

# Fructo-oligosaccharides in Crohn's disease: a prospective randomised double blind controlled trial

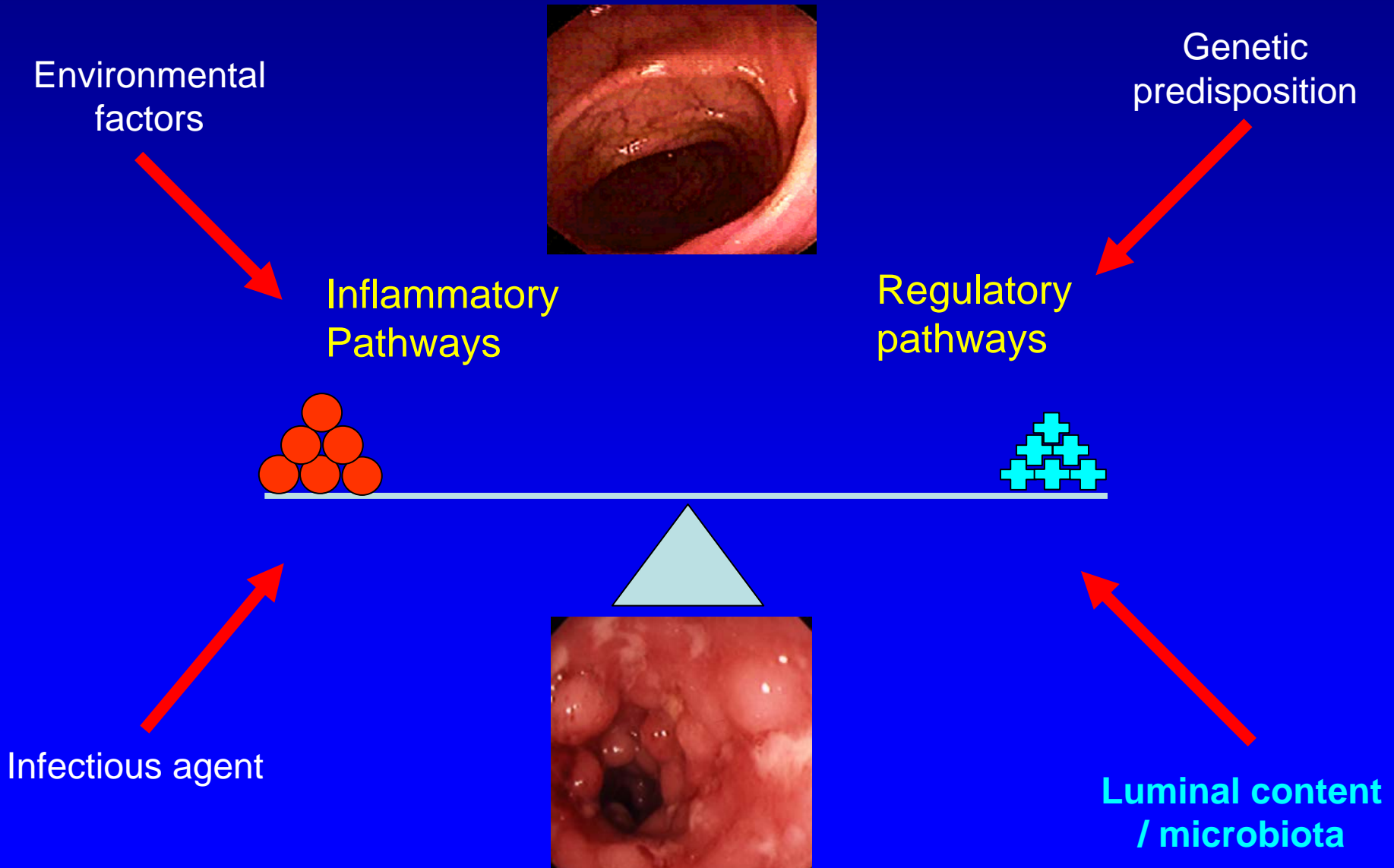
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Principal investigator: Dr James Lindsay

