

TECHNOLOGY

Use of Recombinant Human Activated Protein C to Enhance the Cytoprotective and Anticoagulant Effects of Tissues Transgenic for Human Endothelial Protein C Receptor

OVERVIEW

Organ transplantation is limited by a critical shortage of donor organs. To address this shortage, clinicians have developed transgenic pigs to express human proteins that regulate rejection, inflammation, and thrombosis. Pigs expressing the human Endothelial Protein C Receptor (hEPCR) is a recent advancement in the field and activated via the endogenous Activated Protein C (aPC) to suppress inflammation that may lead to transplant rejection. UMB researchers have developed a method to pretreat hEPCR transgenic tissue with aPC before exposure to human blood to decrease the incidence of subsequent thrombosis, reduces endothelial damage, and decreases thrombin-induced vascular permeability.

This invention is a method to enhance the viability of transplanted tissues and organs by pretreating hEPCR transgenic tissues with exogenous recombinant human aPC, an endogenous enzyme that suppresses inflammation through cytoprotective mechanisms via its binding to hEPCR, to stimulate cytoprotective and anti-thrombotic effects before exposure to cellular and tissue insult.

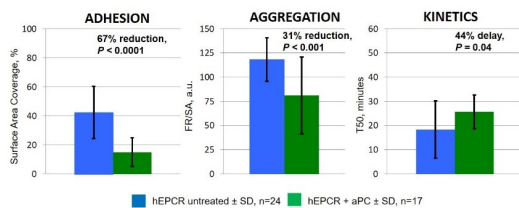


Figure 1. Thrombosis was evaluated using a novel cellular xenoperfusion assay. Porcine aortic endothelial cells were cultured in microfluidic channels. Control endothelia were incubated with media for 6 hours and perfused with blood (n=24). Treated channels were incubated with 0.02 µg/mL aPC in media for 6 hours and perfused with blood + 0.02 µg/mL aPC (n=17). Thrombosis was captured by serial fluorescent imaging and analyzed by percent surface area coverage (SA, %), time to 50% peak SA (T50, minutes) and the fluorescent intensity:SA ratio (FRISA, arbitrary units) as markers of adhesion, thrombosis kinetics and aggregation, respectively.

APPLICATIONS

The unavailability of organs to meet the demand for transplantation has resulted in a major organ shortage crisis. In the United States, a new name is added every 10 minutes to the organ transplant waiting list. Only 33,611 transplants were performed in 2016, and 22 people die on average each day while waiting for a transplant. The organs that are most in demand are the kidneys (82.9%), liver (12.3%), heart (3.4%) and lungs (1.2%). There is a tremendous demand for new methods to address this growing crisis.

ADVANTAGES

Improved survival of Xenogeneic transplant tissues and organs

STAGE OF DEVELOPMENT

This technology has been tested in GalKO.hCD46.hEPCR porcine cultures and tissues using a cellular perfusion assay to model thrombosis under physiological shear flow conditions.

(As of 8//31/2017)- MEW

LICENSING POTENTIAL

UMB seeks to develop and commercialize via an exclusive or non-exclusive license agreement and/or sponsored research with a company active in the area.

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PATENT STATUS

U.S. App. 621/171,661 PCT/US2016/035732

LICENSE STATUS

Available for licensing and commercialization

INVESTIGATOR(S)

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ATTACHMENTS

-  [Download DH-2014-019 Marketing 8.2017.pdf](#)

EXTERNAL RESOURCES

- [Four-dimensional characterization of thrombosis in a live-cell, shear-flow assay: development and application to xenotransplanta](#)

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