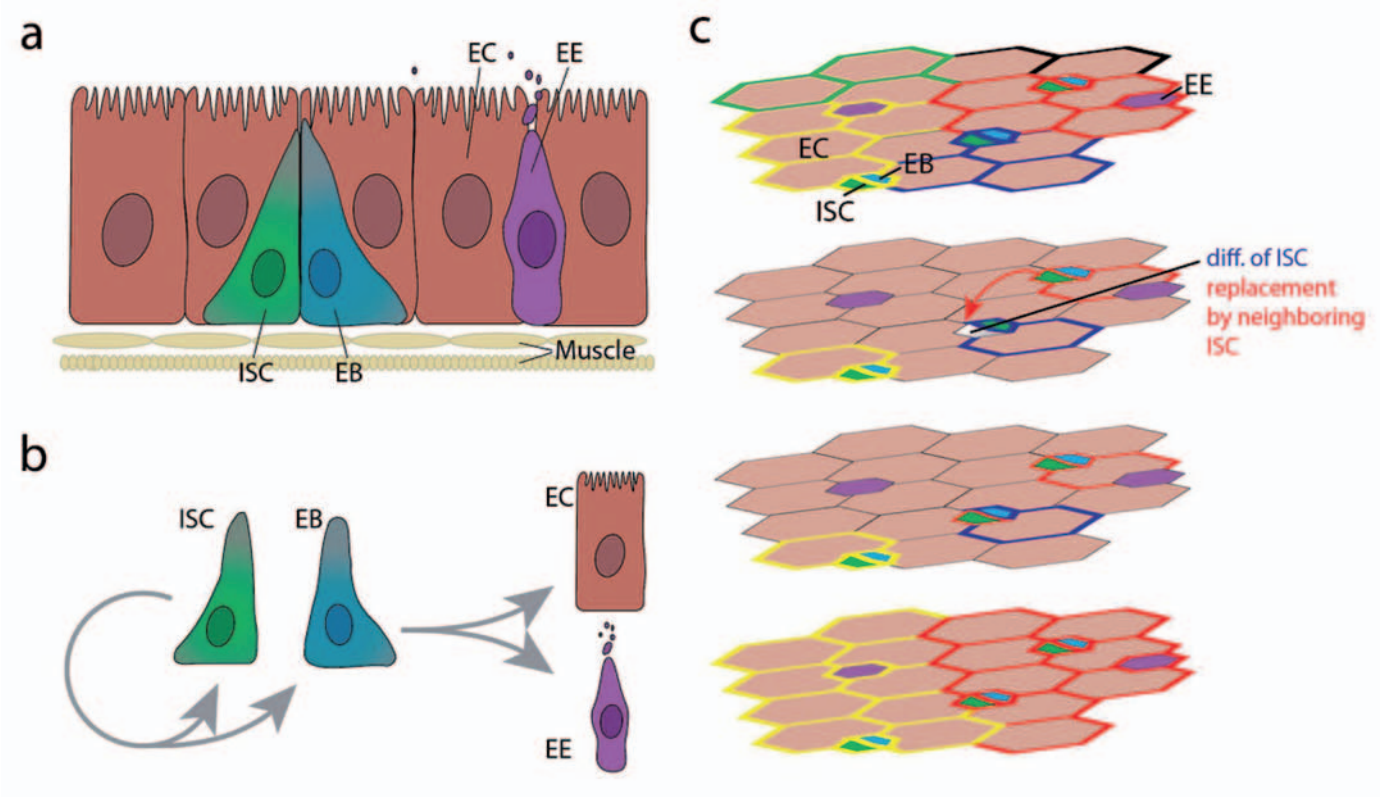
Supplementary information S1 | ***Drosophila* midgut stem cell dynamics**

The *Drosophila melanogaster* midgut is a versatile model system to study intestinal physiology and in particular intestinal stem cell (ISC) biology[1]. The adult *Drosophila* posterior midgut comprises a tube in which the inner lining is predominantly covered with two cell types: absorptive enterocytes (EC) and secretory endocrine (EE) cells (**a**). ISCs continuously proliferate and renew these cells through the generation of enteroblasts (EB), which then commit to differentiation without additional divisions (**b**). Dependent on the microenvironment, EBs differentiate into ECs or EEs. ISCs and EBs are both marked by expression of escargot (esg) and are distributed through the epithelium in small nests[1]. The dominant point of view by which ISCs self-renew and generate EBs is via asymmetrical divisions. However, direct and definitive evidence for this concept is lacking so far. Instead, recent studies revealed that midgut ISCs can self-renew via symmetrical divisions after which differentiation, including terminal loss of ISCs, is dependent on spatial constraints[2,3]. To sustain tissue integrity, ISC loss is compensated by symmetric divisions of nascent ISCs, creating neutral drift dynamics similar to those observed in mice (**c**). This process is regulated by Notch-mediated lateral inhibition[2]. Intriguingly, the esg+ nests can be compared to mammalian crypts, albeit containing considerably fewer ISCs. Nest duplication is much more common than mammalian crypt fission, thereby compensating the relatively frequent loss of nest structures.



1. Ohlstein, B. & Spradling, A. The adult *Drosophila* posterior midgut is maintained by pluripotent stem cells. *Nature* **439**, 470–474,(2006).
2. de Navascues, J. *et al*. *Drosophila* midgut homeostasis involves neutral competition between symmetrically dividing intestinal stem cells. *EMBO J* **31**, 2473–2485,(2012).
3. O'Brien, L. E., Soliman, S. S., Li, X. & Bilder, D. Altered modes of stem cell division drive adaptive intestinal growth. *Cell* **147**, 603–614,(2011)