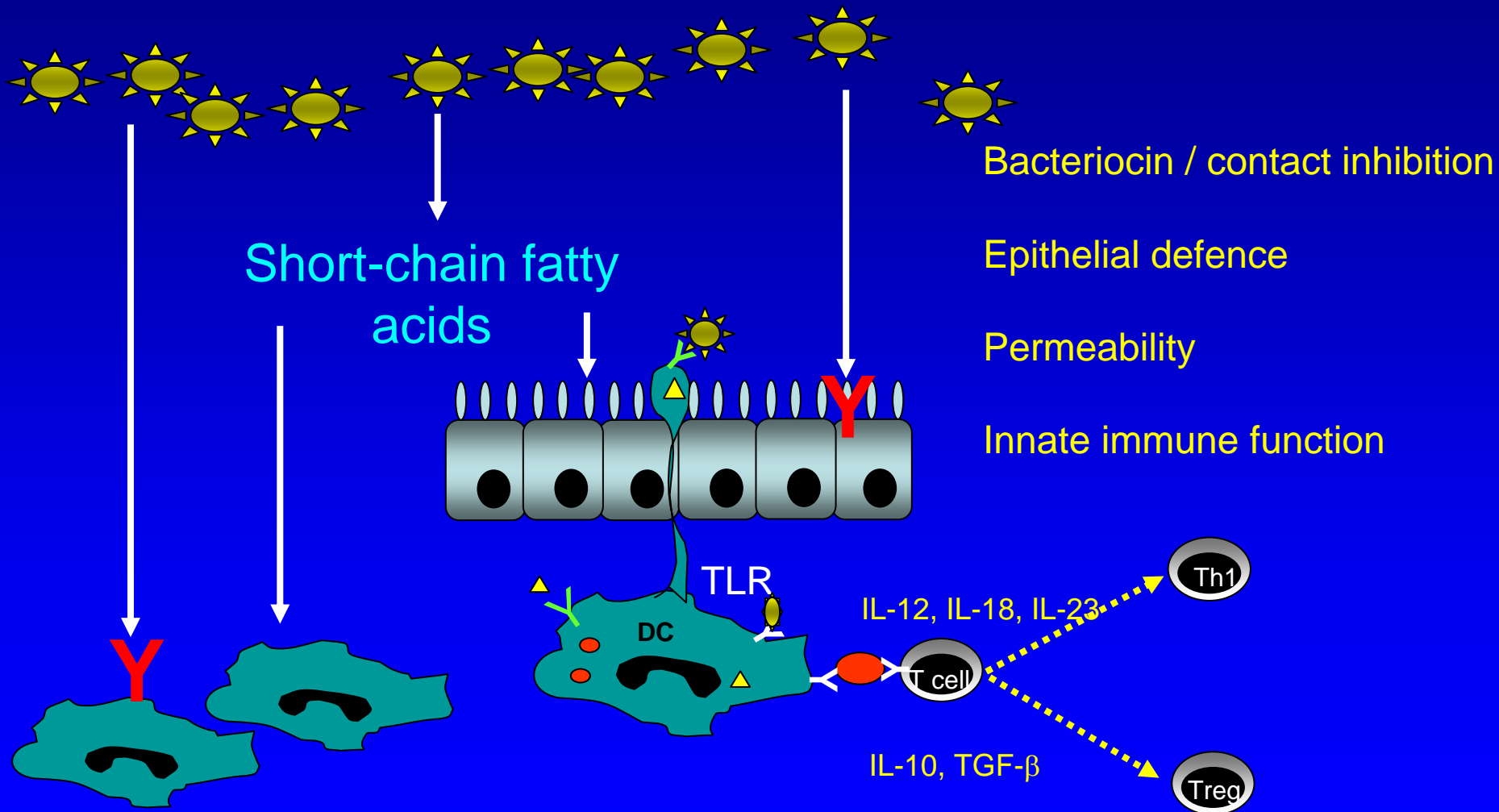
St Bartholomew's Hospital and The Royal London Hospital  
Queen Mary School of Medicine and Dentistry, University of London



