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3-D printed, mechanically robust carrier used to deliver immunosuppressive drug, and cells

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After using a 3-D printer to create a micro but mechanically robust drug and cell carrier for local and sustained delivery of the immunosuppressive drug cyclosporine A (CsA), researchers in Korea have shown in tests with animal models that the carrier, a combination of microspheres and hydrogel, maintained robust integrity and delivered a local, sustained load of CsA in an amount that overcame the need for additional drugs to treat immune rejection.

"Our objective was to show the feasibility of using a subcutaneous 3-D printed drug delivery system to achieve local and sustained CsA release and to investigate the local immunosuppressive effects of the CsA after cell transplantation," explained Dr. Dong-Woo Cho of the Department of Mechanical Engineering at Pohang University of Science and Technology. "The improved load-bearing capacity of the combined microsphere and hydrogel system, and its ability to maintain its integrity and shape during the implantation period, helped to deliver a sustained CsA release, preventing the acceleration of the secretion of cytokines related to immune rejection."

The researchers noted that many trials have attempted CsA delivery based on either microspheres or hydrogels, but most encountered serious problems, such as causing embolisms or organ damage due to migration of the microspheres from the injection site. Also, weak mechanical properties in many other kinds of systems caused premature dissolution and placed limitations on drug load quantity. However, the improved load-bearing capacity of the vehicles and improved structure that the

Korean team developed allowed the sustained release of CsA at the desired site.

"This research could be a fundamental study for overcoming existing cell transplantation limitations, mainly caused by systemic immunosuppression," wrote the researchers, who advocated 3-D printing technology for a variety of medical applications, including printing membranes of various shapes.

Cell-based therapies often require the use of allogeneic (other human donated) cells or xenogenic (different species donated) cells that can stimulate an immune rejection response, requiring the use of immunosuppressive drugs to prevent acute transplant rejection. The introduction of CsA improves the success rate of transplantations, but systemic administration requires high doses of immunosuppressant that can have severe side effects. The benefit of their 3-D printed combination microsphere and hydrogel carrier system is that it provides local rather than systemic drug delivery, say the researchers.

"The carrier we developed could be a promising solution to treating several diseases that require cell-based therapy, such as muscular dystrophy, degenerative disc disease or myocardial infarction," concluded the researchers."

"The 3-D printed carrier is a novel apparatus in cell-based therapeutics that allows for the controlled release of an immunosuppressant," says Wei-Ming Duan, Professor at Capital Medical University Department of Anatomy, Beijing, China, Section Editor for *CELL TRANSPLANTATION*. "This technology could lead to a very promising and innovative delivery system that may benefit allogeneic and xenogenic transplantation. Its applicability for other drugs should also be investigated."

The study will be published in a future issue of *Cell Transplantation* .

More information: www.ingentaconnect.com/content … t-CT-1310_Song_et_al

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