Stem cell motility enables a density-dependent rate of fate commitment during scaled resizing of adult organs

XINXIN DU, LUCY O’BRIEN, INGMAR RIEDEL-KRUSE, Stanford University — Many adult organs grow or shrink to accommodate fluctuating levels of physiological demand. Specifically, the intestine of the fruit fly (the midgut) expands four-fold in the number of mature cells and, proportionally, the number of stem cells when the fly eats. However, the cellular behaviors that give rise to this stem scaling are not well-understood. Here we present a biophysical model of the adult fly midgut. A set of differential equations can recapitulate the physiological kinetics of cells during midgut growth and shrinkage as long as the rate of stem cell fate commitment depends on the stem cell number density in the tissue. To elucidate the source of this dependence, we model the tissue in a 2D simulation with soft spheres, where stem cells choose fate commitment through Delta-Notch pathway interactions with other stem cells, a known process in fly midguts. We find that as long as stem cells exhibit a large enough amplitude of random motion through the tissue (‘stem cell motility’), and explore a large enough ‘territory’ in their lifetime, stem cell scaling can occur. These model observations are confirmed through in vivo live-imaging, where we indeed see that stem cells are motile in the fly midgut.

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