# Pathogenesis of Crohn's disease: *balance within the mucosal immune system*



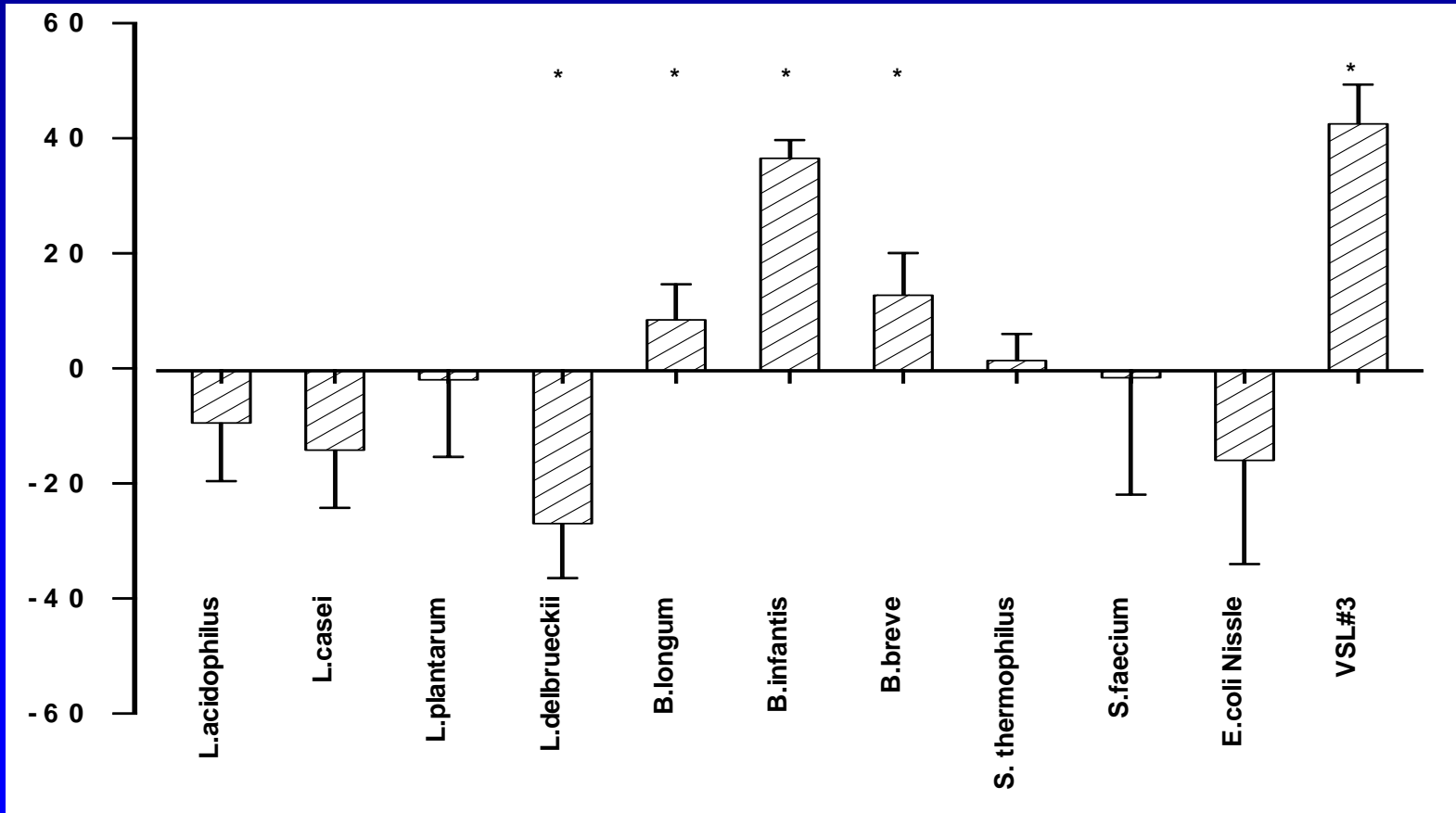
# Regulatory pathways in Crohn's disease: interaction between luminal content and mucosa...



