DBT-Instem study gets new insight on organ development in fruit fly

New Delhi, Oct 08: Organs of fruit fly (Drosophila melanogaster) larva typically comprise post-mitotic cells that are replaced by adult progenitor (imaginal) cells during the pupal period to generate the organs of the adult fly. A recent report from the laboratory of Dr. Arjun Guha from the Regulation of Cell Fate theme at Institute for Stem Cell Science & Regenerative Medicine (DBT-inStem), published in eLife Journal, 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. In 2018, the same group had shown that the co-expression of both positive and negative regulators of cell division enables tracheoblasts to grow in size. Removal of the negative regulator, turning off the ATR/Chk1 pathway in particular, limits growth and leads to cell division. In the current study, Kizhedathu and colleagues reveal how Chk1 is regulated. They 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 is sufficient to stop cell division. The downregulation of Wnts and ensuing cell division activates TGFb signalling that then drives proliferation and other changes.
This work shows how developmental signals actively control the growth and proliferation of tracheoblasts. 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 to the publication: https://elifesciences.org/articles/57056

Contact Person: Amrita Tripathy tripathya@instem.res.in (Communications team)

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