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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 whole-body function in health and disease.

Publications listed on page 103

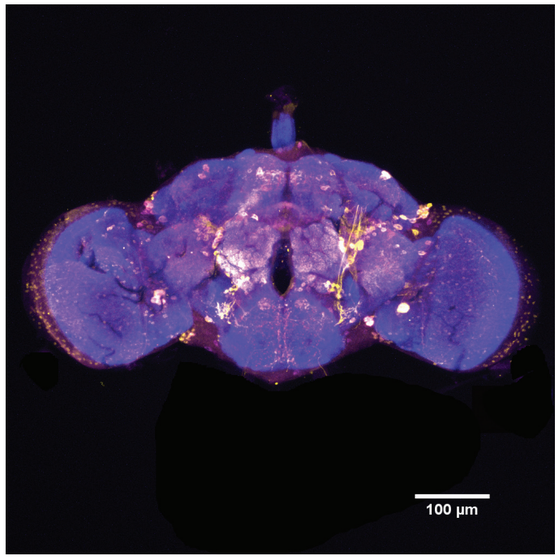

Figure 1
Gut-Brain Crosstalk in health and disease.
Confocal image of the adult *Drosophila melanogaster* brain stained with the neuropil marker NC82 (blue), the neuropeptide protein DH31 (magenta) and a *Dh31* gene expression reporter (yellow).

Image credit: Dr. Sofia Polcowñuk

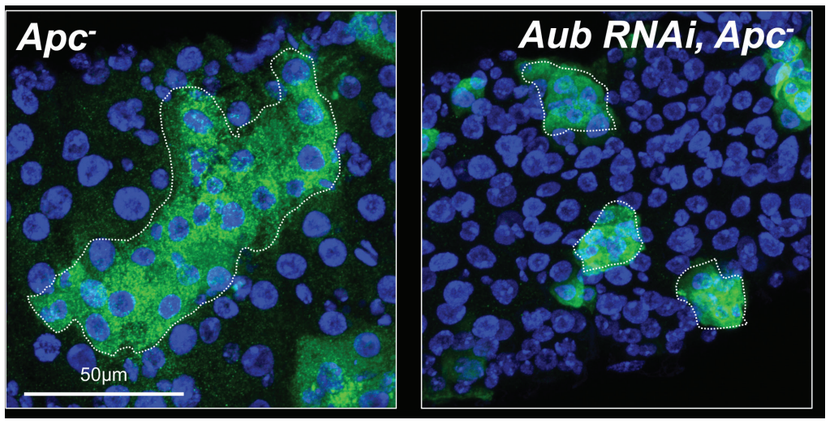

Figure 2
Elucidating the functional role of the PIWI pathway in colorectal cancer:
Clones of adult intestinal epithelial cells (green and outlined) lacking the colorectal cancer tumour suppressor gene *Apc* alone (left panel) or in combination with knockdown of the PIWI protein *PIWIL-1/ Aubergine (Aub)* (right panel). RNAi: RNA interference.

Image credit: Dr. Karen Bellec