Locations**

**Countries of recruitment**

United Kingdom

England

**Study participating centre**

**Barts and The London NHS Trust**

London

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## **Sponsor information**

**Organisation**

Barts and The London NHS Trust (UK)

**ROR**

<https://ror.org/00b31g692>

## **Funder(s)**

**Funder type**

Research organisation

**Funder Name**

Digestive Diseases Foundation (CORE) (UK)

# Results and Publications

## Individual participant data (IPD) sharing plan

### IPD sharing plan summary

Not provided at time of registration

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>	results	01/10/2014		Yes	No