

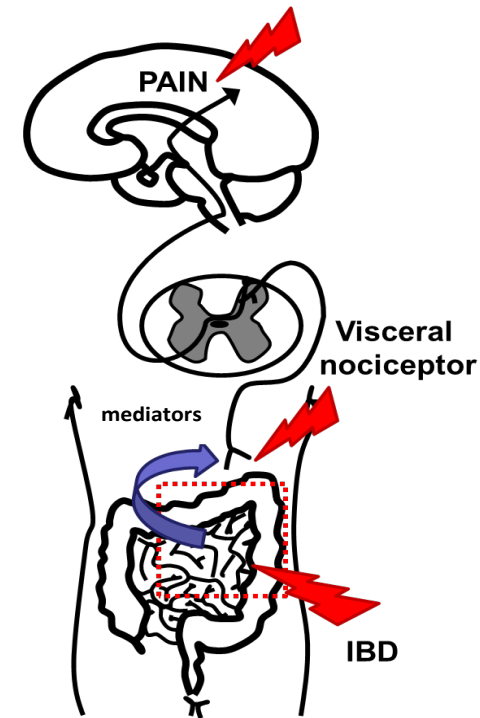
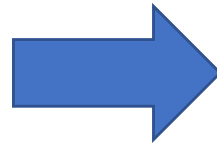
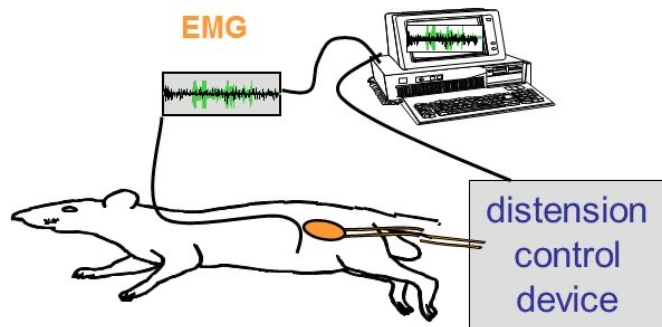
How can we treat visceral pain in GI diseases?

Dr David Bulmer

Department of Pharmacology
University of Cambridge



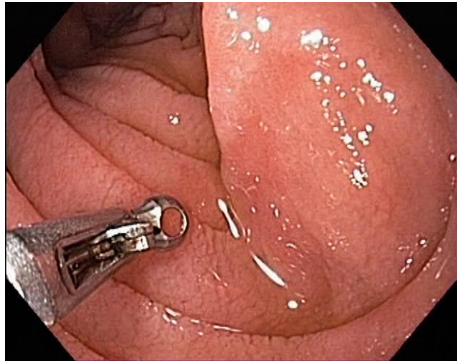
Challenges in 2009



Can we fill the gap between rodent experiments and human clinical studies?



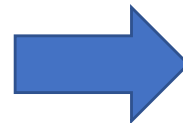
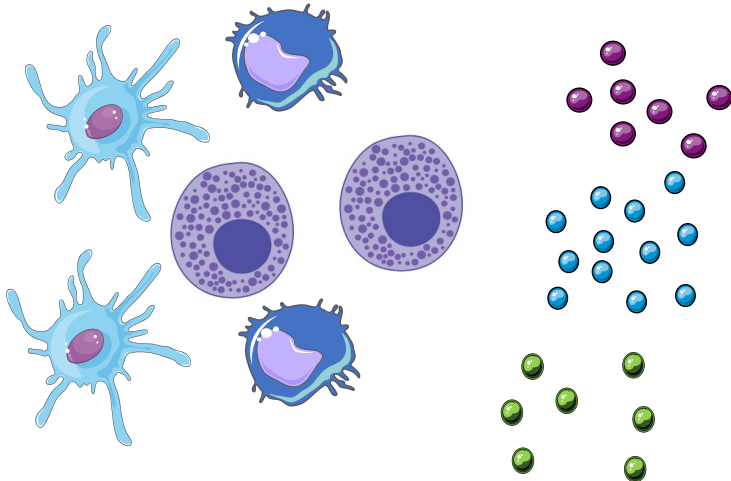
Human tissue



