

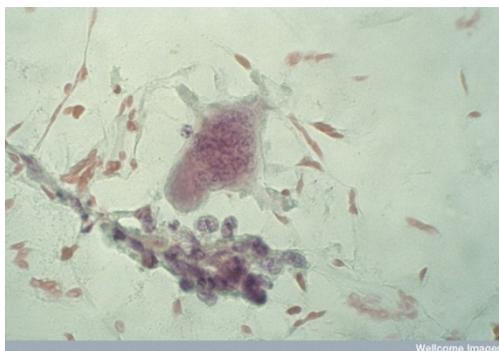
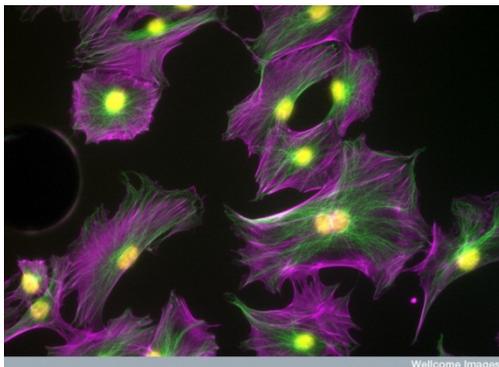
Diabetic bone fracture repair

Written by Danielle Nicholson

Reviewed by Dr. Cynthia Coleman, National University of Ireland Galway



Diabetes mellitus (DM) is a metabolic disorder associated with several complications, including impaired healing. Bone, as important skeletal structure in the body, is affected by the diabetic condition, particularly during fracture healing processes. Fracture healing is a complex, unique physiological process that restores the structural and biological properties of an injured bone. It has been well documented that DM, a systemic disease causes increased healing time by 2-3 times the normal rate.



Top to bottom: Osteoblasts,
Osteocytes, Osteoclasts
Images: Wellcome Images

Bone and its four types of cells

Bone consists of a hard, intercellular material, within or upon which four cell types are found: osteoblasts, osteocytes, osteoclasts and undifferentiated mesenchymal stem cells (MSCs). Osteoblasts are responsible for manufacturing and depositing the protein matrix of new intercellular material on bone surfaces. Osteocytes are osteoblasts that are trapped within intercellular material, residing in a cavity and communicating with other osteocytes and free bone surfaces by means of extensive filament-like extensions that occupy long, meandering channels through the bone. With the exception of certain fish, all bone has this osteocytic structure. Osteoclasts are large cells that, working from bone surfaces, resorb bone by direct chemical and enzymatic attack. Undifferentiated (unspecialized) bone MSCs reside in the loose stromal tissue between the supporting, anchoring strands of connective tissue, along vascular channels, and in the condensed fibrous tissue covering the outside of the bone (periosteum). With appropriate stimuli, MSCs will contribute to the healing process.

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Bone is a dynamic tissue, constantly regenerating thanks to the push and pull of bone-building osteoblasts and bone-destroying osteoclasts.

Healing is a multi-step reaction of the body. Early in this complex process inflammation occurs for approximately 3-7 days. The fracture causes bone marrow to be exposed. Many cell types reside in the bone marrow, including a subgroup of connective tissue or stromal cells called mesenchymal stem cells (MSCs). These cells are recruited to the site of injury and form a protective, rigid cartilaginous structure called a callus. This dense, stiff cartilage clot forms by about day 14 after the fracture. In time, the callus is remodeled and replaced by bone. For diabetes patients, the fracture callus is often smaller than normal. People with diabetes have fewer MSCs in their bones and so have fewer to recruit upon fracture for healing. The MSCs which are present are less likely to contribute to the healing process. In uncontrolled diabetes, MSCs are more likely to be differentiated to adipose tissue (fat cells) since a high blood sugar environment predisposes these cells to behave this way; thus the MSCs are less able to respond to the trauma of a fracture.

Did you know?

Preclinical work has demonstrated that upon achieving adequate blood glucose control, it is possible to overcome the deleterious effects of diabetes mellitus on bone healing.

One of the defining features of MSCs is their ability to specialize or differentiate into cartilage, fat and bone cells once prompted to do so in the laboratory by specific culture conditions. In the body, MSCs can be activated to secrete factors which create a healing environment. They can also differentiate appropriate to their context.

Funded by the European Commission's FP7, REDDSTAR is a three year, 10 partner project that will comprehensively examine if stromal stem cells derived from bone marrow can safely control blood glucose levels while also alleviate damage caused by six diabetic complications. www.REDDSTAR.eu