New hope for patients with chronic wounds

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Most wounds clear up by themselves, but some fail to heal and become chronic. An international team of researchers led from Karolinska Institutet, now unveil the important role of so-called microRNAs in regulating skin wound healing, pointing to new therapeutic possibilities for the treatment of hard-to-heal wounds.

Chronic wounds affect 0.2-1 percent of the population in developed countries and represent an increasing health problem and an economic burden to society. Current treatments focus on optimising controllable factors such as clearing infections. There is a major medical need for treatments that have a direct impact on the wound healing process, and this is why the researchers set out to find therapeutic targets for chronic skin wounds.

Wound healing is a complex process that can be divided into several phases—two of these are the inflammatory and the proliferative phase. During the inflammatory phase, damaged and dead cells, bacteria, and debris are cleared out by immune cells. Next is the proliferative phase, where skin cells multiply and there is growth of new tissue. The transition between these two phases is a critical regulatory point that can determine the outcome of the healing process. Hence, the researchers decided to look for factors that mediate this transition.

MicroRNAs, or miRNAs, are short pieces of genetic code that, instead of coding for proteins, regulate the expression of genes. Since the discovery of miRNAs in 1993, many studies have shown that miRNAs are involved in a range of diseases.

"There is very little known about the expression and function of miRNAs in human skin wounds, but we have previously shown that miRNAs play important roles in the regulation of the cells in the outermost layer of the skin, also called keratinocytes", says Dr. Ning Xu Landén, principal investigator at the department of medicine, Solna, Karolinska Institutet.

In a news tudy, published in the *Journal of Clinical Investigation*, the researchers collected skin biopsies from the edge of wounds, and looked for changes in miRNA expression during the healing process. They found one miRNA of particular interest, miR-132. Its expression increased during the inflammatory phase and then peaked again in the proliferative phase—just what the researchers were looking for.

They found that in the inflammatory phase, miR-132 caused less immune cells to move to the wound, whereas a lack of miR-132 meant more immune cells and hence increased inflammation. During the proliferative phase, miR-132 promoted keratinocyte growth, while a lack of miR-132 decreased cell growth and wounds took longer to heal.

"Our results show that miR-132 is important during the transition from the inflammatory to the proliferative phase and therefore acts as a critical regulator of skin wound healing", says Xu Landén. "Due to its pro-healing capacity, miR-132 may be an attractive therapeutic target for chronic skin wounds. Our goal is to develop a microRNA-based treatment to promote healing."

More information: 'MicroRNA-132 enhances transition from inflammation to proliferation during wound healing Healing', Dongqing Li, Aoxue Wang, Xi Liu, Florian Meisgen, Jacob Grünler, Ileana R. Botusan, Sampath Narayanan, Erdem Erikci, Xi Li, Lennart Blomqvist, Lei Du, Andor Pivarcsi, Enikö Sonkoly, Kamal Chowdhury, Sergiu-Bogdan Catrina, Mona Ståhle, Ning Xu Landén, *J Clin Invest*, online first

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