

A role for cell competition in the elimination of aberrantly specified cells

Supervisory team:

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Project description:

Cells in an organ take life and death decisions based on the input they receive from their immediate neighbours. For example, some cancer cells cause their healthy neighbours to commit suicide. Indeed, cells with higher levels of the oncogene Myc slowly expand and occupy larger territories at the expense of normal cells. This phenomenon, known as cell competition, was first discovered in *Drosophila* and is conserved in mammals. Conversely, other pre-cancerous cells, such as scrib mutants, are recognized and eliminated by neighboring wild-type cells, suppressing carcinogenesis via another form of cell competition. Altogether, cell competition can be defined as a range of cell interactions that enable cells within tissues to compete for space and survival cues. During competition, the less fit cells are eliminated from the tissue and referred to as “losers”, whereas the remaining cells are called “winners”. Research in the last two decades identified several molecular players in the process, but which mechanisms are common to all forms of cell competition remain unclear. Likewise, aberrantly specified cells, cells of wrong identity in the wrong place, are eliminated from tissues during development (see Figure), ensuring functional adult organs. Whether this is a form of cell competition is unknown and is the subject of this studentship.

In the Hamaratoglu Lab, we have been developing quantitative assays and identified several players with roles in the elimination of aberrantly specified cells. Our unpublished results highlight a role for JNK signalling in the elimination of aberrantly specified cells; JNK was shown to be activated during cell competition as well. There are also differences between the two processes. In cell competition, the genetic identity of the cell determines winner or loser status. For example, Myc expressing cells would always be winners in competition with wild-type cells. However, the identity of the majority determines the winners during elimination of aberrantly specified cells.

The Piddini Lab has world-renowned expertise in cell competition, and is currently investigating the links between metabolism and cell competition. Together, we will determine the commonalities between cell competition and the elimination of mis-specified cells, we will test molecular players identified in cell competition for roles in the other process and vice versa.

You will join a dynamic and international research group and will be trained in the use of genomics, genetics, and microscopy techniques to investigate cell-cell interactions. You will also become a part of the interactive Cardiff and Southwest *Drosophila* communities.

Our aim as the SWBio DTP is to support students from a range of backgrounds and circumstances. Where needed, we will work with you to take into consideration reasonable project adaptations (for example to support caring responsibilities, disabilities, other significant personal circumstances) as well as flexible working and part-time study requests, to enable greater access to a PhD. All our supervisors support us with this aim, so please feel comfortable in discussing further with the listed PhD project supervisor to see what is feasible.