'Open wide' for new stem cell potential: Stem cells of the oral mucosa stay young

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While highly potent embryonic stem cells are often the subject of ethical and safety controversy, adult-derived stem cells have other problems. As we age, our stem cells are less pliant and less able to transform into the stem cells that science needs to find breakthrough treatments for disease.

An exception to this can be found in the stem cells of oral mucosa, the membrane that lines the inside of our mouths. These cells do not seem to age along with the rest of our bodies. In his lab at Tel Aviv University's Goldschleger School of Dental Medicine, Prof. Sandu Pitaru and his graduate students Keren Marinka-Kalmany, Sandra Treves, Miri Yafee and Yossi Gafni, have successfully collected cells from oral mucosa and manipulated them into stem cells.

Though taken from adult tissues, these oral stem cells are almost as easy to manipulate as embryonic stem cells, Prof. Pitaru discovered. His research, which has been published in the journal *Stem Cells*, opens a new door to stem cell research and potential therapies for neurodegenerative, heart, and autoimmune diseases, as well as diabetes.

The healing powers of Wolverine

Dentists have long been aware of some of the unique properties of the oral mucosa, says Prof. Pitaru. "Wounds in the oral mucosa heal by regeneration, which means that the tissue reverts completely back to its original state," he says. A wound that might take weeks to heal and leave

a life-long scar on the skin will be healed in a matter of days inside the mouth, regardless of the patient's age. Except for the mouth, this type of healing usually occurs only in very young organisms and lower amphibians, such as the lizards that can regenerate their tails.

Prof. Pitaru set out to determine if oral mucosa could be a source for young, fetal-like stem cells with this unique healing ability. Even when obtained from an older patient, he says, these stem cells still have properties of young or primitive stem cells — which have a high capacity to be transformed into different tissues. Prof. Pitaru and his fellow researchers have already succeeded in coaxing oral mucosa stem cells into becoming other significant cells, including bone, cartilage, muscle, and even neurons.

All this, says Prof. Pitaru, is derived from a miniscule biopsy of tissue, measuring 1 by 2 by 3 millimeters. "We are able to grow trillions of stem cells from this small piece of tissue," he explains. The site of the biopsy is readily accessible, and patients experience minimal discomfort and require almost no healing time. This makes the mouth a convenient site for harvesting stem cells.

A safe and effective alternative

Prof. Pitaru and his fellow researchers are currently in pre-clinical trials, implanting these stem cells into various tissues within small rodents. Their projects include researching the impact of the innovative cells as a treatment for chronic heart failure; neurodegenerative diseases; inflammatory autoimmune diseases such as Crohn's disease; and diabetes.

These diseases are most likely to affect the elderly, and the oral mucosa stem cells would offer a more safe and effective alternative to both embryonic and adult-derived stem cells. Despite their therapeutic

potential, patients would be required to take immunosuppressant therapies when being treated with implanted embryonic cells to ensure that the body does not reject the foreign cells. Once implanted, embryonic stem cells often cause tumors to form, Prof. Pitaru says. "Stem cells taken from the tissue of elderly patients have growth limitations and reduced functional capacities."

Stem cells derived from the oral mucosa, however, avoid the pitfalls of their predecessors. Because they stay young, they behave as fetal cells, but there is no danger of rejection because they are taken directly from the patient. And they show no signs of developing the aggressive tumors that surround implantation of embryonic stem cells. With limited risk and high therapeutic potential, these cells could step in to fill a major medical need, Prof. Pitaru concludes.

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