

Way to block immune rejection after transplant surgery



A water-based gel, 'hydrogel,' has shown promising results in animal trials

Individuals who have had transplant surgery need drugs that suppress their immune system and prevent it from turning on the new organ. Indian scientists have helped develop a gel that can hold and slowly release an immune-suppressing drug.

The water-based gel, known as a 'hydrogel', put together by a team of scientists from the U.S., India and Switzerland has shown promising results in animal trials. The gel could allow transplant recipients ward off organ rejection with less frequent application, reducing the amount of immunosuppressant they receive and thereby limiting the drug's toxic side-effects.

The research has just been published in *Science Translational Medicine*.

Screening

The scientists screened hundreds of substances in a list of agents 'generally recognised as safe' compiled by the U.S. Food and Drug Administration. Triglycerol monostearate (TGM) was identified as suitable for making the hydrogel.

This molecule, when appropriately processed in water, self-assembles into tiny fibres, which then clump to form bundles, said Praveen Kumar Vemula of the Institute for Stem Cell Biology and Regenerative Medicine in Bangalore, one of the paper's corresponding authors.

The processing was carried out in the presence of tacrolimus, a widely used immunosuppressant, so that the drug got encapsulated in the TGM bundles as the hydrogel formed.

The hydrogel could be given as an injection after transplantation. The TGM fibres would be broken up by enzymes produced by inflammation at the site of surgery, releasing the drug they held, explained Dr. Vemula.

He and his graduate student, Ashish Dhayani, had worked out how the hydrogel could be made.

The tacrolimus-containing hydrogel was tested in rats that had one leg transplanted from another animal. The hydrogel was injected into the transplanted leg a day after the operation.

Immune rejection

A single injection of the hydrogel was sufficient to block immune rejection of the limb for more than 100 days, the scientists noted in their paper.

This was longer and achieved with a much lower dose of tacrolimus than reported in previous studies where rats with a transplanted leg were subjected to 14-day or 90-day courses of daily injections of only the immunosuppressant.

The development of a single-dose sustained-release drug delivery system is important for better patient compliance with an immunosuppression regime, the paper noted.

The experiments carried out on rats with a transplanted leg were a proxy for human hand and face transplants, which carried a higher risk of immune rejection, according to Dr. Vemula.

But the rat experiments also suggested that the hydrogel could be beneficial in other sorts of transplantation too, such as those involving the kidney or liver, he pointed out.

In such cases, the hydrogel could not be injected directly into the transplanted organ and would instead have to be given to a readily accessible part of the body like the arm.

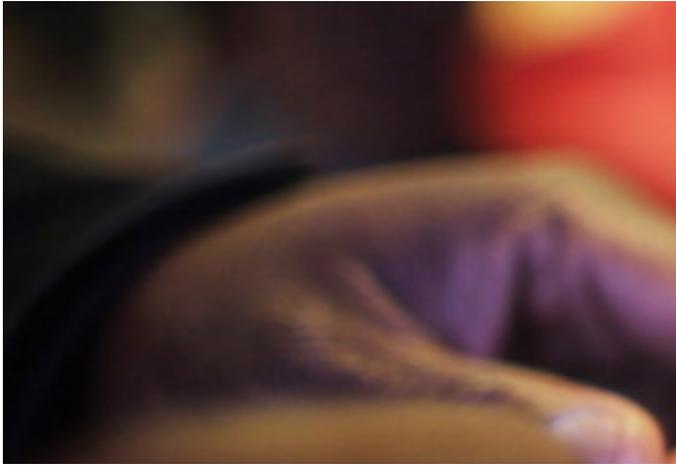
Even when rats received the hydrogel injection in the leg on the other side, immune rejection of the transplanted limb was on average avoided for 75 days.

Although the duration was lower than when the hydrogel was injected into the transplanted leg, it was still more than twice as long as when the rats received a single dose of tacrolimus alone.

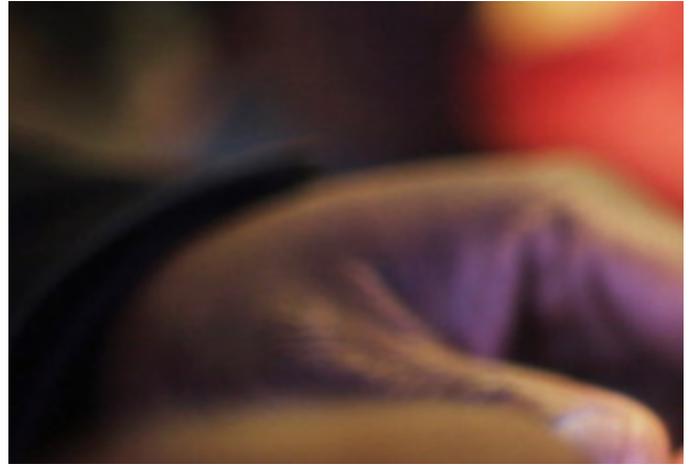
"We now need to test the efficacy of hydrogel encapsulation of immunosuppressants in animal models of kidney and liver transplants," Dr. Vemula told this correspondent.

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