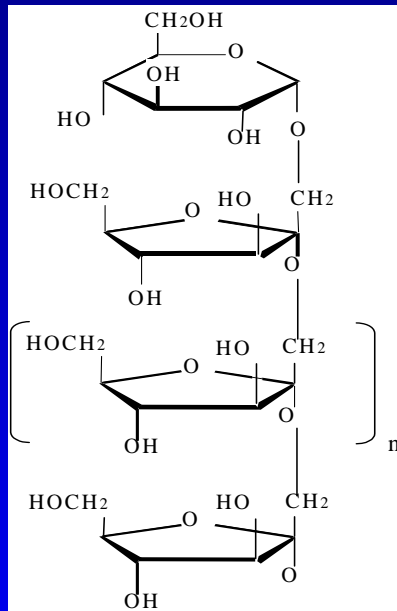
# Regulatory pathways in Crohn's disease

interaction between microbiota and adaptive responses...

Probiotic VSL enhances DC immunoregulatory function in vitro



# Prebiotics: Fructo-oligosaccharide / inulin



Not hydrolyzed in upper GI tract

Selectively fermented

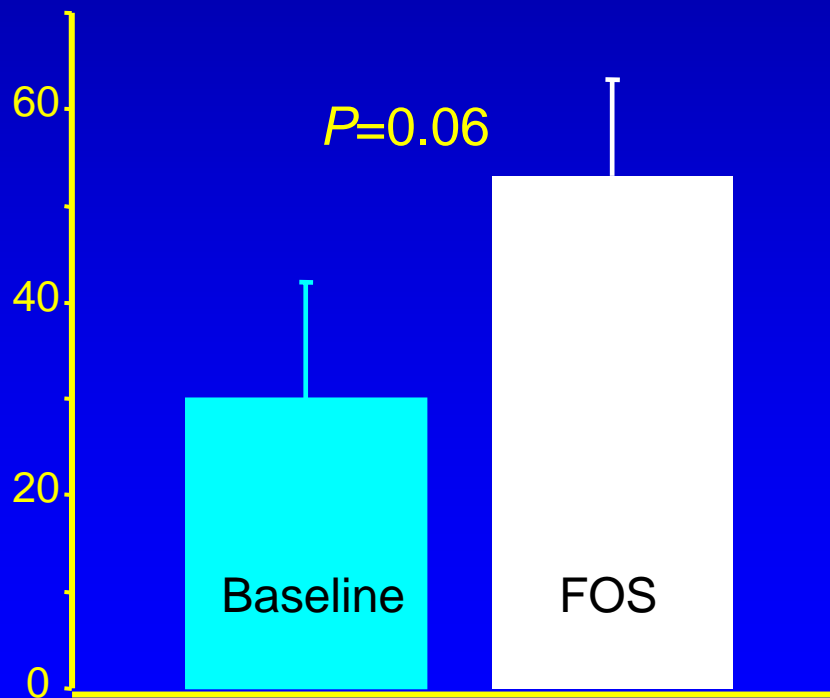
Increase faecal and mucosal bifidobacteria

