

# NATURE'S HEALING MATRIX\*

BY DR. DROR SELIKTAR



In recent years, the medical community has turned to sophisticated therapeutic paradigms such as gene therapy to treat complicated ailments. Some of the most persistent medical problems are hardly deserving of such complicated solutions – despite our ineffectiveness in treating them. Perhaps the most pronounced of these is wound healing. Evolution has equipped us with a highly capable mechanism for dealing with cuts, abrasions, fractures and other accidental tissue damage. In such events, healing is almost always initiated with the formation of a blood clot that fills the defect and acts as a provisional matrix – recruiting cells and starting the process of rebuilding functional tissue. Despite its potent healing properties, there are problems with

nature's biomaterial, particularly when the injury is too large for functional tissue regeneration.

In large-size tissue damage, otherwise known as critical size defects, the standard fibrin clot that forms in the injury site dissolves too rapidly, providing insufficient time for the normal repair process and giving way to crude connective scar tissue in place of functional repair tissue.

This may also happen with smaller defects, depending on the healing potential of the type of tissue (cartilage, nerve, or heart muscle) that has been damaged. A closer look at the structural properties of the fibrin clot reveals a problem in its design.

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Its loose, open-pore structure, combined with fibrin's high susceptibility to degradation, gives the blood clot matrix a limited lifetime in the injury site – up to two weeks.

Motivated by the desire to improve nature's healing biomaterial, my laboratory sought ways of slowing down the natural breakdown of the clot at the injury site to allow functional tissue repair in critical size defects. The idea is to synchronize between the dissolution of the fibrin clot matrix and the ability of the body to repair itself without leaving unwanted scar tissue. We approached this problem by modifying the structural properties of the fibrin clot using man-made polymer

technologies. Our aim was to create a bioartificial blood clot using a molecularly modified precursor of fibrin called fibrinogen.

The fibrinogen is fused with a common biomedical polymer called polyethylene glycol (PEG). A dense gel-like matrix is created from the PEG-fibrinogen solution using a simple light-activated reaction – similar to what is done in the dentist's office using polymer fillings. This safe and effective technology, called Gelrin™, provides a biologically active matrix for healing critical size defects and other difficult healing applications.

The Gelrin technology has a number of advantages over other biologic or synthetic materials used for tissue regeneration.

Gelrin can be custom-tailored for specific types of tissue repair. With more synthetic constituent in the network, the degradation of the material inside the injury site slows down significantly. Though seemingly counterintuitive, the slow degrading biosynthetic blood-clot material actually improves the healing characteristics. The Gelrin composition that proved most effective in bone regeneration contained nearly four times more PEG than fibrinogen.

Beyond applications requiring more than a simple provisional matrix, the Gelrin technology may also be a useful tool when combined with more potent stimulants for tissue regeneration, including stem cell therapy. Because of its biocompatible properties and its ability to harden directly in the injury site, Gelrin can also be an excellent biomaterial for localized stem cell delivery in cardiac or nerve tissue repair.

Gelrin has already proven highly effective in treating complicated articular cartilage injuries in pre-clinical studies. Articular cartilage lines the ends of long bones to provide near-frictionless lubrication during joint movement. This tissue has a limited capacity to repair itself and once it is injured, the motion of the joint becomes increasingly painful. Cartilage injuries in adult sheep were treated with a single injection of Gelrin and showed remarkable healing after four months. These amazing results will serve as the basis for further studies in humans.

Although more studies are required before Gelrin makes its clinical debut, there is little doubt that this innovative biomaterial technology will become a welcome addition to the arsenal of medical technologies used in tissue repair.

Regentis Biomaterials Ltd., a start-up company in the Technion incubator, has acquired the technological license for Gelrin in all orthopedic indications, and plans to begin clinical trials testing Gelrin for cartilage repair within the next 18 months. ■

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***Articular cartilage defects from the knee joint being treated with Gelrin. The Gelrin biosynthetic matrix has the biological properties of a natural material and the physical characteristics of a synthetic polymer.***