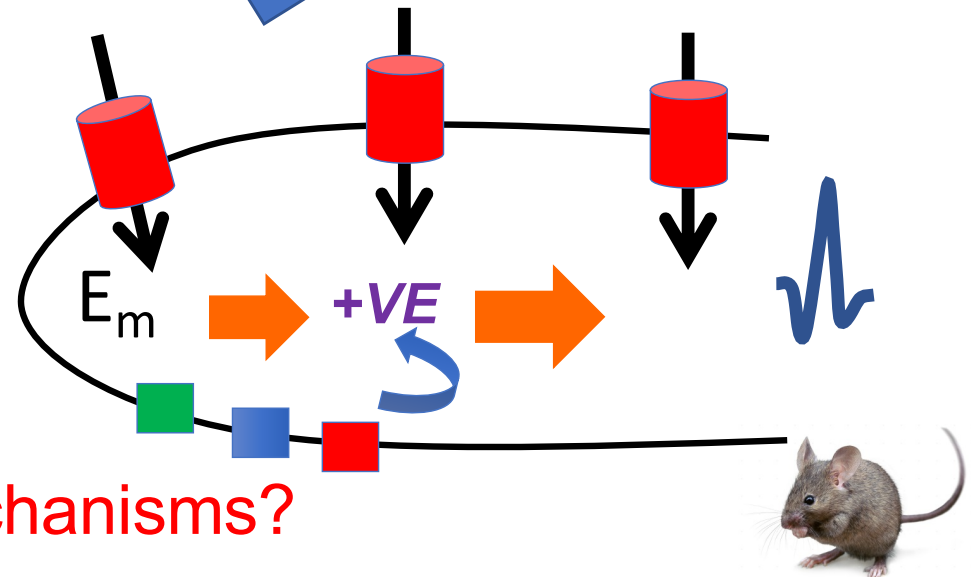
Translate input



+ve mediators?

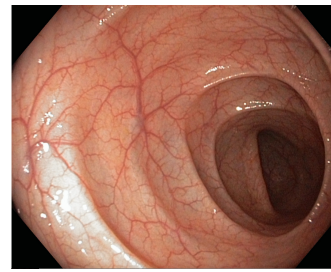


mechanisms?



Nociceptor – pain sensing nerve

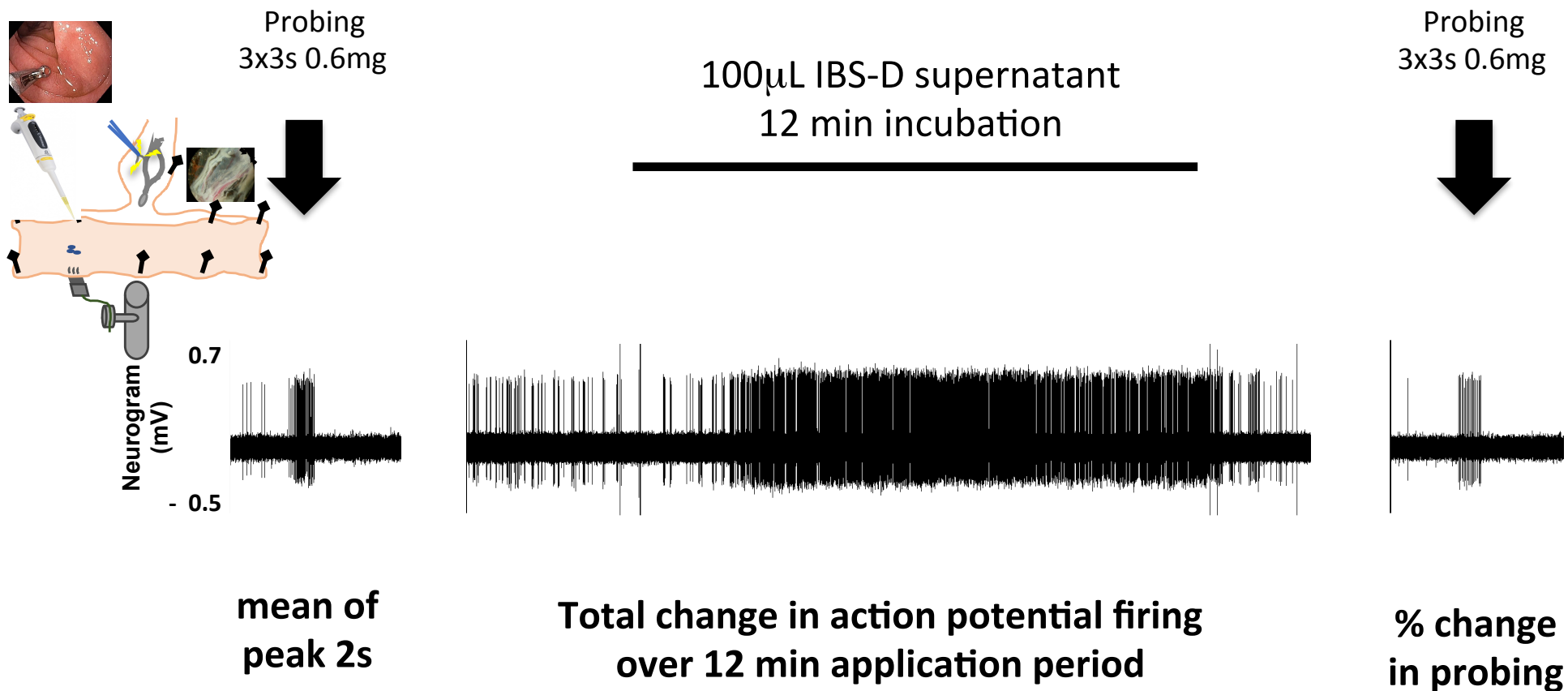
IBS-D (Diarrhoea)



