Medical Xpress

The immune system can delay healing of bone fractures

March 22 2013

(Medical Xpress)—Researchers at Charité – Universitätsmedizin Berlin have succeeded in demonstrating an association between delayed bone fracture healing and increased concentration of specific immune cells in the blood of the patient. Results of the study show that the adaptive immune system responds to the fracture in a similar way as to an infection and attempts to fight against it. The study appears in the current issue of the journal *Science Translational Medicine*.

In their study, the team of researchers led by Prof. Georg Duda and Prof. Hans-Dieter Volk, directors of the Berlin-Brandenburg Center for Regenerative Therapies (BCRT) at Charité, examined the role of the acquired immune system in the process of fracture healing. Their study focused on so called CD8+ T-cells, which recognize pathogens (e.g. a bacteria or viruses) through specific receptors and eliminate them by releasing certain proteins (cytokines). The researchers found an association between delayed bone healing and elevated concentrations of a sub-group of CD8+ T-cells - known as TEMRA cells - in the patient's blood. These cells indicate an aged immune system. They do not require a direct pathogen contact to become activated, but instead, respond directly to inflammatory signals. "Our study suggests that TEMRA cells misinterpret the fracture as a pathogen infection. In case of a fracture, they migrate to the side of injury and locally release specific cytokines, which compromises the function of pro-regenerative cells, resulting in a delayed healing," says Dr. Simon Reinke, one of the two lead authors of the study. The researcher then took these studies into mice and found that depletion of CD8+ T cells by a specific antibody therapy

significantly improved the healing, whereas adding CD8+ T cells impaired fracture regeneration.

"Our study establishes a mechanistic link between the individual immune profile and the fracture healing outcome," states the other lead author of the study, Dr. Sven Geißler. In the future, this knowledge could be used for the early prediction of the healing outcome and for the targeted intervention. Thus, it opens the opportunity for the development of new therapies to improve and accelerate the healing of bone fractures or potentially other tissue injuries.

More information: Reinke, S. et al. Terminally Differentiated CD8+ T Cells Negatively Affect Bone Regeneration in Humans. *Sci. Transl. Med*. 5, 177ra36 (2013).

Provided by Charité - Universitätsmedizin Berlin