Produce short-chain fatty acids

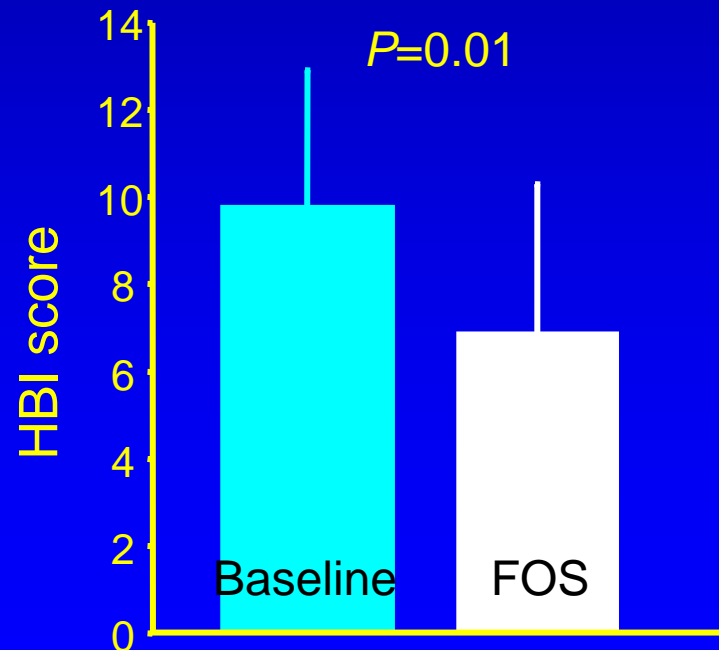
Enhance calcium absorption

# Open label trial of fructo-oligosaccharide in Crohn's disease

Increased DC IL-10



Reduced disease activity



# Double blind placebo controlled trial of FOS vs placebo in Crohn's disease

## Inclusion criteria

- Crohn's disease for at least 3/12
  - Radiological / endoscopic diagnosis
- Active disease (CDAI 220-450)
- Raised inflammatory markers
  - CRP *or*
  - ESR *or*
  - Platelet count
- Stable medication
  - Prednisolone <10mg
- Aged 18-65
- No pre / probiotic
- No recent antibiotics
- Must have functioning colon
- Not pregnant or lactating
- No other significant disease

# Double blind placebo controlled trial of FOS vs placebo in Crohn's disease

## Outcome measures

### **Primary endpoint**

- Clinical response week 4

### **Secondary endpoints**

- Remission week 4
- Response / remission week 12
- Change in HBI / CDAI
- Reduction in CRP weeks 4/12
- Increase in IBDQ