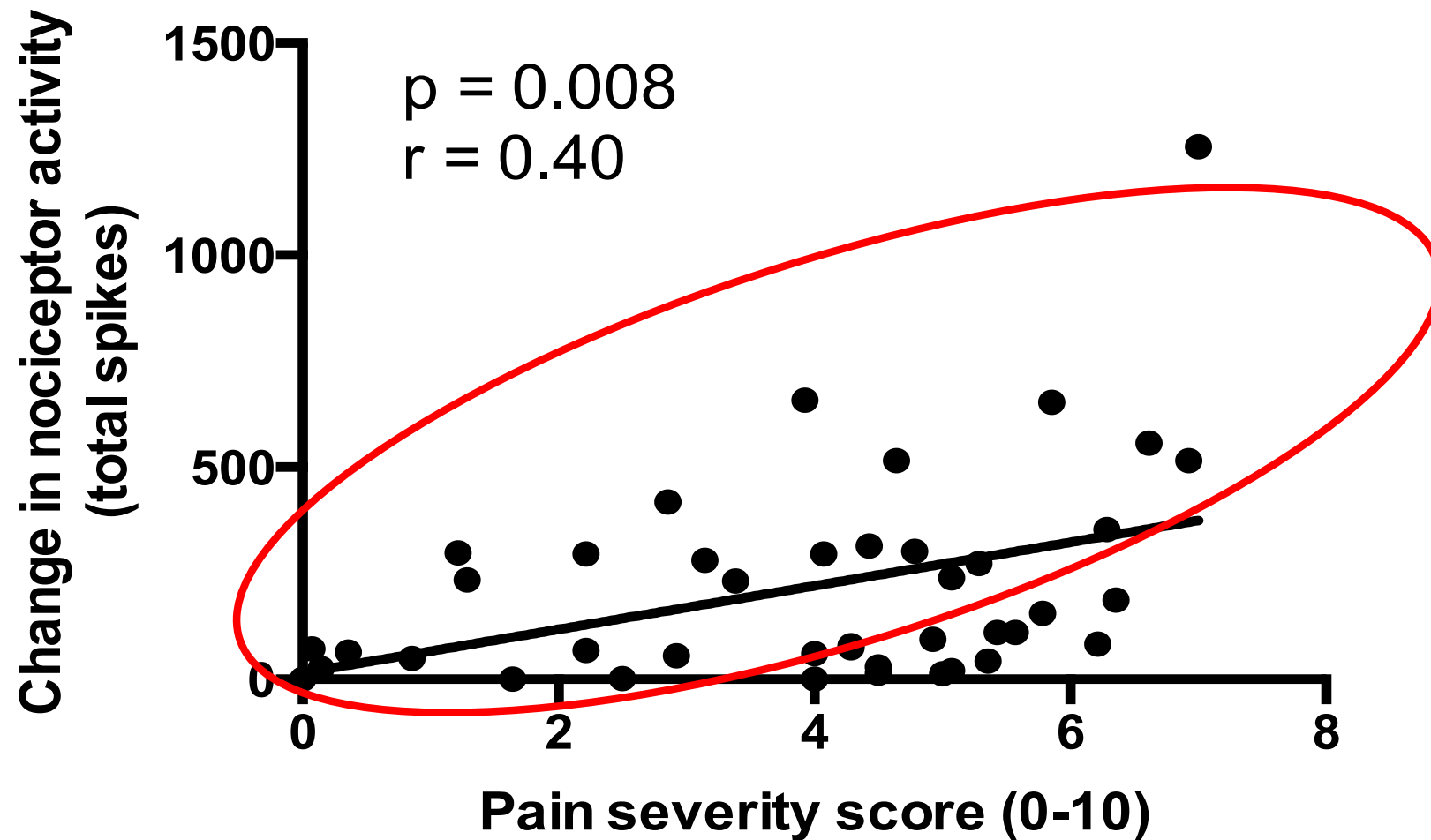
Robin Spiller
University of
Nottingham



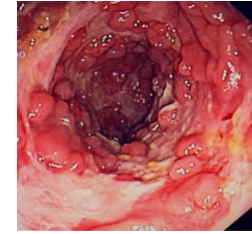
- 42 IBS-D patients (ROME III)
- Mean of daily scores from 14 day symptom diary
- Sensory symptoms
 - Pain severity (0-10)
 - Urgency to defecate (0-10)
- Motility symptoms
 - Stool frequency
 - Stool consistency
- Psychological
 - Anxiety
 - Depression



