Research Highlights

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# Nanotubes guide mesenchymal stem cells toward becoming bone

Megan Scudellari[1]

**The surface a cell grows on can control its fate**

In the continuing quest to direct stem cell differentiation, some researchers have set aside chemistry in favour of topography. Studies have shown that physical factors, such as rigidity of the extracellular environment, can influence stem cell fate in lieu of growth factors or chemical substances[1, 2]. Now, collaborators at the University of California, San Diego have directed the differentiation of human mesenchymal stem cells solely by altering the size of the nanotubes on which the cells are grown[3].

The researchers, led by Shu Chien and Sungho Jin, grew human mesenchymal stem cells (hMSCs) on arrays of nanotubes that ranged from 30–100 nm in diameter as well as on a flat plate of titanium that served as a control culture. After 24 hours, hMSCs on the 70 and 100 nm nanotube surface grew pronounced filopodia and elongated 10 times the length of the cells on the 30 nm culture. The researchers speculate that this occurs as the cells stretch to reach extracellular matrix proteins across the wide nanotubes. "Different sized nanotubes can indeed direct cells to different shapes," concludes Chien. And not just shapes: the elongated hMSCs showed several signs of differentiating into osteoblasts, or bone forming cells. The researchers' analysis showed two common osteogenetic protein markers, osteopontin and osteocalcin, as well as osteoblast gene expression.

"The results are pretty convincing," says Matthew Dalby of the University of Glasgow, UK, who was not involved in the study. It is noteworthy that the researchers used titanium oxide as their substrate, says Dalby, who has done similar experiments but with polymer arrays. A load-bearing metal, titanium is well tolerated *in vivo* and is approved for various clinical applications, such as dental implants. "It's a significant step in the right direction," he says. Both Dalby and Chien hope the technology may someday be used in bone implant procedures.

What remains unknown is exactly how changing the geometry of a cell's external environment affects gene transcription and subsequent differentiation. One working hypothesis is that as cells adjust their cytoskeletons to adhere to external surfaces, intracellular tension induces signaling events.

Until recently, researchers always focused on the chemical factors of cell signaling, "but mechanical factors are being recognized as an important way to induce signaling inside the cell," says Chien. "It's a very hot field right now."

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## References

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## Author affiliations

1. Megan Scudellari is a freelance writer based in Durham, North Carolina.

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