UKE Paper of the Month Januar 2017
Science Translational Medicine, 2016, Vol 8, Issue 363

Cardiac repair in guinea pigs with human engineered heart tissue from induced pluripotent stem cells

Florian Weinberger*, Kaja Breckwoldt*, Simon Pecha*, Allen Kelly, Birgit Geertz, Jutta Starbatty, Timur Yorgan, Kai-Hung Cheng, Katrin Lessmann, Tomas Stolen, Marielle Scherrer-Crosbie, Godfrey Smith, Hermann Reichenspurner, Arne Hansen, Thomas Eschenhagen

**These authors contributed equally to this work.*

ABSTRACT:
Myocardial injury results in a loss of contractile tissue mass that, in the absence of efficient regeneration, is essentially irreversible. Transplantation of human pluripotent stem cell–derived cardiomyocytes has beneficial but variable effects. We created human engineered heart tissue (hEHT) strips from human induced pluripotent stem cell (hiPSC)–derived cardiomyocytes and hiPSC-derived endothelial cells. The hEHTs were transplanted onto large defects (22% of the left ventricular wall, 35% decline in left ventricular function) of guinea pig hearts 7 days after cryoinjury, and the results were compared with those obtained with human endothelial cell patches (hEETs) or cell-free patches. Twenty-eight days after transplantation, the hearts repaired with hEHT strips exhibited, within the scar, human heart muscle grafts, which had remuscularized 12% of the infarct area. These grafts showed cardiomyocyte proliferation, vascularization, and evidence for electrical coupling to the intact heart tissue in a subset of engrafted hearts. hEHT strips improved left ventricular function by 31% compared to that before implantation, whereas the hEET or cell-free patches had no effect. Together, our study demonstrates that three-dimensional human heart muscle constructs can repair the injured heart.

STATEMENT:
"A heart attack destroys cardiac muscle, resulting in a fibrotic scar. We created a living patch for injured hearts using endothelial and cardiac cells grown from human induced pluripotent stem cells. These three-dimensional strips were placed over injured areas of guinea pig hearts. 28 days later, the injured area was partly remuscularized, and the heart pumped ~30% better than just after the injury. The grafts also contained new blood vessels and, in some cases, were electrically coupled to the healthy parts of the heart. These human heart patches may one day help patients recover cardiac function after a heart attack."

BACKGROUND:
This interdisciplinary work was mainly performed at the Department of Experimental Pharmacology and Toxicology in the group of Professor Thomas Eschenhagen, who invented the technology of three-dimensional engineered heart tissue (EHT). It was part of the PhD thesis of Dr. Kaja Breckwoldt, which was supervised by Dr. Florian Weinberger. Her work was honoured with the Follow-up prize at a Young Investigators Competition (2014) and the Karl Heinz Hölzer-Promotionspreis for Interdisciplinary Medical Research (2015). The surgeries were performed by Dr. Simon Pecha from the UHZ, who received the Philip K. Caves Award (2015). This work aims at translating the finding in animals to first-in-human therapy and will be supported by a research grant from the DZHK.