## **RESEARCH HIGHLIGHTS**

## Journal club



## THE DEATH AND GROWTH CONNECTION

It is commonly assumed that cell proliferation, cell growth and cell migration are the main drivers of tissue growth. However, two papers published in 2004 demonstrated that cell death is more intimately related to tissue growth than previously anticipated. The Morata and Steller groups found independently that dying cells produce mitogens that promote the proliferation of neighbouring cells.

To investigate the consequences of apoptotic cell death within a growing tissue, the authors developed a very elegant approach in which dying cells lingered without being removed from the tissue. This was achieved in flies by dying cells produce mitogens that promote the proliferation of neighbouring cells

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overexpressing an inhibitor of the apoptotic signalling cascade (cyclin-dependent kinase 5 (CDK5; also known as p35), which allows cells to survive a fatal injury.

Using this approach the authors made some key observations. When cells became committed to die they began to express evolutionarily conserved mitogens such as bone morphogenetic protein (BMP) and WNT (called Decapentaplegic (DPP) and Wingless in flies, respectively). Moreover, if the WNT pathway was impaired, proliferation of cells neighbouring the dying tissue was no longer observed.

Finally, through genetic approaches the authors revealed that the molecular link between apoptotic and mitogen signalling was the JUN-N-terminal kinase (JNK) pathway, which is essential for the activation of *wingless* and *dpp* expression in apoptotic cells.

The field was aware that both cell death and proliferation events can be vital for a properly shaped and functional tissue during development. However, such a direct link between the apoptotic machinery and the stimulation of proliferation was a novel and very exciting discovery.

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ORIGINAL RESEARCH PAPERS Perez-Garijo, A. et al. Caspase inhibition during apoptosis causes abnormal signalling and developmental aberrations in Drosophila. Development 131, 5591–5598 (2004) | Ryoo, H. D. et al. Apoptotic cells can induce compensatory cell proliferation through the JNK and the Wingless signaling pathways. Dev. Cell 7, 491–501 (2004)