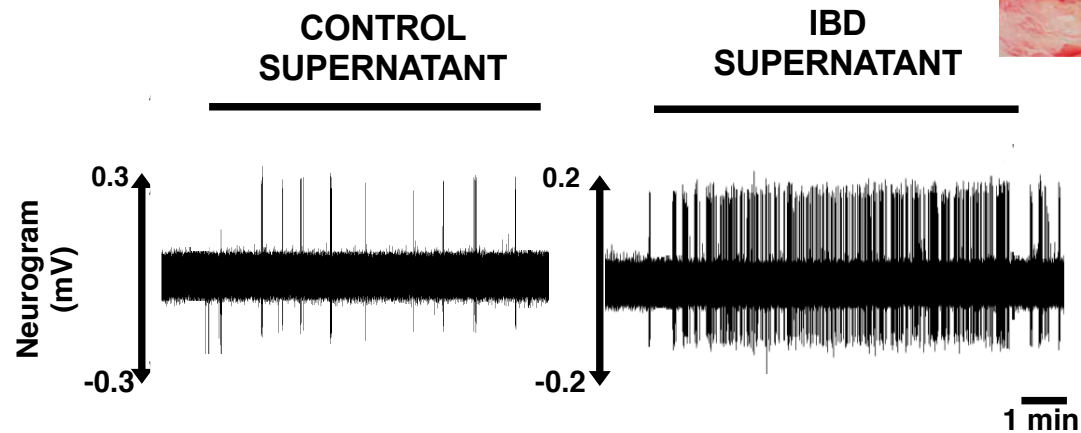
Correlation with pain score



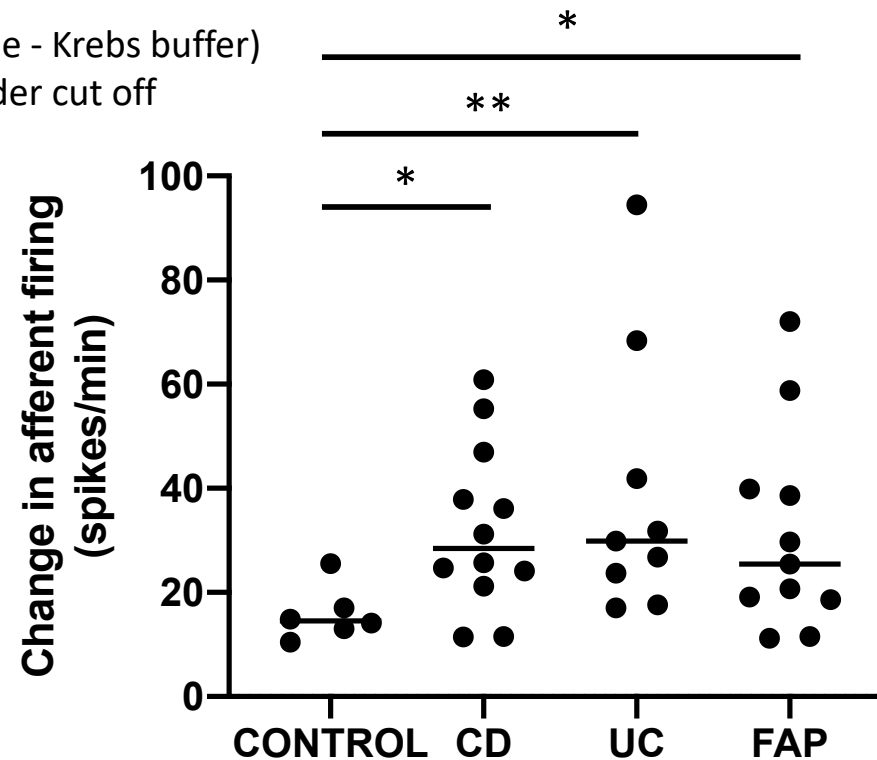
Paediatric IBD & FAP



Nick Croft
QMUL

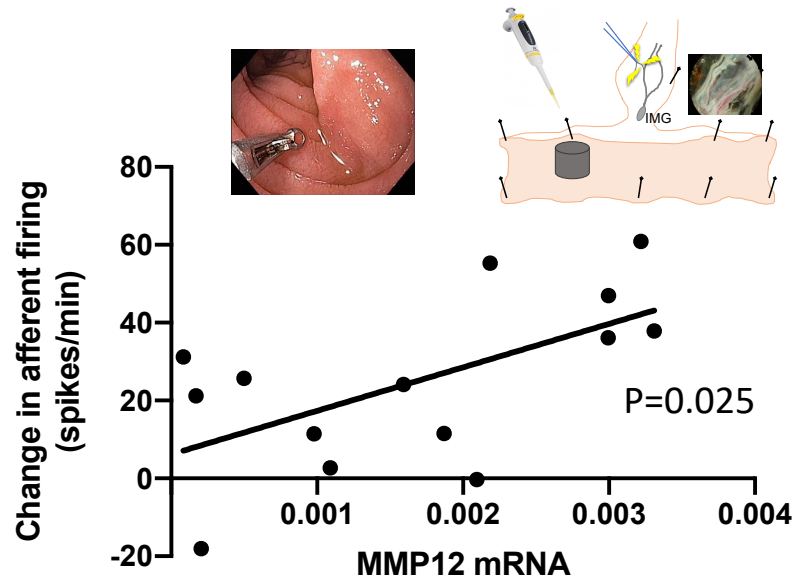


