Scar-free Healing

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Scarring of the skin after injury, surgery, burn or trauma in a person can result in several medical problems, such as loss of function, restriction of movement and psychological damage. Though treatments such as pressure garments, hydrocortisone injections, or silicone dressings are on the market, none of these have proved effective and often yield unpredictable results. It has been discovered that mammalian embryonic wounds heal perfectly with no scar, whereas adult mammals develop scars. Mark Ferguson and Sharon Kane of the UK have investigated the cellular and molecular reasoning behind the difference, and are in the process of marketing drugs based on their findings.

Scars can occur after trauma, surgery or an injury to any tissue or organ in the human body. They happen as a result of a repair mechanism which replaces the normal missing tissue with an extracellular matrix. This extracellular matrix consists of fibronectin and collagens I & II. Scars vary in appearance- they can be flat and pale, raised (if too much collagen is produced), sunken (for example, acne scars), or stretched (such as stretch marks from pregnancy). They can pose several different medical risks. In the eye, scars can lead to hazy vision or even blindness, PNS/CNS scars can lead to neural malfunction, gastrointestinal or reproductive organ adhesions can cause infertility or bowel failure, and ligament scars can restrict movement and prevent normal function.

The differences between and embryo and adult must be investigated to find out why one leaves scars and the other does not. An embryo's immune system is still in the midst of development, so response to an injury is different than that of an adult. An embryo also has fewer inflammatory cells (meaning a reduced number of neutrophils, lymphocytes, monocytes and macrophages), and those that are present are less differentiated than an adult's. Since embryos are rapidly developing, they are growing with an expansion of skin volume, so they contain high levels of morphogenetic factors involved in skin growth, remodeling, and morphogenesis. There are several consequences that come as a result of this altered inflammatory response and skin morphogenesis. Types of growth factor present, amounts of such growth factors and the length of time they remain all are different in an embryo.

Growth factors play an important role in development. TGFβ, or transforming growth factor beta, is a secreted protein that exists in three isoforms and is important in controlling proliferation, cell differentiation and other functions in most cells. It plays a role in immunity, cancer, heart disease and diabetes. PDGF is another protein that regulates cell growth and division, and plays a significant role in blood vessel formation. Embryos have high levels of TGFβ3 and endogeneous FGFs. Adult wounds have high levels of TGFβ1 and large quantities of PDGF.

Using this data, scientists have found a way to manipulate the healing wounds of adults to heal without a scar. They have developed new pharmaceutical agents that alter the ratio of TGFβ isoforms (either elevating TGFβ3 or reducing TGFβ1 and 2). For example, on adult mice, rats and pigs, it was found that applying neutralizing antibodies to TGFβ1 and TGFβ2 to healing adult wounds results in improved scarring. Also, prevention of activation of TGFβ1 and 2 at the wound site by competitive inhibition also results in improved scarring. Human trials have recently begun and have progressed well. Though the treatments have only been conducted in the skin, these pharmaceuticals are quite likely to find use in other tissues or organs, such as the eye, abdominal and reproductive organs, nerves, and ligaments. All of these share similar molecular and cellular mechanisms with dermal scarring, so the same techniques are applicable.

References:

Mark W. J. Ferguson and Sharon O'Kane, "Scar-free healing: from embryonic mechanisms to adult therapeutic intervention." *Philosophical Tranactions of The Royal Society Lond B Biological Sciences*. 359 (2004): 839-850.