DNA Damage Response intertwines with tissue homeostasis in D. melanogaster

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Abstract

It is a common knowledge that caspases are required downstream of DNA damage for executing cell death function. Counter-intuitively, we show, for the first time, that initiator caspase Dronc acts upstream of DNA Damage Response (DDR) signalling via ATM where Dronc plays a dual role by initiating DDR or apoptosis depending upon the required threshold of activation in damaged cells of Wingdisc tissue. Tissue homeostasis ensues when p53, while promoting cell death via hid, also simultaneously upregulates JNK cell-autonomously, thereby triggering a parallel response of cell protection via countering both hid/rpr system. The context specificity of this circuitry became evident when JNK & p53 roles got inverted in the same tissue during rad51 versus atm null mutant genomic stress backgrounds. Such a paradigm unveils plasticity associated with the mechanistic circuitry involving cell death and cell protective responses within a tissue resulting in tissue-homeostasis functions giving rise to no obvious phenotype in repair mutant flies, whereas the same in mammalian system leads to embryonic lethality.