- 50% responder rate (vehicle - Krebs buffer) used to determine responder cut off

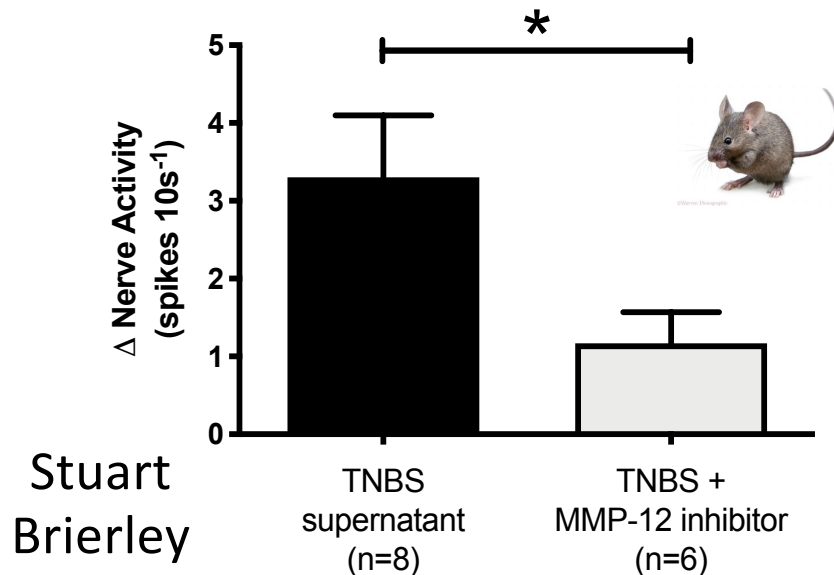
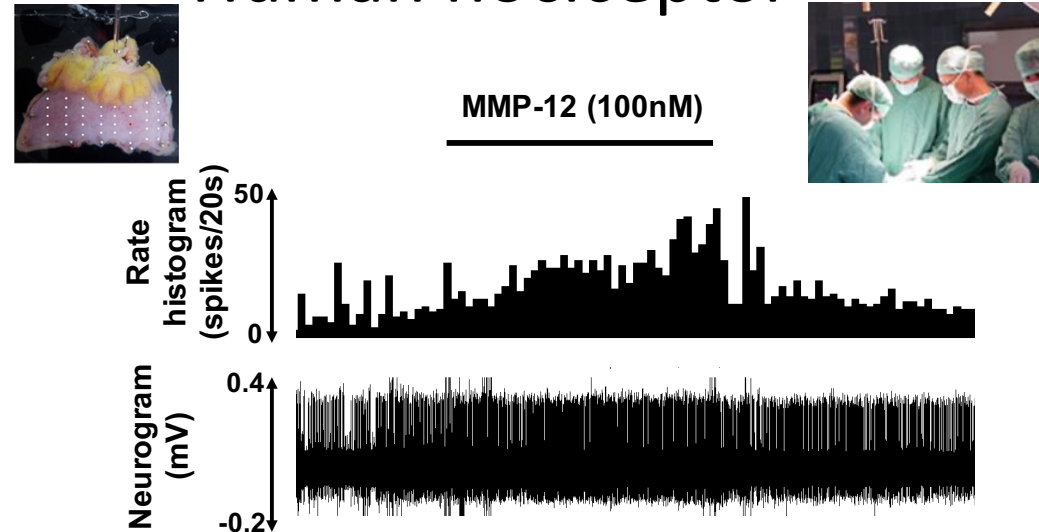


