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Tendon regeneration in rats

The use of genetically modified adult stem cells may provide a new approach to treating common musculoskeletal injuries, according to results from a new study in rats.

Tendon and ligament injuries are both very common and difficult to treat. Each year ~200,000 Americans undergo tendon or ligament repair procedures, including autografts, allografts, and implantation of synthetic prostheses. None of these treatment options represents a successful long-term solution to the injury.

Now, in the April issue of the *Journal of Clinical Investigation*, Dan Gazit of Hebrew University–Hadassah Medical Center (Jerusalem, Israel) and colleagues report Achilles tendon repair in rats using mesenchymal stem cells (MSCs) engineered to look and act like tenocytes. Researchers have previously shown that MSCs differentiate into fat cells, as well as bone-, cartilage-, muscle-, and tendon/ligament-forming cells. Gazit's team demonstrated that an MSC line engineered to overexpress two proteins, Smad8 and BMP2, differentiated into tenocytes. On transplantation into the site of an Achilles tendon injury in rats, these cells induced tendon regeneration and collagen production.

Because Smad8 and BMP2 activity are not limited to musculoskeletal tissues, these results may have therapeutic implications that extend beyond orthopedic medicine.

One-two punch against cancer

By combining tumor-targeted immune cells with a cancer-killing virus, researchers have created a potent new anticancer weapon in mice. The method may one day be used to target metastatic cancer while preserving healthy tissue.

Traditional chemotherapy agents attack both cancerous and healthy cells. Newer immune cell-based therapies and the use of oncolytic viruses, which selectively infect cancer cells, show greater specificity but have been used with limited effectiveness.

In a recent study Christopher H. Contag and colleagues at the Stanford University School of Medicine (Stanford, CA) have combined both strategies; they packaged vaccinia viruses engineered to infect only cancer cells inside cytokine-induced killer (CIK) cells, which have been shown to target and kill a variety of tumors. After systemic delivery the viruses remain dormant inside the cells long enough for them to locate the tumors, and then they burst out, killing the cancer cells. In immunodeficient mice with human ovarian cancer xenografts, the combined strategy eradicated the tumors in all mice tested. After 90 days they showed no signs of relapse or treatment-related toxicity (*Science*, 24 March).

If similar results can be achieved in humans, cancer patients may soon have the option of more effective treatments, without the side effects common with chemotherapy.

Picking out the bad guys

A new study illustrates how identification of the subtle differences between cancerous and healthy stem cells could be a key step toward developing safer and more effective therapies.

Only in old western movies does the villain wear a black hat that easily distinguishes him from the white-clad hero. Real bad guys are harder to spot. For example, the stem cells involved in acute myeloid leukemia (AML) are nearly indistinguishable from healthy hematopoietic stem cells (HSCs). Fortunately, the differences do exist if one looks closely enough, as Sean Morrison and colleagues at the University of Michigan (Ann Arbor) demonstrate in an article from *Nature* (published online 5 April; doi: 10.1038/nature04703).

They found that deletion of the gene for the tumor suppressor PTEN has notably different effects in the two types of stem cells. AML appears quickly in mice lacking hematopoietic expression of PTEN, and transplantation of diseased marrow cells led to the onset of leukemia in formerly healthy mice. Healthy HSCs lacking PTEN, conversely, dwindled in number and proved incapable of reconstituting marrow formation in marrow-depleted animals.

According to the authors, this observation illustrates how differently the same biochemical pathways can operate in healthy and diseased cells; finding and understanding these differences could help researchers to develop more efficiently targeted therapies.