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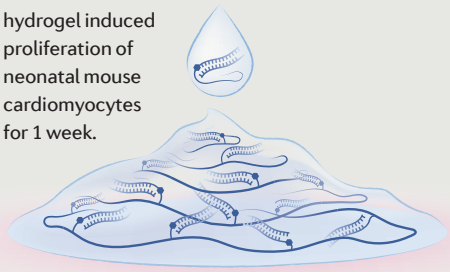
CARDIAC REGENERATION

A hydrogel–miRNA complex stimulates heart recovery

Use of a degradable hydrogel to deliver the microRNA miR-302 gradually into the injured myocardium induces sustained production of new cardiomyocytes and leads to improvements in heart function in mice after ischaemic heart injury, according to a study led by Jason Burdick and Edward Morrisey. "The concept of promoting cardiomyocyte proliferation as a means to regenerate the heart is gaining traction in the field," says Morrisey. "This process circumvents issues of engraftment of exogenous cells, which remains very difficult and is prone to issues of immunological tolerance," he explains.

The research team had previously shown that miR-302 induces cardiomyocyte proliferation in mouse hearts through the inhibition of Hippo signalling. In the new study, the investigators developed a hyaluronic acid hydrogel designed for injection and sustained release of miR-302 mimics into infarcted myocardium. "The use of the hydrogel to deliver the miRNA is very important to provide localization of the miRNA to prevent any off-target effects that may occur if the miRNA is delivered systemically," explains Burdick. Other potential benefits of the hydrogel are the enhancement of tissue retention and protection of miRNAs from degradation.

In vitro, sustained release of miR-302 mimics from the hydrogel induced proliferation of neonatal mouse cardiomyocytes for 1 week.



> a single injection of gel–miR-302 complex in the heart led to local and sustained cardiomyocyte proliferation for 2 weeks

In adult mice, a single injection of gel–miR-302 complex in the heart led to local and sustained cardiomyocyte proliferation for 2 weeks. Intramyocardial injection of gel–miR-302 after myocardial infarction (MI) induced an expansion of cardiomyocyte numbers in a clonal fashion, with increased cell numbers at the infarct border zone, and led to improvements in heart function, as shown by decreased end-diastolic (39%) and end-systolic (50%) volumes, and improved ejection fraction (32%) and fractional shortening (64%) at 4 weeks after MI in treated compared with control mice. "The next step will be to test this methodology in large-animal models as a step towards human therapies," say Burdick and Morrisey.

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ORIGINAL ARTICLE Wang, L. L. *et al.* Sustained miRNA delivery from an injectable hydrogel promotes cardiomyocyte proliferation and functional regeneration after ischaemic injury. *Nat. Biomed. Eng.* http://dx.doi.org/10.1038/s41551-017-0157-y (2017)

FURTHER READING Boon, R. A. & Dimmeler, S. MicroRNAs in myocardial infarction. *Nat. Rev. Cardiol.* **12**, 135–142 (2015)