unpublished

Macrophage Metalloelastase (MMP-12)



Human nociceptor



Stuart
Brierley

Where next?

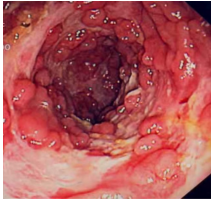
Ewan St
John Smith



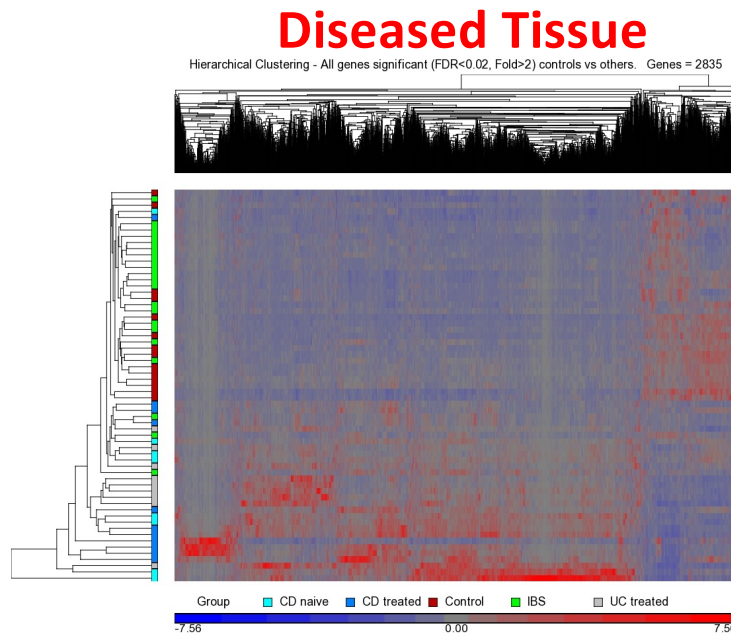
James
Hockley



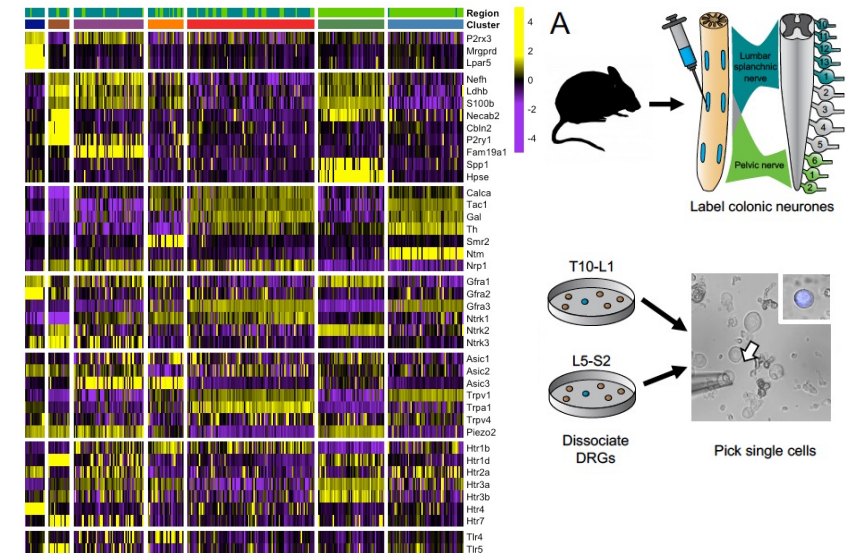
RNA Seq



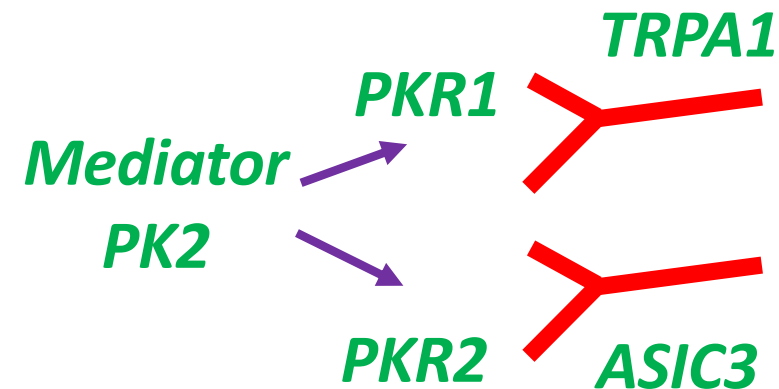
CD vs
UC vs
IBS vs
Control



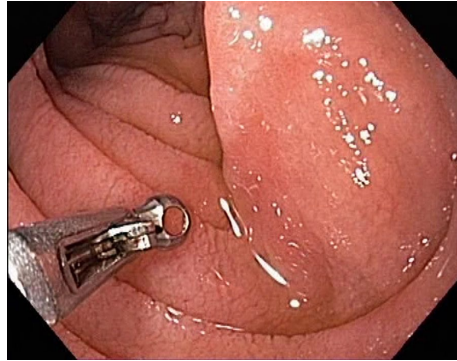
Sensory Neuron



	FOLD CHANGE	P VALUE
MMP8	122.6	0.000085
MMP1	73.9	0.000209
PROK2	48.8	0.000295
IL11	44.2	0.000364
CXCR1	36.3	0.000114
CXCL6	33.1	0.000040
CXCR2	23.9	0.000026



