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Injection of encapsulated embryonic stem cells improves cardiac structure and function following myocardial infarction in the absence of tumor formation

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Regenerative medicine approaches utilizing stem cells to increase heart performance represent an important potential therapeutic approach for the treatment of myocardial infarction (MI). Two challenges in the use of embryonic stem cells (ESCs) in cardiovascular regenerative medicine is the poor differentiation of these cells into cardiomyocytes and additional concerns with the formation of tumors following implantation. Here we use an innovative encapsulation technology coupled with a pre-differentiation approach that increases the differentiation of ESCs into cardiomyocytes and reduces tumor formation following direct injection into the infarct zone of mouse hearts. Mouse ESCs were encapsulated in alginate microcapsules with an aqueous liquid core using coaxial electrospray and cultured for 7 days to form pluripotent ES cell aggregates that were then treated with BMP-4 and bFGF for three days to induce early differentiation into the cardiac lineage. Mice were subjected to permanent surgical occlusion of the left ascending artery and 2x10⁵ of the encapsulated aggregated cells were injected in to the infarct zone. Encapsulated ESCs increase survival time as well as cardiac structure and function compared to mice treated with ESCs alone. Labeling of ESC cells showed the appearance of new cells in the infarct zone that expresses cardiomyocyte markers such as troponin. Additionally, while injection of ESC alone would produce tumor formation at the injection site, no tumor formation was observed with encapsulated ESC. We conclude that direct injection of encapsulated ESC in an infarct zone allows for improved pathology and reduced tumorigenesis following experimental induction of MI in mice.

Biography

Noah Weisleder received his PhD in Cell Biology from Baylor College of Medicine and conducted Postdoctoral studies in Physiology at Robert Wood Johnson Medical School. Currently, he is an Associate Professor of Physiology and Cell Biology at The Ohio State University and an Investigator in the Davis Heart and Lung Research Institute. He has authored numerous manuscripts on muscle physiology, cardiovascular disease, membrane repair and calcium homeostasis. He is an inventor on multiple U.S. and international patents. These inventions led to formation of TRIM-edicine, a biotechnology company developing protein therapeutics where he is a Founder and Chief Scientific Officer.

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