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The death and growth connection

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When we think about tissue growth we think of it as driven by cell proliferation, growth and migration processes. However, two papers in 2004 demonstrated that cell death is more intimately related to cell proliferation and growth than we had previously anticipated. The Morata and Steller groups found independently that cells about to die begin producing mitogens that in turn activate proliferation of neighboring cells.

In order to investigate the consequences of apoptotic cells within a growing tissue, the authors adopted a very elegant approach in which cells that were about to die lingered without being eliminated. This was achieved in flies by overexpressing an inhibitor of the apoptotic cascade (p35/cdk5) to let the cells survive a fatal injury.

By this approach the authors were able to make the following observations. Once cells were committed to die they began to express evolutionarily conserved mitogens such as Wnt and BMP (called Wingless and Dpp in flies). When the Wnt pathway was impaired, proliferation of neighboring cells was no longer observed as consequence of cell death. Finally through genetic approaches the authors revealed that the molecular link between the apoptotic and the mitogen pathways was via the JNK pathway, which is essential for *dpp* and *wingless* to be turned on in apoptotic cells.

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

References and links

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- 2. Ryoo, et al. Apoptotic cells can induce compensatory cell proliferation through the jnk and the wingless signaling pathways. Developmental Cell. 2004; 7:491–501. [PubMed: 15469838]