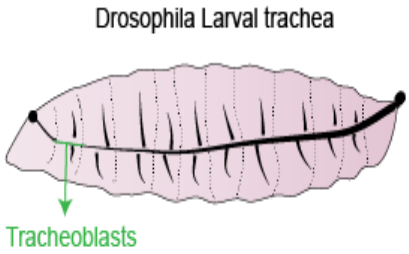
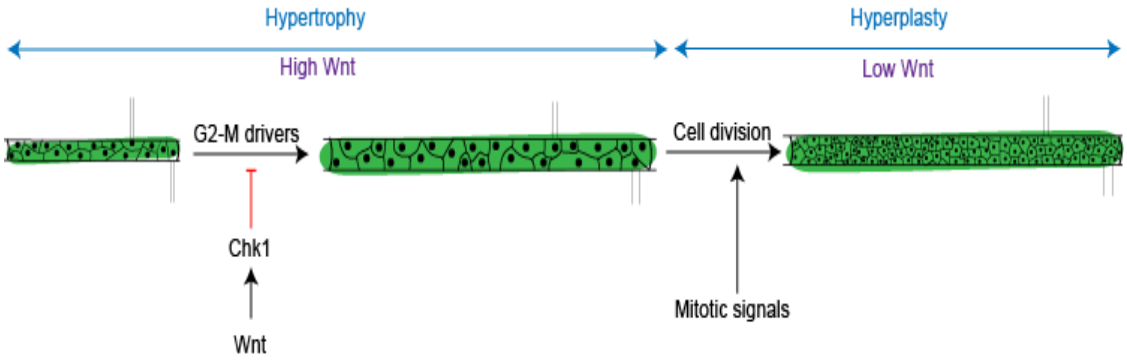
Ways to get bigger: How cells switch from growing in size to increasing in number

A website report titled '*ways to get bigger: how cells switch from growing in size to increasing in number*' is based on a publication published in the journal *eLife* in September 2020, from Dr. Arjun Guha's laboratory at Institute For Stem Cell Science and Regenerative Medicine (inStem), Bengaluru. The report describes that the size of an organ or tissue is determined both by the number of cells it has and the size of each of those cells. The increase in size during development and thereafter is thought to occur in one of two ways: 'hyperplasia' or 'hypertrophy'. The fruit fly, *Drosophila melanogaster*, is an excellent system to study how cells switch between hypertrophy and hyperplasia.





During the course of development, *Drosophila* transforms from a larva into an adult fly. As the adult form is very different from the larval form, the fly almost literally makes itself again from small patches of 'progenitor' (imaginal) cells set aside in the larval body. Arjun Guha's lab at Regulation of Cell Fate (RCF) theme at inStem focuses on studying a subset of the progenitor cells that give rise to the respiratory system of the adult fly. The team focuses on a subset of larval cells of the respiratory (tracheal) system (also known as tracheoblasts) that are not

replaced but become imaginal cells instead. These larval cells proliferate and contribute towards the development of adult tracheal structures. Arjun and his group have been investigating mechanisms underlying the switch from the larval to the imaginal fate.

This study investigates the regulation of a cell fate in the respiratory (tracheal) system of the *Drosophila* larva. Some tracheal cells in the larva (hereafter called tracheoblasts) are unusually versatile cells. These cells make up air-filled tracheal tubes, grow in size (~11 fold in volume) to enable tube growth, and then divide, alter gene expression and generate the respiratory system of the adult fruit fly. The current study focuses on how the growth and proliferation of tracheoblasts are regulated. Not the least, the research findings also reveal how Chk1 is regulated and further show that Wnt signalling, mediated by four different Wnt proteins acting together, increases Chk1 expression in growing cells. High levels of Chk1 in cells with ATR are sufficient to stop cell division. The down-regulation of Wnts and ensuing cell division activates TGFb signalling that then drives proliferation and other changes.

A fascinating finding of this work, as per the team, is while the cells have high Wnt/Chk1 and are paused in G2, these cells also are unable to respond to signals that promote division. This goes to show how signals in a cellular environment instruct cells to stop and start cell cycle; thereby facilitating growth in cell size and/or number. Interestingly, the role of Wnts in the regulation of Chk1 could also be relevant to cancer cells that are resistant to chemotherapy and radiation since high Chk1 expression can protect against DNA damage.

Link: https://elifesciences.org/articles/57056