LOCAL AND SYSTEMIC FUNCTIONS OF THE ADULT INTESTINE IN HEALTH AND DISEASE

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Research in our laboratory aims to elucidate the mechanisms by which intestinal stem cells (ISCs) adapt and respond to changes in their micro- and macro-environment, how the intestine senses and controls whole-body homeostasis, and how intestinal dysfunction can lead to broader organismal instability.

We use the fruit fly *Drosophila melanogaster* as a primary research model system due to its unparalleled genetic power and amenability for multi-organ *in vivo* studies combined with experiments in mammalian systems.

The adult intestine is a major barrier epithelium and coordinator of multi-organ functions. Stem cells constantly repair the intestinal epithelium by adjusting their proliferation and differentiation to tissue intrinsic, as well as micro- and macro-environmental signals. How these signals integrate to control intestinal and whole-body homeostasis is largely unknown. Addressing this gap in knowledge is central to an improved understanding of intestinal pathophysiology and its systemic consequences.

Combining Drosophila and mammalian model systems, the laboratory has discovered fundamental mechanisms driving intestinal regeneration and tumourigenesis and outlined complex inter-organ signalling regulating health and disease. We have three interrelated areas of research in the lab.

1 Identify and characterise stem cell intrinsic adaptations underpinning intestinal regeneration and tumourigenesis.

2 Elucidate interactions between the intestine and its microenvironment influencing intestinal regeneration and tumourigenesis.

3 Characterise how long-range signals from the intestine impact the whole-body in health and disease.

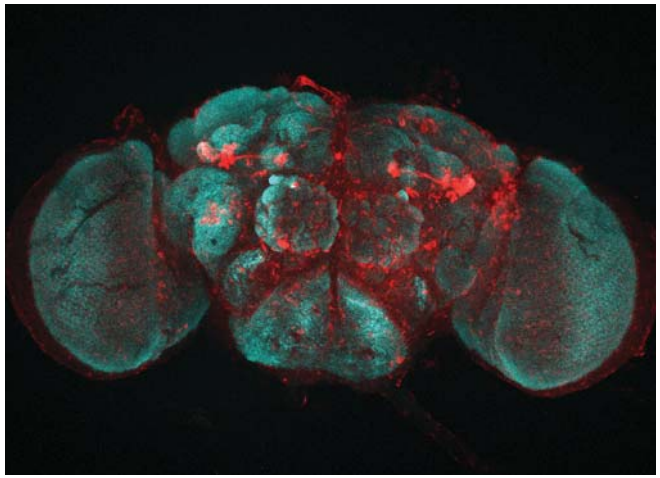

Figure 1: Gut/brain crosstalk in health and disease . Confocal image of the adult Drosophila melanogaster brain stained with the neuropil marker NC82 (Cyan), and a JAK/Stat signaling activity reporter (red).

Image credit: Dr Jack Holcombe

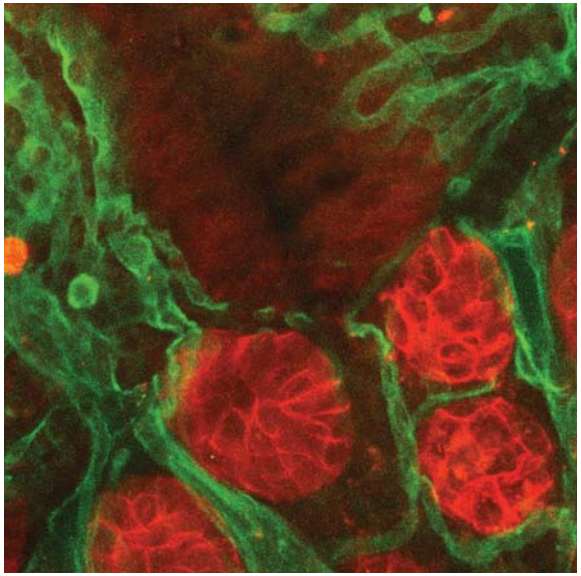

Figure 2: Gut/vasculature interactions in the adult intestine. Small intestinal epithelium (red) and associated blood vasculature (green).

Image credit: Jade Phillips

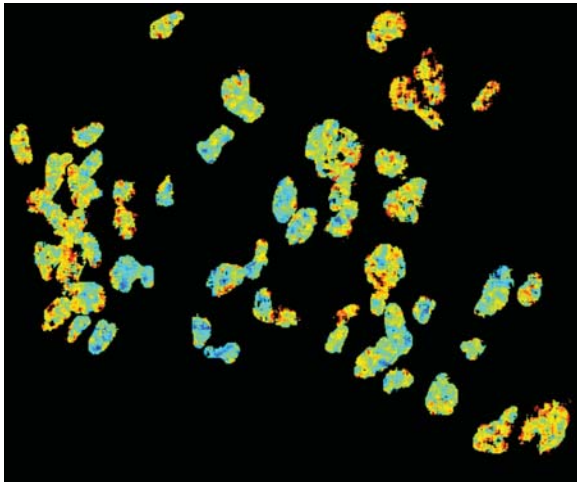

Figure 3: Metabolic adaptations of intestinal stem cells in health and disease. Oxidative phosphorylation FRET sensor in Drosophila adult intestinal stem cells (cyan and yellow).

Image credit: Yuanliagzi Tian