MedicalXpress

Precise and persistent cell sabotage: Control of siRNA could aid regenerative medicine, cancer therapy

August 27 2012

Some of the body's own genetic material, known as small interfering RNA (siRNA), can be packaged then unleashed as a precise and persistent technology to guide cell behavior, researchers at Case Western Reserve University report in the current issue of the journal, *Acta Biomaterialia*.

The research group, led by Eben Alsberg, associate professor in the departments of Biomedical Engineering and Orthopedic Surgery, have been pursuing experiments that seek to catalyze stem cells to grow into, for example, bone and cartilage cells, instead of fat, smooth muscle and other cell types.

Beyond tissue engineering, the scientists believe that their technology could be used to starve a tumor by blocking growth of blood vessels that carry nutrition to a malignancy. Or the siRNA could bring on cancer cell death by interfering with other cellular processes.

siRNA is a short section of double-stranded RNA that inhibits gene expression. The molecule can jam up the machinery that produces specific proteins important to cell processes.

A current challenge to using siRNA to block growth of cancerous tumors or guide cell behavior in tissue engineering, is that the tiny material rapidly disperses when injected in the bloodstream or directly into target

tissues.

Alsberg, Khanh Nguyen, a postdoctoral researcher, and Phuong N Dang a doctoral student here, packaged siRNA in a mix of polymeric materials. Under ultraviolet light, the mix is induced to form hydrogels connected by a network of polymer threads.

As the threads of the hydrogels break down, the siRNA molecules are cut loose to redirect the fate of the targeted cells. Ultimately, this system can be injected into a target tissue and application of light from outside the body will induce hydrogel formation.

"Local delivery helps target the siRNA to specific cell populations of interest, such as cancer cells in a tumor or stem cells in a bone fracture," Alsberg said. "The ability to alter cell behavior with siRNA can depend on the length of exposure time to the genetic material.

"We can tune the material properties so we can control the dose and rate at which cells are exposed to siRNA. This capacity may prove to be therapeutically valuable."

Tests showed the siRNA effectively interfered with a signal pathway of cells surrounding and inside the hydrogels over an extended period of time.

By adjusting the formula, essentially adding more hands that hold onto the siRNA in the hydrogel complex, the team increased the amount to time target cells are exposed to siRNA from a few days up to a few weeks, thus prolonging the sabotage of undesired cell development.

Provided by Case Western Reserve University