

Name of Research Group:  
Nerve Gut Research Laboratory

Name(s) of supervisors:  
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### **Title and short description of projects offered for 2009:**

#### **Satiety signals from the stomach**

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Obesity is a national priority area for research, and controlling satiety signalling is an important target in its treatment. The most successful current treatment for obesity is bariatric surgery which targets the stomach by restricting its volume, resulting in a smaller meal being required to give the same feeling of fullness. Vagal sensory nerves in the stomach are responsible for these feelings of fullness. Determining how gastric peptides known to influence food intake interact with vagal sensory nerves is the subject of this project, along with investigating how these interactions change in obesity. To achieve this we will first determine expression of peptidergic (leptin, ghrelin and NPW) receptors in gastric sensory neurones and the effect of leptin, ghrelin and NPW on their electrophysiological responses to mechanical stimuli. Then we shall determine changes in function of afferents in obesity and changes in expression of leptin, ghrelin and NPW receptor mRNA.

Key references:

1. Cummings DE, Overduin J. Gastrointestinal regulation of food intake. **Journal of Clinical Investigation** 2007;117:13-23.

2. Elder KA, Wolfe BM. Bariatric surgery: a review of procedures and outcomes. **Gastroenterology** 2007;132:2253-71.
3. Page AJ, Slattery JA, Milte C, Laker R, O'Donnell TA, Brierley SM, Dorian CL, Blackshaw LA. Ghrelin selectively reduces mechanosensitivity of upper gastrointestinal vagal afferents. **American Journal of Physiology** 2007; 292: G1376-1384
4. Peters JH, McKay BM, Simasko SM, Ritter RC. Leptin-induced satiation mediated by abdominal vagal afferents. **American Journal of Physiology** 2005;288: R879-84.
5. Caminos JE, Bravo SB, Garcia-Rendueles ME, Ruth Gonzalez C, Garces MF, Cepeda LA, Lage R, Suarez MA, Lopez M, Dieguez C. Expression of neuropeptide W in rat stomach mucosa: Regulation by nutritional status, glucocorticoids and thyroid hormones. **Regulatory Peptides** 2008;146:106-11.

### **TRP channels as sensors and effectors in visceral sensory nerves**

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Chronic pain is a major unresolved clinical problem, and pain from internal organs represents the major manifestation of this. The likely cause is increased activation of peripheral sensory mechanisms, so understanding how hypersensitivity of sensory nerves occurs would advance the design of new therapies. TRP channels are key candidates contributing to pain because they are primary mechano- and chemosensors, plus they can be effectors, mediating excitation after activation of other receptors. Plant extracts are known as traditional cures, and their potential in modern medicine is emerging. The best current treatments for visceral pain are in fact alternative medicines, which probably act via TRP channels. We shall look for TRP channels in colonic sensory neurons, determine their mechano and chemosensory properties and how they are influenced by inflammatory mediators and plant extracts. We shall also reveal if TRPs are linked with symptoms by increased expression in tissue from patients with visceral pain.

Key references:

1. Blackshaw LA, Brookes SJ, Grundy D, Schemann M Sensory transmission in the gastrointestinal tract. **Neurogastroenterology and Motility** 2007; 19(1 Suppl):1-19.
2. Brierley SM, Page AJ, Hughes PA, Adam B, Liebrechts T, Cooper NJ, Holtmann G, Liedtke W, Blackshaw LA. A selective role for TRPV4 ion channels in visceral sensory pathways. **Gastroenterology** 2008 (On line, January 2008).

3. Sipe W, Brierley SM, Martin CM, Phillis BD, Spreadbury I, Grady EF, Liedtke W, Vanner S, Blackshaw LA, Bunnett NW. Transient receptor potential vanilloid 4 mediates protease activated receptor 2-induced sensitization of colonic afferent nerves and mechanical hyperalgesia. **American Journal of Physiology** 2008; 294(5): G1288-98
4. Adam B, Liebrechts T, Best J, Bechmann L, Lackner C, Neumann J, Koehler S, Holtmann G. A combination of peppermint oil and caraway oil attenuates the post-inflammatory visceral hyperalgesia in a rat model. **Scand J Gastroenterol.** 2006;41(2):155-60.
5. von Arnim U, Peitz U, Vinson B, Gundermann KJ, Malfertheiner P. STW 5, a phytopharmakon for patients with functional dyspepsia: results of a multicenter, placebo-controlled double-blind study. **Am J Gastroenterol.** 2007; 102(6): 1268-75.

### **Nutrient sensing in the gut**

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Detection of nutrients in the intestine is of crucial importance in the control of motility, glycaemia, and energy intake, and yet we know little of the fundamental aspects of this process. Altered nutrient signalling occurs in diabetes, as evidenced by changes in gastric emptying and gut motility in response to nutrient infusions. Altered function of epithelial sensory mechanisms are strongly implicated in these disturbances. Intestinal nutrients are detected by highly specialised epithelial cells, known as enteroendocrine cells, which sample the lumen and release neuroactive mediators into the subepithelial space, which then activate sensory fibres in the vagus nerves. Several types of enteroendocrine cells exist, which contain a wide range of mediators. The aims of this project are to determine 1. which taste receptors exist in intestinal epithelium, 2. their mechanism of coupling in enteroendocrine cells, 3. which mediators enteroendocrine cells release, 4. how they activate vagal sensory nerves.

Key references:

1. Sutherland K, Young RL, Cooper NJ, Horowitz M, **Blackshaw LA**. Phenotypic characterization of taste cells of the mouse small intestine. **American Journal of Physiology** 2007; 292:G1420-1428. (IF: 3.7) C
2. Horowitz M, O'Donovan D, Jones KL, Feinle C, Rayner CK, Samsom M. Gastric emptying in diabetes: clinical significance and treatment. **Diabetes Medicine.** 2002;19(3):177-94.

3. Kim M, et al. D-glucose releases 5-hydroxytryptamine from human BON cells as a model of enterochromaffin cells. **Gastroenterology** 2001;121:1400-6.
4. Rindi G, et al. The "normal" endocrine cell of the gut: changing concepts and new evidences. *Annals of the N Y Academy of Sciences* 2004;1014:1-12.
5. Imeryuz N, et al. Glucagon-like peptide-1 inhibits gastric emptying via vagal afferent-mediated central mechanisms. **American Journal of Physiology** 1997;273:G920-7.