Researchers use nanoscale 'patches' to sensitize targeted cell receptors

November 25 2013, by Matt Shipman

Researchers from North Carolina State University and Duke University have developed nanoscale "patches" that can be used to sensitize targeted cell receptors, making them more responsive to signals that control cell activity. The finding holds promise for promoting healing and facilitating tissue engineering research.

The research takes advantage of the fact that cells in a living organism can communicate via physical contact. Specifically, when targeted receptors on the surface of a cell are triggered, the cell receives instructions to alter its behavior in some way. For example, the instructions may cause a stem cell to differentiate into a bone cell or a cartilage cell.

These receptors respond to specific ligands, or target molecules. And those ligands have to be present in certain concentrations in order to trigger the receptors. If there aren't enough target ligands, the receptors won't respond.

Now researchers have developed nanoscale patches that are embedded with tiny protein fragments called peptides. These peptides bond to a specific cell receptor, making it more sensitive to its target ligand – meaning that it takes fewer ligand molecules to trigger the receptor and its resulting behavior modification.

"This study shows that our concept can work, and there are a host of potential applications," says Dr. Thom LaBean, an associate professor of

materials science at NC State and senior author of a paper describing the work. "For example, if we identify the relevant peptides, we could create patches that sensitize cells to promote cartilage growth on one side of the patch and bone growth on the other side. This could be used to expedite healing or to enable tissue engineering of biomedical implants."

"What's important about this is that it allows us to be extremely precise in controlling cell behavior and gene expression," says Ronnie Pedersen, a Ph.D. student at Duke University and lead author of the paper. "By controlling which peptides are on the patch, we can influence the cell's activity. And by manipulating the placement of the patch, we can control where that activity takes place."

The patch itself is made of DNA that researchers have programmed to self-assemble into flexible, two-dimensional sheets. The sheets themselves incorporate molecules called biotin and streptavidin which serve to hold and organize the peptides that are used to sensitize cell receptors.

"These peptides can bind with cell receptors and sensitize them, without blocking the interaction between the receptors and their target ligands," Pedersen says. "That's what makes this approach work."

More information: The paper, "Sensitization of Transforming Growth Factor-β Signaling by Multiple Peptides Patterned on DNA Nanostructures," was published online Nov. 8 in the journal *Biomacromolecules*. pubs.acs.org/doi/abs/10.1021/bm4011722

Abstract
We report sensitization of a cellular signaling pathway by addition of functionalized DNA nanostructures. Signaling by transforming growth factor β (TGFβ) has been shown to be dependent on receptor clustering. By patterning a DNA nanostructure with closely spaced peptides that

bind to TGF? receptor, we observe increased sensitivity of NMuMG cells to TGFβ ligand. This is evidenced by translocation of secondary messenger proteins to the nucleus and stimulation of an inducible luciferase reporter at lower concentrations of TGFβ ligand. We believe this represents an important initial step toward realization of DNA as a self-assembling and biologically compatible material for use in tissue engineering and drug delivery.

Provided by North Carolina State University