# Effect of Sex and Reproductive Status on Adult *Drosophila* Midgut Tumours

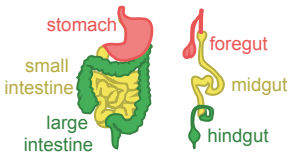
Emily Strachan, Bruno Hudry, Irene Miguel-Aliaga, Susumu Hirabayashi

https://lms.mrc.ac.uk/research-group/gut-signalling-and-metabolism/
https://lms.mrc.ac.uk/research-group/metabolism-cell-growth/

MRC London Institute of Medical Sciences, London, UK
Institute of Clinical Sciences, Faculty of Medicine, Imperial College London, London, UK

Contact: emily.strachan15@imperial.ac.uk

# Background




The *Drosophila* midgut, analogous to the human small intestine, is a highly sexually dimorphic organ.

The intestinal stem cells (ISC) that replenish the intestinal epithelium of adult flies divide more often in females.

Unexpectedly, sex differences in proliferation are intrinsically controlled by the sexual identity of the ISC.

**SEX** - Female guts are more proliferative than male guts in response to damage, and produce larger *Notch*$^{RNAi}$ (*N*$^{RNAi}$) and *Ras*$^{V12}$*APC*$^{Q8}$ (*RasApc*) tumours. After masculinisation of the adult ISC with sex determinating *tra* downregulation, virgin female *N*$^{RNAi}$ tumours are reduced to the size of virgin male tumours (Figure 1a: Hudry et al., 2016).

**REPRODUCTIVE STATUS** - After mating females undergo extensive intestinal remodelling, increasing their energy input and changing their lipid metabolism to prepare for energy intensive egg laying (Reiff et al., 2015). This remodelling is also expected to change the female tumour phenotype (Figure 1b).

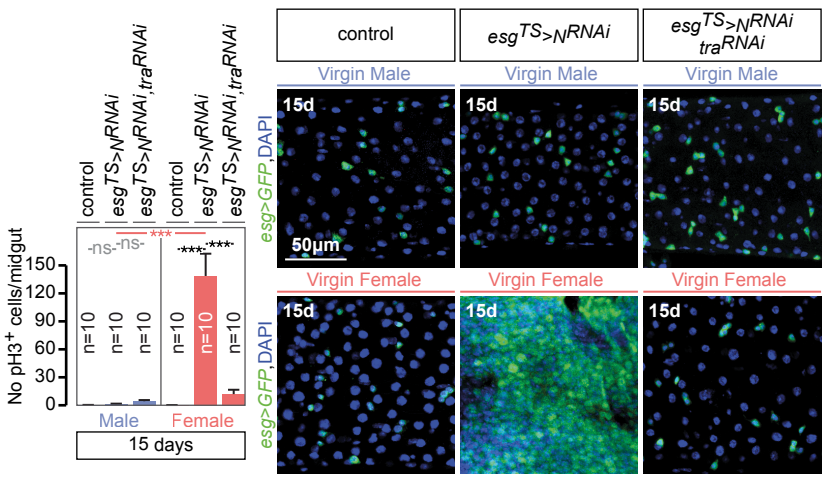
# Aim

**1.** To explore the molecular mechanisms underlying the sex bias of *Drosophila* tumours, and to characterise how female midgut tumours change upon mating.

**2.** To see if this sexual dimorphism and reproductive bias is consistent across different tumour models.

# Results

**a** *Notch*$^{RNAi}$ tumours in virgin males, virgin females and the effect of *tra*$^{RNAi}$ masculinisation




**b** *Ras*$^{V12}$*APC*$^{RNAi}$ tumours in virgin females, mated females and virgin males

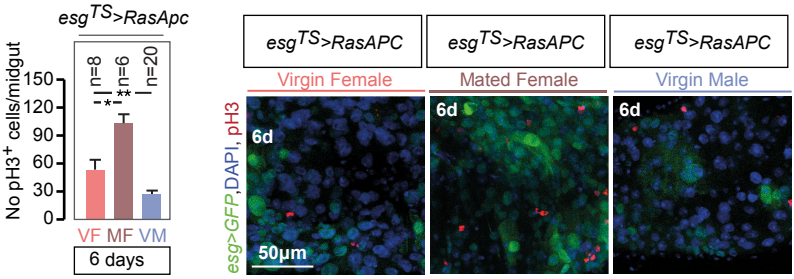



**FIGURE 1:** Tumours can be generated by driving oncogenes or downregulating tumour supressors in intestinal stem cells (ISC) and enteroblast (EB) progenitors using the esg-TS driver.

**a** - Tumour (quantified by the number of pH3-positive cells) resulting from adult ISC/ EB-driven *Notch* downregulation and its modulation by *tra* (*tra* downregulation masculinises the fly midgut) in virgin female and virgin male midguts (adapted from Hudry et al., 2016).

**b** - Tumour (quantified by the number of pH3-positive cells) resulting from adult ISC/EB-driven *Ras*$^{V12}$*APC*$^{RNAi}$ (*RasAPC*) expression in virgin females (VF), mated females (MF) and virgin males (VM) (Unpublished, 2021).

Confocal images show intestinal progenitor coverage of representative posterior midgut portions for each genotype (DNA: DAPI, in blue; ISC/EB marker: GFP, in green; pH3-positive cells: anti-pH3, in red). n denotes the number of midguts that were analysed for each genotype.

# Further Reading

Hudry B, Khadayate S, Miguel-Aliaga I. The sexual identity of adult intestinal stem cells controls organ size and plasticity. Nature. 2016;530(7590):344-8.
Reiff T, Jacobson J, Cognigni P, Antonello Z, Ballesta E, Tan KJ, et al. Endocrine remodelling of the adult intestine sustains reproduction in Drosophila. Elife. 2015;4:e06930.