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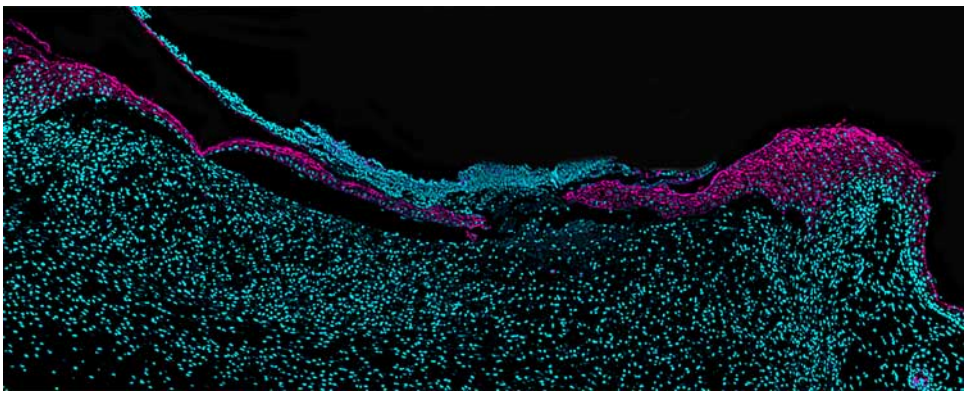
Miller School Researchers Identify Molecule that Suppresses Skin Tumors and May Promote Wound Healing

We're one step closer to solving a mystery of why diabetic foot ulcers rarely develop skin tumors. It turns out that a molecule called microRNA 193b-3p has the potential to both suppress skin cancer and promote wound healing, Irena Pastar, Ph.D., Marjana Tomic-Canic, Ph.D., and colleagues at the University of Miami Miller School of Medicine reveal in new research.



Immunohistochemistry of a healing wound after miR193b-3p treatment in vivo showing epithelial fronts (pink) moving toward each other to achieve closure of the wound.

The new findings were published May 11 as the cover story in the prestigious journal *Science Translational Medicine*. Dr. Pastar and Tomic-Canic are both corresponding authors.

Non-healing or chronic wounds, such as diabetic foot ulcers (DFUs), and malignant tumors, such as squamous cell carcinomas, share common biological traits, said Dr. Tomic-Canic, professor and vice chair of research and the Director of Wound Healing and Regenerative Medicine Research Program in the Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery at the Miller School.

These tumors and ulcers are “like two sides of the same coin,” added Dr. Pastar, who is research associate professor. And although other wounds can become cancerous, skin tumors are very rare in patients with diabetic foot ulcers.

Discovering the Dual Role

To find out why, Drs. Pastar and Tomic-Canic and colleagues evaluated microRNAs, small RNA molecules that orchestrate healing, in both DFUs and acute wound samples from people. Through this work, they discovered the dual role of miR193b-3p, which was more active in DFUs and less active in acute wounds. They also confirmed their findings using a diabetic mouse wound model.

The new breakthrough comes with a caveat. Although activation of microRNA 193b-3p suppresses skin cancer in DFUs, too much of a good thing, or “super-activation” of this mechanism also impairs re-epithelialization and cell migration in the same ulcers. Those two processes are necessary for DFU wound healing.

Wound Healing Team.

Therefore, finding the right balance with microRNA 193b-3p could be the key. In addition, this biological mechanism could be targeted with therapeutics in the future.

The next step in the research could be to further explore the multiple mechanistic components of tumor suppression to advance development of therapies that benefit both people with cancer and non-healing diabetic foot ulcers.

Best of Two Worlds

“Our findings revealed a specific molecule, microRNA 193b-3p, and its downstream targets that can be fine-tuned to achieve the best of the two worlds – tumor suppression and wound healing at the same time,” Dr. Tomic-Canic said.

“Both wounds and tumors represent such complex clinical problems that only a multi-disciplinary team, such as the one at UM’s Wound Healing Program, can tackle them, she added.

“Our dedicated patients, clinicians and scientists are working together to teach us why tumors are not forming, wounds aren’t healing and, at the same time, provide solutions for new therapeutics.”

Other Miller School faculty involved in study, “Dichotomous role of miR193b-3p in diabetic foot ulcers maintains inhibition of healing and suppression of tumor formation,” include Ivan Jozic, Ph.D.; Rivka C. Stone, M.D., Ph.D.; Tongyu C. Wikramanayake, Ph.D.; Robert S. Kirsner, M.D., Ph.D.; and Hadar Lev-Tov, M.D.

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