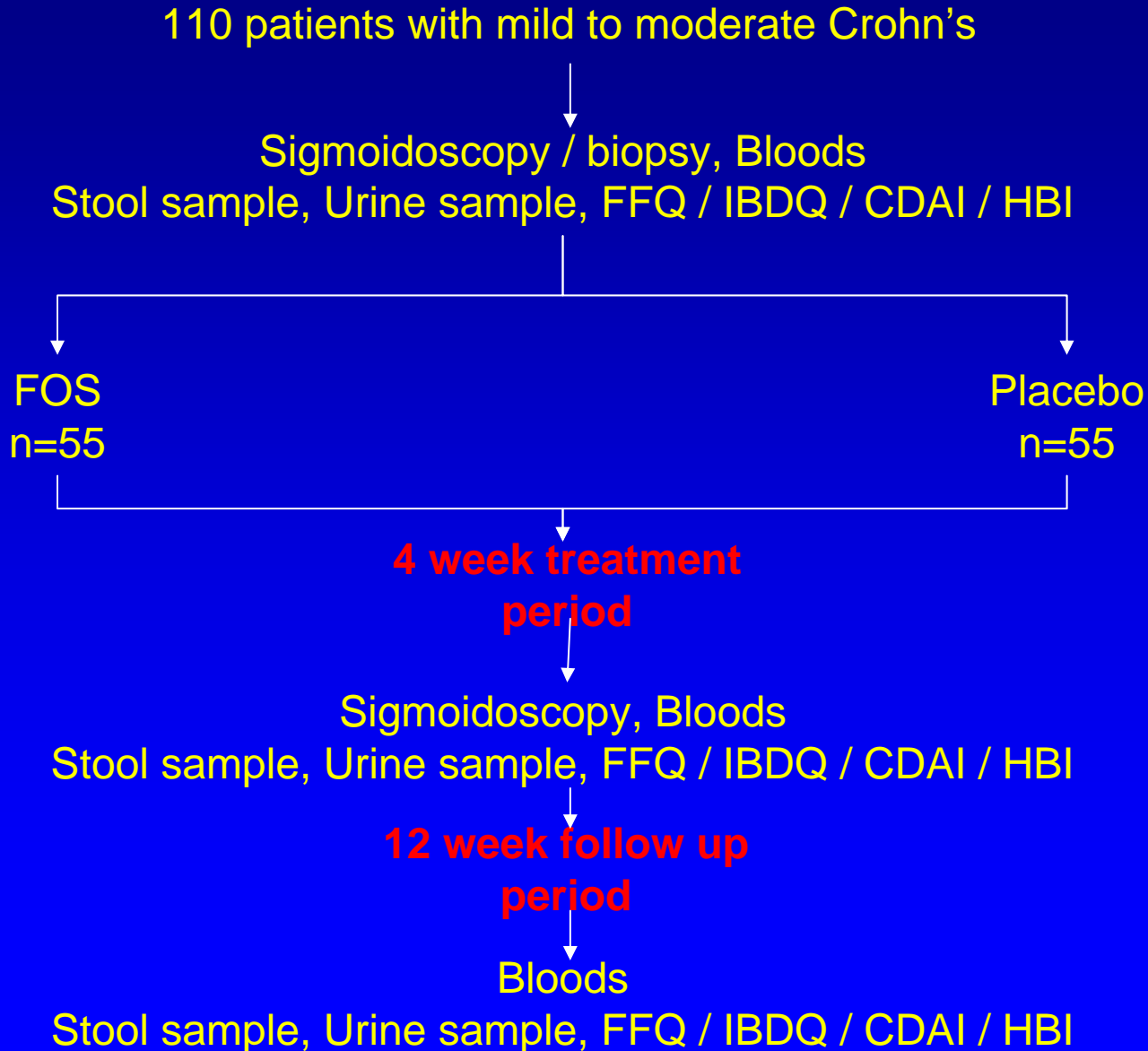
### **Microbiological endpoints**

- Baseline faecal / mucosal microbiota
- Change in microbiota at week 4 / 12

### **Immunological endpoints**

- LP dendritic cell phenotype at baseline
- LP dendritic cell phenotype at week 4

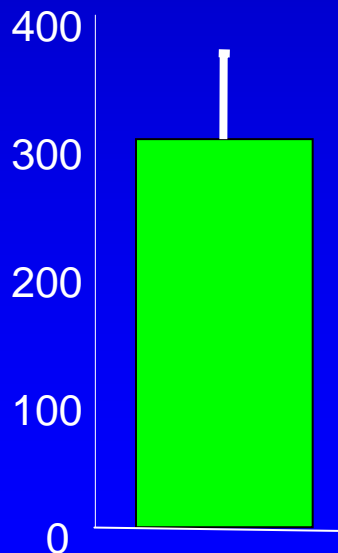
# Schematic diagram of study visits



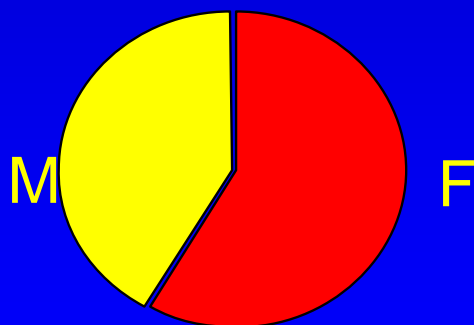
# Double blind placebo controlled trial of FOS vs placebo in Crohn's disease: *interim results*

96 pts screened  
47 pts recruited  
8 pts withdrawn

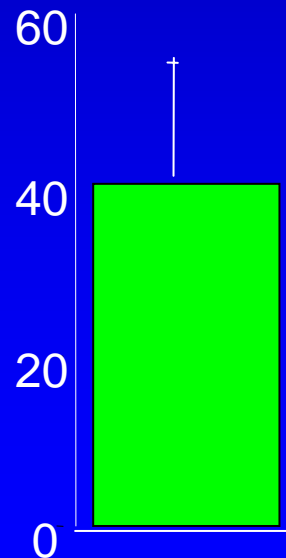
Baseline CDAI



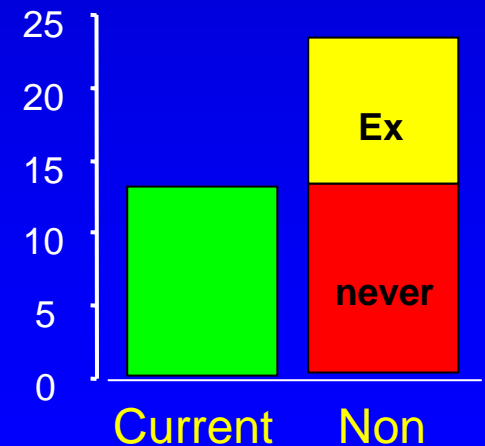
Sex ratio



Age



Smoking status



# Double blind placebo controlled trial of FOS vs placebo in Crohn's disease: *baseline microbiota*

Baseline microbiota is not affected by disease location

	Colonic only (N=8)	Ileo-colonic (N=30)	sig
Total bacteria	10.4 (0.3)	10.2 (0.5)	NS
Total cells	10.4 (0.3)	10.3 (0.4)	NS
Bifidobacteria	10 (0.3)	9.9 (0.5)	NS
Bacteroides	9.9 (0.3)	9.8 (0.5)	NS
Clostridia Sp	10 (0.4)	9.7 (0.5)	NS

