The innate immune system condemns weak cells to their death

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In cell competition the strong eliminate the weak, thereby ensuring optimal tissue fitness. Molecular biologists at the University of Zurich and Columbia University have now demonstrated that the innate immune system plays a key role in this important mechanism. However, cancer cells also make use of this: they can cause cells that are important for healthy tissue to die.

The "survival of the fittest" principle applies to cells in a tissue - rapidly growing and dividing cells are the fit ones. A relatively less fit cell, even if healthy and viable, will be eliminated by its more fit neighbors. Importantly, this selection mechanism is only activated when cells with varying levels of fitness are present in the same tissue. If a tissue only consists of less fit cells, then no so-called cell competition occurs. Molecular biologists from the University of Zurich and Columbia University are the first researchers to demonstrate in a study published in the scientific journal *Science* that this cellular selection process requires the innate immune system.

Innate immune system recognizes weaker cells

Using the fruit fly as a model the researchers demonstrate that during cell competition programmed cell death is activated in the weaker cells. This apoptosis is induced by the signaling protein "Spätzle" that docks onto Toll-related receptors. The Toll-related receptors are part of the ancient innate immune system and normally trigger a defense reaction to

bacterial or fungal infection, but as shown by Meyer and colleagues it can also trigger apoptosis in relatively less fit cells. "Less fit cells are recognized and eliminated with the help of the communication pathway in the innate immune system", is how primary author Stefanie Meyer explains this astounding phenomenon. According to Professor Konrad Basler it is not yet clear whether the initial signal comes from the winner cells or the weaker loser cells. "We still don't know whether this involves the voluntary or forced suicide of the less-fit cells."

When the wrong ones win

Sometimes the stronger cell is not a healthy cell, for example during the development of a tumor cancer cells can "outcompete" their weaker neighbors. In this case it is the healthy cells that fall behind in terms of fitness and are consequently condemned to death by the cell competition mechanism. "Cancer cells use the innate immune system to drive out the healthy cells", sums up Laura Johnston from Columbia University. These new findings are of particular interest for cancer research and early detection of the disease. According to the researchers the innate immune system could serve to identify faster growing but not yet malignant cells - and thus represent a way to combat the disease at an early stage.

More information: Stefanie Meyer, Marc Amoyel, Cora Bergantinos, Claire de la Cova, Claus Schertel, Konrad Basler, Laura Johnston, An ancient defense system operates in cell competition to eliminate unfit cells from developing tissues. *Science*. December 4, 2014. DOI: 10.1126/science.1258236

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