Senescent cells play an essential role in wound healing

December 11 2014

Buck faculty Judith Campisi and Postdoc Marco Demaria. Credit: The Buck Institute

Senescent cells have a bad-guy reputation when it comes to aging. While cellular senescence - a process whereby cells permanently lose the ability to divide when they are stressed - suppresses cancer by halting the growth of premalignant cells, it is also suspected of driving the aging process. Senescent cells, which accumulate over time, release a continual

cascade of inflammatory cytokines, chemokines, growth factors and proteases. It is a process that sets up the surrounding tissue for a host of maladies including arthritis, atherosclerosis and late life cancer.

But in a study publishing online in advance of the December 22nd edition of *Developmental Cell*, Buck Institute faculty Judith Campisi, PhD, postdoctoral fellow Marco Demaria, PhD and colleagues show that senescent cells act as good-guys when it comes to wound healing. Moreover, they identified a single factor secreted by senescent cells that cause them to promote wound healing. It's a crucial discovery for researchers (including Campisi) who are working on developing treatments to clear the body of senescent cells as a way to stem the development of age-related disease.

"What is most exciting is that we are now able to identify what senescent cells express that makes them beneficial," said Campisi, senior scientist on the study. "This means we will be able to simply provide that factor while we eliminate senescent cells to prevent a deleterious side effect before it even occurs."

Postdoctoral fellow, Marco Demaria, PhD, lead author of the study, used two different mouse models: in the first, which was developed in collaboration with colleagues at the Erasmus, Harvard and Einstein Medical Schools, senescent cells can be visualized and eliminated in living animals; in the second, which was developed by Eiji Hara, Naoko Ohtani and colleagues at the Japanese Foundation for Cancer Research, mutations in two key genes block the senescence program. Demario showed that following a skin wound, senescence occurs early on in cells that produce collagen and line blood vessels. Demaria said the senescent cells accelerated wound closure through the secretion of PDGF-AA, a growth factor contained within blood platelets, making it the "good guy" in this portrayal of senescence. "We were able to apply recombinant PDGF-AA topically to mice that had senescent-free wounds," said

Demaria. "It rescued delayed wound closure and allowed the mice to heal normally."

The researchers also found that senescent cells were present only for a short time during tissue repair, in contrast to the persistent presence of senescent cells in aged or chronically damaged tissues. Moreover, they say the fact that PDGF-AA was activated very early upon senescence induction in cell culture suggests the time-dependent regulation of secretory factors might, in part, explain the beneficial vs. deleterious effects of senescent cells.

Campisi says the finding shows that, in addition to preventing cancer in the young, cellular senescence might play a beneficial role in human health, perhaps throughout the entire lifespan. "It is essential that we understand the full impact of senescence," Campisi said. "The possibility of eliminating senescent cells holds great promise and is one of the most exciting avenues currently being explored in efforts to extend healthspan. This study shows that we can likely harness the positive aspects of senescence to ensure that future treatments truly do no harm." The researchers now plan to explore the role of senescent cells in other examples of tissue injury.

Provided by Buck Institute for Age Research