No effect of baseline CDAI / medication / age / years since diagnosis

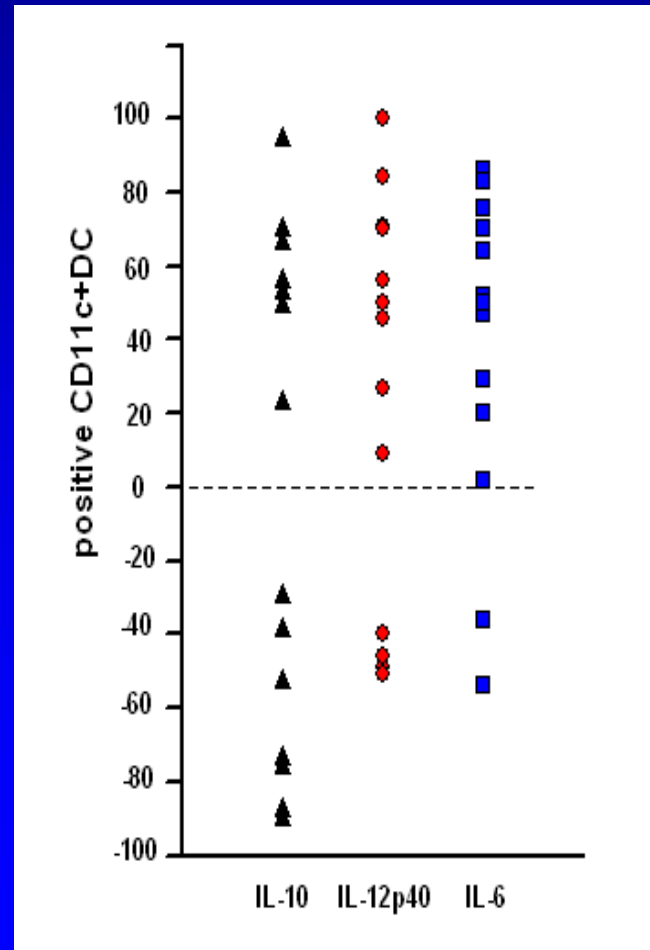
# Double blind placebo controlled trial of FOS vs placebo in Crohn's disease: *baseline microbiota*

Effect of smoking on baseline microbiota in patients with Crohn's disease

	Smokers	Non-smokers	sig
%Bac (EUB)	47.3 (14.8)	36.5 (14.9)	p=0.043
%Bac (DAPI)	39.6 (12)	31.5 (12.7)	p=0.070

	Smokers	Non-smokers	sig
Bac/Bif	1.1 (0.4)	0.9 (0.3)	p=0.019

# Double blind placebo controlled trial of FOS vs placebo in Crohn's disease : *baseline immunology*



## Double blind placebo controlled trial of FOS vs placebo in Crohn's disease : *baseline immunology*

Compared with patients with no detectable IL-10 producing DC, those with IL-10 positive colonic DC have significantly higher:

1. Faecal concentrations of total bacteria ( $10.6 \pm 0.2$  vs  $10.2 \pm 0.4$  log<sub>10</sub>/g,  $p=0.049$ )
2. Bifidobacteria ( $10.3 \pm 0.2$  vs  $9.8 \pm 0.5$  log<sub>10</sub>/g,  $p=0.039$ )
3. Bacteroides ( $10.2 \pm 0.3$  vs  $9.6 \pm 0.5$  log<sub>10</sub>/g,  $p=0.025$ )

There were no significant differences in individual bacterial strains and concentrations when comparing IL-6 or IL-12p40 positive DC, with IL-6 and IL12p40 negative DC

# Double blind placebo controlled trial of FOS vs placebo in Crohn's disease : conclusions

Microbiota exert inflammatory and immunoregulatory effect on the intestine

Prebiotics increase bifidobacteria and enhance regulatory responses

DBPCT ongoing: recruitment on schedule

# The London Prebiotic Research Group: *Acknowledgments*

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