Researchers engineer reconstructive tissue for transplant

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A breakthrough by Israeli researchers could speed recovery and limit scarring and disfigurement for patients who have suffered large soft tissue trauma - as often occurs with serious injury or cancer surgery. By biomedically engineering a muscle flap that includes a patient's own blood vessels, the team has created tissue that could one day be transferred to other parts of the body along with the patient's blood supply, speeding recovery and limiting scarring for patients who have suffered serious tissue trauma.

Led by Professor Shulamit Levenberg, of the Department of Biomedical Engineering and the Russell Berrie Nanotechnology Institute at the Technion-Israel Institute of Technology, the scientists fabricated the muscle flap using a variety of added cells and connective tissues to strengthen it. They then tested the flap by reconstructing deep abdominal wall tissue defects in mice.

Their paper describing how the muscle flap was engineered, its advantages, and its successful use when tested in an animal model, appears this week in the Online Early Edition of the *Proceedings of the National Academy of Sciences*.

According to Levenberg, successful reconstruction of large, soft tissue defects has been a clinical challenge in the past. Current techniques - involving grafts and synthetic material - often fail because of lost blood supply.

To improve outcomes, the researchers developed the unique muscle flap using a patient's own tissues (autologous), added important and advantageous cellular components to strengthen it, and engineered the flap in such a way as to vascularize to include the patient's own blood vessels so that the patient retains their own blood supply during the reconstruction process.

"We set out to design and evaluate an engineered muscle flap with robust vascularization," says Levenberg, whose research focuses on vascularization of engineered tissues. "Proper vascularization is essential for successfully integrating the flap within the host."

Their study, said the researchers, provides evidence that tissue-specific cells, such as myoblasts (cells that form muscles), endothelial cells (the thin layer of cells that lines the interior surface of blood vessels), and fibroblasts (the cells providing the structural framework for animal tissues), are necessary for successful muscle flap engineering as the added cells "rapidly and more effectively integrated within the host tissue."

"The cell types integrated in the engineered flaps dictate the muscle flap's mechanical strength," adds Levenberg.

The researchers report that within one week of transferring the engineered muscle flaps into the test mice the flaps were "viable, highly vascularized," and demonstrated "firm attachment to the surrounding tissues." They also note that the muscle flaps had the mechanical strength to support the "abdominal viscera," or organs in the abdominal region.

Their positive results, say the researchers, will not only stimulate more research, but also lead to clinical studies with human patients. They also suggest that there are far-reaching uses of the muscle flap as it can be transferred as a "free flap" to reconstruct defects in other parts of the body. This advantage could circumvent the need to harvest and transfer large amounts of tissue, avoiding many of the current complications.

"When the flap is made with a viable blood vessel network, larger quantities of tissue, even a whole organ, can be implanted and then coupled to the main vessel trunk by attaching the blood vessel network of the engineered tissue to host vessels," conclude the researchers.

More information: "An engineered muscle flap for reconstruction of large soft tissue defects," by Shandalov Yulia et al. *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1402679111

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