Isolated organ viral, theraputic or cell therapy delivery

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Value proposition

Cardiovascular diseases (CVD) remain the leading cause of death worldwide. The number of CVD patients with heart failure (HF) in the US is approaching 6.5 million adults and is estimated to increase by 46% in the next decade. HF has no cure and about 50% of people who develop HF die within five years of diagnosis. Cardiac transplantation is the gold standard therapy for heart failure patients, but is fraught with post-transplant complications such as graft dysfunction, allograft vasculopathy, rejection, and immunosuppression complications. The Organ Care System (TransMedics, Inc.) is an example of a clinically tested blood perfusion system that could mitigate ischemic injury during organ preservation and replace the cold static storage strategy. Once on the device, the heart is maintained in a nonworking, but metabolically active mode. While the main goal of perfusion storage is to reduce ischemia reperfusion injury, perfusion storage uniquely isolates the metabolically active cardiac graft, potentially enabling biological modification. There continues to be a need for improvement in cardiac transplantation and gene therapy approaches that can address some of these complications, especially organ preservation.

Technology

The technology provides a novel and clinically applicable method of viral vector delivery that allows biological modification of cardiac allografts prior to implantation for the purpose of improving post-transplant outcomes. The inventors examined the influence of components (such as proprietary solutions, donor blood, and *ex vivo* circuitry tubing and oxygenators) of the Organ Care System (TransMedics, Inc.) on viral vector transduction using a cell-based luciferase assay. The inventors found that the perfusion solution nor the *ex vivo* circuitry influence viral vector transduction. Rahter, the serum or plasma fractions of the donor blood significantly inhibited viral vector transduction. Enzymatic assessment of luciferase activity in tissues obtained post-transplant revealed wide-spread and robust luciferase activity in all regions of the allograft compared to the native recipient heart. Extension of this technology may be useful in the treatment of end stage heart failure.

Advantages

- *ex vivo* perfusion as an approach to deliver a viral vector to a donor heart during storage
- Global gene expression isolated selectively to cardiac allografts