‘Super-Hero’ Stem Cells Survive Radiation to Regrow Muscles

Radiation-resistant stem cells take on a major role in muscle repair when regular stem cells are damaged by radiation.

May 8, 2019 By Nicholas Weiler

Muscle damage is a common side effect of radiation therapy for cancer treatment, and is made worse because the very stem cells responsible for repairing injured muscles typically bear the brunt of radiation damage.

Now UC San Francisco researchers have discovered a new type of stem cell in mouse muscles that is resistant to radiation and other forms of cellular stress. The findings have implications for improving recovery for cancer patients undergoing radiotherapy and could even lead to treatments to protect future astronauts from the ravages of deep-space radiation.

Annarita Scaramozza, PhD, of the UCSF Department of Orthopaedic Surgery, discovered the small population of stem cells — identifiable by their expression of a gene called *Pax3* — which normally remain inactive within mouse muscles. But when some stressful event — such as radiation exposure — wipes out the muscles’ main pool of stem cells, these cells leap into action and can help regrow damaged muscles.

“It was remarkable to see how these reserve cells that we’d previously overlooked were able to withstand levels of radiation that severely damaged all other stem cells, and then wake up and start regrowing the damaged muscles,” Scaramozza said. “They were like superhero stem cells.”

The results were published April 18 in Cell Stem Cell, alongside a second study showing that these resilient reserve stem cells are not just resistant to radiation, but also take over when regular stem cells are damaged by environmental toxins found in plastics and other pollutants.

Scaramozza and colleagues in the laboratory of Andrew Brack, PhD, also found that regular stem cells can be made radiation-resistant by treating them with anti-oxidizing agents that are well tolerated in humans.

“Traditionally, radiotolerance has been defined by virtue of survival post-stress. Now that we have predictive markers, we can understand how reserve stem cells are protected, and potentially identify strategies to boost their numbers ahead of radiation therapy. This should help patients

recover more rapidly," said Brack, an associate professor of orthopaedic surgery and member of the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research at UCSF who was the study's senior author.

Though the study was conducted in mice, future studies will determine whether the number of these reserve cells can be boosted therapeutically to improve muscles' ability to withstand radiation exposure in the clinic or in the depths of space.

"Of course, we also have to be careful, because these cells could harbor mutations that allow them to trigger cancerous growths when they become activated following radiation exposure," Brack said. "It may be that these cells are able to act as both friend and foe."

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