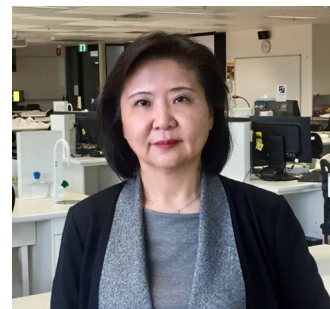


THERAPEUTIC TARGETS FOR INFLAMMATORY BOWEL DISEASE, INTESTINAL MOTILITY DISORDERS AND BLADDER DYSFUNCTION

Associate Professor **Lu Liu**

(Gastrointestinal & Bladder Disease (GBD) Research Group)



You are welcome to have a chat with A/Prof Lu Liu about the projects via Zoom during the SOMS Research Information Session on *Wednesday 6 July 2022 between 4 pm and 5:30 pm*: <https://unsw.zoom.us/j/7346703713>

Other times, please make an appointment with her via email: lu.liu@unsw.edu.au

CLINICAL IMPLICATIONS OF BASIC RESEARCH

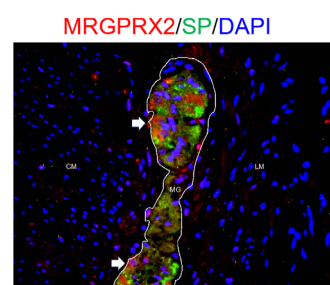
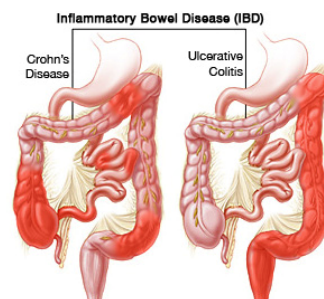
The goal: uncovering the causes of and developing therapeutics for gut and bladder diseases

PROJECT 1: Mas-related G protein-coupled receptors in the human colon and bladder: in health and disease

G protein-coupled receptors (GPCRs) are the largest family of receptor proteins that mediate a great range of body functions. Approximately 30% of therapeutic drugs target GPCRs. In recent years, a new GPCR family, named Mas-related GPCRs (MRGPRs), consisting of more than 50 members was discovered. They are known to mediate pain sensation and inflammation.

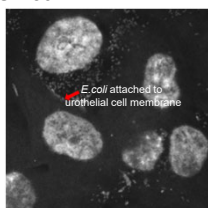
Information on MRGPRs in the gastrointestinal tract is very limited. My group has recently found that MRGPR subfamilies D, F and X2 are expressed in the human colon with different expression profiles. For instance, the D receptor subtype is primarily expressed on smooth muscle, and reduced expression was seen in the colon of patients with ulcerative colitis but not in Crohn's disease. The X2 receptor, expressed in lamina propria immune cells and enteric neurons, is substantially downregulated in the colon of diverticular disease patients. The F receptor is significantly downregulated in colonic longitudinal muscle of slow transit constipation, which is an intractable functional colonic motor disorder occurring in young to middle-aged females, indicating that this receptor may be implicated in peristaltic activities. Based on our novel findings, further investigation is needed to explore which neuronal cells (motor or sensory) and specialised immune cells express MRGPRs, whether these receptors are involved in regulating colonic motor functions and neuroimmune interactions and what clinical significance of altered expression is disease colon.

To date, there is almost no information on MRGPRs in the urinary bladder. The profile of this large family expressed in the bladder is novel and will fill the knowledge gap.

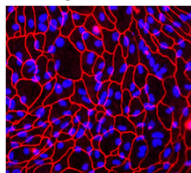


Double labelling of MRGPRX2 (red) and substance P (green) in myenteric ganglia of human colon

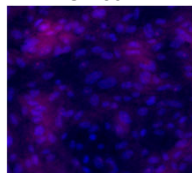
E. coli UT189 treated urothelial cells



Control



E. coli UT189 treated



E. coli, UT189 treated urothelial cells showed a complete loss of tight junction structure

PROJECT 2: Nonantibiotic management of urinary tract infection

A urinary tract infection (UTI) is a term for infections that involve any part of the urinary tract, causing considerable morbidity. UTIs are highly prevalent, affecting 150 million people each year worldwide. Antibiotic resistance UTIs are on the rise globally, making them very hard to treat. Therefore, there is a need to look for nonantibiotic alternatives to treat and prevent UTIs.

Studies have shown that cranberry products, d-mannose, ibuprofen and intravesical glycosaminoglycans may relieve symptoms caused by UTI and reduce UTI recurrence rates. However, there is no report on the underlying mechanisms. Using the MDCK cell line and porcine bladder, the best model for the human bladder, we will study the effect of cranberry, d-mannose and ibuprofen on *E. coli* UT189 caused diminished urothelial integrity and increased permeability. Their effects on *E. coli* UT189-induced changes in cytokine production, cell viability, oxidative stress, and the programmed death-ligand 1 (PD-L1) will also be investigated.

Both projects are suitable for honours, masters and PhD

Well established techniques applied to the projects

Immunohistochemistry and immunocytochemistry, Western blot, real-time PCR, cell culture and tissue explant culture, isolated organ pharmacology, ELISA, fluorescent and luminescent assays etc.

Collaborators for the projects

Human colon: A/Prof Li Zhang (BABS, UNSW); Dr D Shevy Perera (Colorectal surgeon, St George Hospital)

Bladder: A/Prof Kylie Mansfield (Uni of Wollongong); Prof Kate Moore (urogynaecologist, St George Hospital)