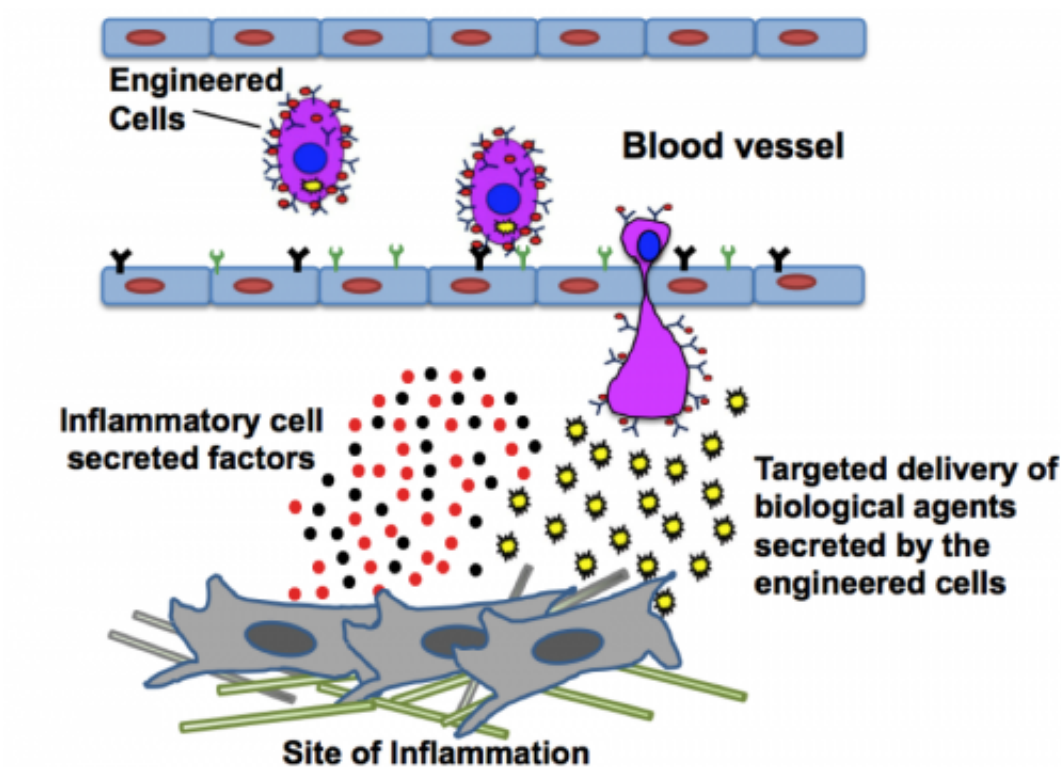


Stem cells engineered to become targeted drug factories

October 4 2013, by Joseph Caputo



Engineered mesenchymal stem cells are targeted to a site of inflammation to secrete anti-inflammatory interleukin-10 proteins. Credit: Jeffrey Karp

(Medical Xpress)—A group of Brigham and Women's Hospital, and Harvard Stem Cell Institute researchers and collaborators at MIT and MGH have found a way to use stem cells as drug delivery vehicles.

The researchers inserted modified strands of messenger RNA into connective tissue [stem cells](#)—called mesenchymal stem cells—which stimulated the cells to produce adhesive surface proteins and secrete interleukin-10, an anti-inflammatory molecule. When injected into the bloodstream of a mouse, these modified human stem cells were able to target and stick to sites of inflammation and release biological agents that successfully reduced the swelling.

"If you think of a cell as a drug factory, what we're doing is targeting cell-based, drug factories to damaged or diseased tissues, where the cells can produce drugs at high enough levels to have a therapeutic effect," said research leader Jeffrey Karp, PhD, a Harvard Stem Cell Institute principal faculty member and Associate Professor at the Brigham and Women's Hospital, Harvard Medical School and Affiliate faculty at MIT.

Karp's proof of concept study, published in the journal *Blood*, is drawing early interest from biopharmaceutical companies for its potential to target biological drugs to disease sites. While ranked as the top sellers in the drug industry, biological drugs are still challenging to use, and Karp's approach may improve their clinical application as well as improve the historically mixed, clinical trial results of mesenchymal stem cell-based treatments.

Mesenchymal stem cells have become cell therapy researchers' tool of choice because they can evade the immune system, and thus are safe to use even if they are derived from another person. The researchers' method of engineering the cells with messenger RNA is also harmless, as it cannot integrate into a cell's genome, which can be a problem when DNA is used (via viruses) to manipulate gene expression.

"This opens the door to thinking of messenger RNA transfection of cell populations as next generation therapeutics in the clinic, as they get

around some of the delivery challenges that have been encountered with biological agents", said Oren Levy, co-lead author of the study and Instructor of Medicine in Karp's lab. The study was also co-led by Professor Weian Zhao at University of California, Irvine who was previously a postdoctoral fellow in Karp's lab.

One such challenge with using [mesenchymal stem cells](#) is they have a "hit-and-run" effect, since they are rapidly cleared after entering the bloodstream, typically within a few hours or days. The Harvard/MIT team demonstrated that rapid targeting of the cells to the inflamed tissue produced a therapeutic effect despite the cells being rapidly cleared. The scientists want to extend cell lifespan even further and are experimenting with how to use messenger RNA to make the stem cells produce pro-survival factors.

"We're interested to explore the platform nature of this approach and see what potential limitations it may have or how far we can actually push it," Zhao said. "Potentially, we can simultaneously deliver proteins that have synergistic therapeutic impacts."

More information: [bloodjournal.hematologylibrary ... 3-04-495119.abstract](#)

Provided by Harvard University

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