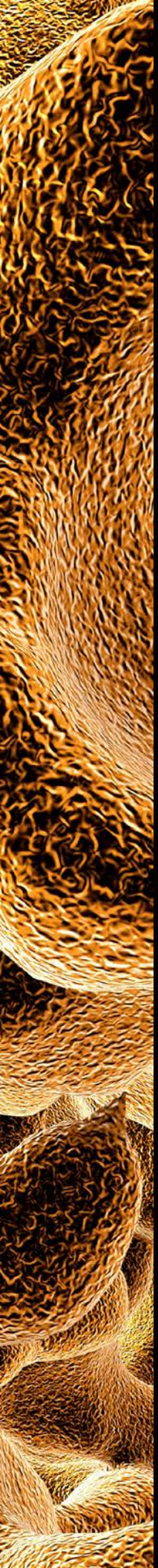

Laying bare the skeleton foundations

New research concludes that the proper organization of the cell skeleton during bone cell formation is regulated by TGFβ1, a key growth factor

A crucial growth factor, TGFβ1 reorganizes the cellular skeleton during bone cell differentiation, according to new research that may offer a path towards treating osteoporosis.

A team of Saudi researchers, led by Amer Mahmood of King Saud University, investigated the activity of TGFβ1, which is key to the differentiation of bone and fat cells from bone marrow stem cells. The researchers treated stem cell cultures with TGFβ1 to induce differentiation, and analyzed which genes were affected. They identified around 3,000 genes which responded to TGFβ1. Genes related to a component of the cell skeleton known as actin were surprisingly common among TGFβ1-regulated genes, leading the team to suspect that TGFβ1 might influence differentiation by regulating the cell skeleton.

The researchers examined the actin filaments in cells cultured with and without TGFβ1. "After treatment with TGFβ1, we saw that the cytoskeleton became very organized, forming bundles like many ropes collected together," says Mahmood. When the team added an inhibitor of TGFβ1, the actin "became completely disorganized — like someone had messed with all the ropes, leaving some pieces on top of each other and some laying in other places where they should not be."

To confirm the importance of actin in differentiation, the team treated the cell cultures with CYD, a chemical that disrupts the cell skeleton by interfering with the formation of actin filaments. Stem cells treated with CYD didn't differentiate into bone cells, even when the culture was also treated with TGFβ1. Instead, CYD enhanced the differentiation of stem cells into fat cells, again regardless of whether TGFβ1 was added. Analysis of gene expression in these cultures uncovered 13,000 genes affected by CYD, including many actin-related genes and 218 genes that were upregulated by TGFβ1, but downregulated by CYD.

Mahmood believes that the effect of TGFβ1 on the cell skeleton makes cells more likely to become bone cells, whereas fat cell differentiation may be less sensitive to the actin distribution, since fat cells don't need to be held in a specific shape. "I think the change in actin pattern leads to differentiation, which again makes changes to the actin, which further reinforces the differentiation process," he says.

These findings clarify the role of TGFβ1 in bone cell formation and highlight the importance of the cell skeleton in this process. The team hopes that TGFβ1 could be used as a treatment for diseases such as osteoporosis, an idea they're now testing in mice.

Elsafadi, M., Manikandan, M., Almalki, S., Mobarak, M., Atteya, M., et al. TGF 1-Induced differentiation of human bone marrow-derived MSCs Is mediated by changes to the actin cytoskeleton. *Stem Cells International* **2018**, 6913594 (2018).

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