MedicalXpress

Potential therapeutic target for wound-healing and cancer identified

May 12 2014

A Jackson Laboratory research team led by Professor Lenny Shultz, Ph.D., reports that a protein involved in wound healing and tumor growth could be a potential therapeutic target.

In one of nature's mixed blessings, the mechanisms that work to heal cuts and wounds, rebuilding damaged cells, can also go out of control and cause cancer. But understanding those mechanisms could lead to new ways of stimulating healing in wound patients and dialing back cancerous proliferation.

An inactive rhomboid protease, iRhom2, is normally a short-lived protein that controls a cascade of events involved in wound healing as well as tumor growth. By introducing mutations in Rhbdf2, the gene that encodes the iRhom2 protein, the researchers extended the protein's duration and wound-healing power. And while the altered protein also contributed to the growth of already-present tumors, it did not trigger the spontaneous development of new tumors.

Epidermal growth factor receptor (EGFR) signal transduction plays a major role in growth, proliferation and differentiation of mammalian cells. "In *Drosophila*," explains Vishnu Hosur, a postdoctoral associate in the Shultz lab, "iRhoms, are cardinal regulators of EGFR signaling. In humans, iRhoms have been implicated in EGFR-mediated keratinocyte proliferation and cancer growth, but the molecular mechanisms underlying these biological functions have not been well defined."

In this study, the researchers used molecular, cell biological, in vivo genetic and bioinformatics approaches to identify the EGFR ligand amphiregulin as a physiological substrate, and demonstrate a role for iRhoms in amphiregulin-EGFR-dependent wound healing. Furthermore, they showed how iRhom mutations that increase EGFR signaling, under the right circumstances, can drive cancer development.

"This study demonstrates the significance of mammalian iRhoms in regulating an EGFR signaling event that promotes accelerated wound healing and triggers tumorigenesis," Shultz says. "It provides a paradigm shift in our understanding of rhomboid enzymes and their emerging role in diverse biological functions. Given their ability to regulate EGFR signaling in parallel with metalloproteases, iRhoms can be potential therapeutic targets in impaired wound healing and cancer."

Provided by Jackson Laboratory