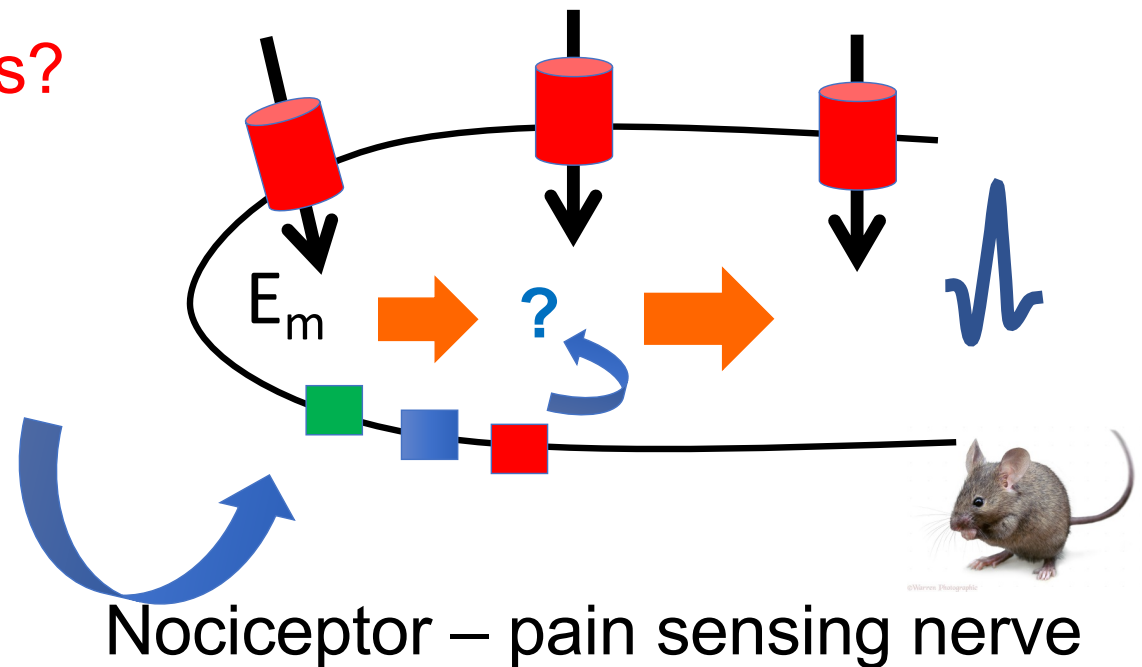
Visceral nociception in IBD



Translate input



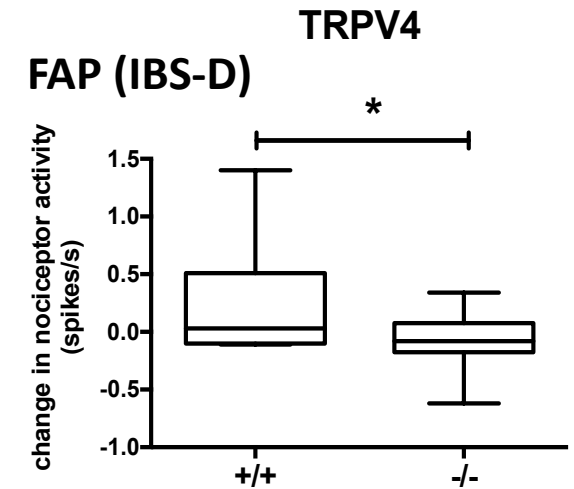
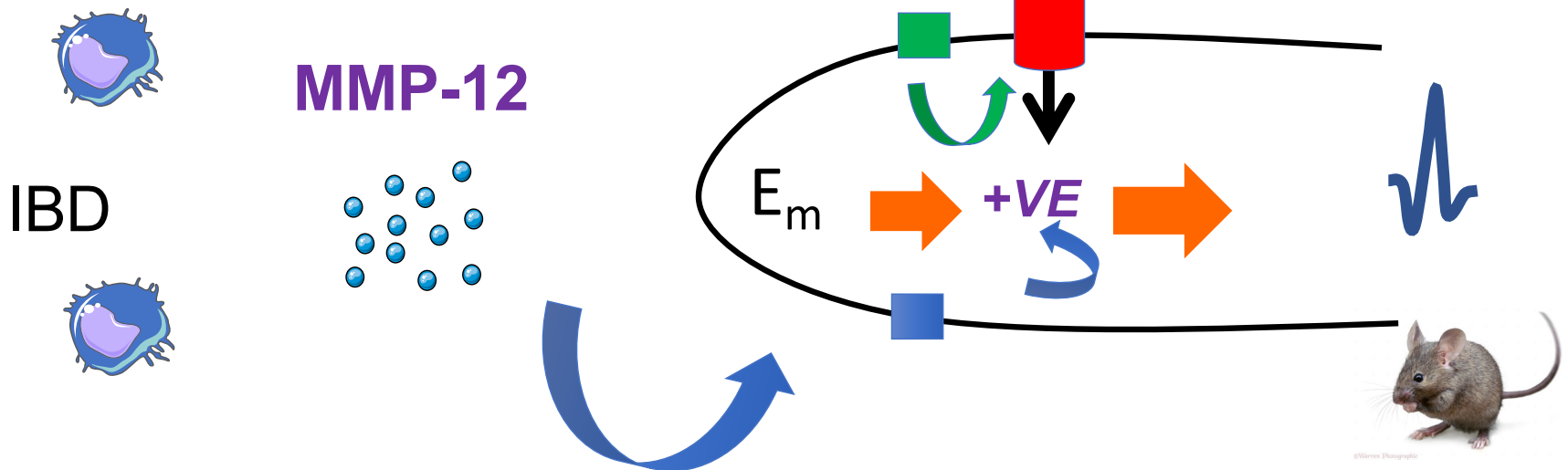
Translate output



Visceral nociception in IBD/IBS

Challenges

- Tractability
- Efficacy - disease
- Side effects – disease



Opportunity

Challenges

- Expertise

