# Live imaging reveals how wound healing influences cancer

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Researchers in the United Kingdom and Denmark have studied the "see-through" larvae of zebrafish to reveal how wound healing leads to skin cancer. Live imaging shows neutrophils, the protective inflammatory cells of the body's immune system, diverted from an induced wound to any nearby precancerous skin cells. The newly arrived neutrophils cause rapid division of these skin cells, which may cause them to progress to melanoma. The results are published in *The EMBO Journal*.

"Our results provide direct visual evidence of a physical link between wound-associated inflammation and the development of skin cancer," says EMBO Member Paul Martin, professor at Bristol University and the University of Cardiff. "White blood cells, in particular neutrophils, that typically serve as part of the body's built-in immune system are usurped by nearby precancerous skin cells in a way that leads to the proliferation of tumour cells in our zebrafish model experimental system of human melanoma."

Scientists have known for some time that inflammation is one of the ten hallmarks of cancer. Cancer has also been described as a "wound that does not heal." However details about how physical damage to body tissues might influence the progress of cancer have remained scarce.

The researchers used genetically modified larvae of zebrafish to watch the relationship between wound-associated inflammation and melanoma as the cancer took hold in the living fish. The cellular events and changes were observed by live imaging with a special confocal laser-scanning

microscope.

In further experiments, the researchers were also able to show that a specific type of signaling molecule released by neutrophils, prostaglandin E2, is part of the signal that drives the splurge of cell growth linked to the cancer in their experimental system. High levels of neutrophils were also detected in human clinical samples of melanomas that had been obtained from individuals whose cancers had open ulcers. Importantly, neutrophils were linked to increased proliferation of melanoma cells and poor survival, which suggests that these findings in fish may have considerable relevance to cancer patients.

The authors note that the findings of the study may have implications for cancer surgery. Minimally invasive surgery is beneficial to cancer patients in many situations and often the preferred treatment. However, particularly in cases where all cancerous tissue cannot be removed, the inflammatory response might influence the remaining cancer cells in the body. "Our studies to date suggest that several strategies might improve outcomes for patients including the possible use of therapeutics to dampen damage-induced inflammatory responses," adds Martin.

Further work is in progress to better understand the relationship between the inflammatory response and skin cancer in the zebrafish model system. Studies are also needed to investigate what therapeutic or other strategies might bring better interventions for patients who have adverse tissue inflammation due to planned (for example biopsy or surgery) or unplanned (e.g. ulceration) tissue damage.

**More information:** The wound inflammatory response exacerbates growth of pre-neoplastic cells and progression to cancer, *The EMBO Journal*, 2015.

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