A stem cell target for expanding waistlines?

June 16 2011

Researchers may have found the key to developing a method to rid the body of stem cells responsible for driving fat expansion. According to a report in the June 16 *Cell Stem Cell,* a Cell Press publication, they've landed the first protein marker on the surface of those so-called adipose stromal cells (ASCs), which serve as progenitors of the cells that make up fat tissue.

"Our long-term goal is to identify an approach to inactivate these cells in disease," said Mikhail Kolonin of University of Texas Health Science Center at Houston. "By administering a peptide with a toxin to ASCs, we could deplete these cells." In past studies, he has used a similar approach to develop a therapy targeting the blood vessels that feed fat tissue.

The first step to targeting ASCs was to find a marker on their surfaces that uniquely identifies them. The method the research team developed relies on billions of viral particles each displaying a different peptide on its outer coat. The goal was to find one or more that binds specifically to ASCs in live mice and to then use it as "bait" to isolate the target receptor.

That exercise led them to a previously undescribed fragment of decorin, a multifunctional protein regulating cell adhesion, proliferation, and migration. Interestingly, the team shows that this new marker (referred to as delta-decorin) interacts with a hormone known as resistin. Despite resistin's fame in scientific circles for its connection to obesity and insulin resistance, its receptor had remained elusive.

"The expansion of fat tissue is the foundation of obesity," Kolonin said. "For that to happen, you need progenitors to proliferate and spread around." The effects of resistin in ASCs, acting via decorin, appear to be responsible.

The findings may have other benefits as well. Although ASCs may be part of the problem in the case of obesity, they can also be harvested for use in regenerative therapies and hundreds of clinical trials are now underway. "The lack of markers for the cells has been limiting in the clinical context," Kolonin explained, because it has made it difficult to tell whether administered cells are stable and whether they end up where they should be.

"These cells can be useful, but they are also potentially dangerous," he said, noting that they've been linked to cancer progression. The new findings show it is possible to direct probes to stromal cells in vivo in an organ-specific manner. In the future, the identified cell surface biomarker can be exploited for imaging or therapeutic ASC targeting.

But there is more work to do. "While identification of decorin as a prospective ASC marker makes a step toward stem cell targeting applications, cell surface molecules differentially expressed on progenitor cells in other organs are yet to be identified," the researchers write. "Other peptides isolated in our study, based on their homing to lung, muscle, and bone marrow stromal cells, set the foundation for subsequent identification of protein interactions marking stromal progenitors of these organs."

More information: Daquinag et al.: “An Isoform of Decorin Is a Resistin Receptor on the Surface of Adipose Progenitor Cells.” *Cell Stem Cell* July 8, 2011.

Provided by Cell Press