ratio (53%) that increased in combination with EPA by 216% ($p < 0.01$). Similar results were observed for EPA in combination with rosuvastatin. When either statin was combined with EPA, there was also decreased ONOO− release compared to statin alone ($p < 0.01$).

CONCLUSION: In combination with high intensity statins, EPA enhanced NO bioavailability in dysfunctional human ECs. The ability of EPA to reverse vascular EC dysfunction may lead to reduced ischemic events in statin-treated patients, as evidenced in outcome trials.

Amarin Pharma Inc., Elucida Research LLC

P010
IMMUNE ANALYSIS OF TISSUE ENGINEERED PORCINE AORTIC VALVE LEAFLETS AFTER ALPHA-GALACTOSE CLEAVAGE

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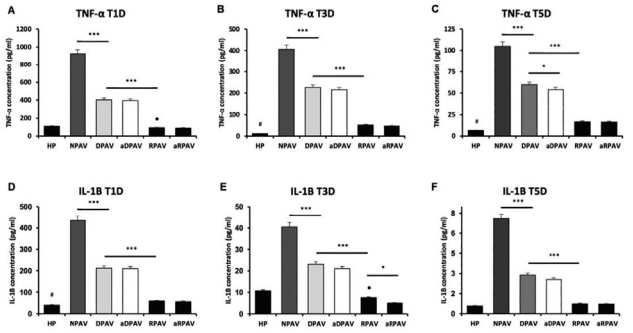
BACKGROUND: Bioprosthetic heart valves are prone to structural valve deterioration (SVD) due to an inflammatory immune response resulting in calcification, stenosis, and ultimately valve failure. The antigenicity of xenografts is thought to underlie the immune response, with galactose-α-1,3-galactose (alpha-gal) the principal antigen of investigation. The objective of this study is to further characterize the role of alpha-gal in SVD and determine whether the addition of alpha-gal cleavage to tissue engineered porcine aortic valve (PAV) leaflets will attenuate the xenoreactive humoral immune response.

METHODS AND RESULTS: Samples of human pericardium, bone marrow, and whole blood were collected from patients undergoing elective cardiac surgery. PAV leaflets were excised from the hearts of female juvenile Yorkshire pigs, decellularized with or without alpha-gal cleavage via green coffee bean alpha-galactosidase, and recellularized with allogeneic human mesenchymal progenitor cells (hMSCs). These tissue-engineered constructs, as well as native PAV leaflets and autologous human pericardium, were exposed to human blood. At 1, 3, and 5 days proinflammatory cytokine production was quantified via enzyme-linked immunosorbent assays. On days 1, 3, and 5 there was a significant reduction in TNF-α and IL1-β concentration in the serum exposed to decellularized and recellularized PAV leaflets as compared to native PAV leaflets, as well as a significant reduction in the recellularized PAV tissue compared to the decellularized tissue. Compared to the decellularized tissue, the addition of alpha-gal cleavage reduced the TNF-α concentration on day 5. Similarly, as compared to the recellularized tissue, the addition of alpha-gal cleavage reduced the IL1-β concentration on day 3.

CONCLUSION: Allogenic recellularization of PAV tissue with hMSCs attenuates the xenoreactive immune response. Independent of the decellularization and recellularization processes, alpha-gal cleavage reduced the xenoreactive immune response to PAV tissue only at select time points. Therefore, other antigenic epitopes on xenogeneic tissue in addition to alpha-gal likely contribute to the immune-mediated SVD affecting bioprosthetic heart valves.



TNF-a production after (A) 1 day of blood exposure; (B) 3 days of blood exposure; (C) 5 days of blood exposure (n = 6). IL-1B production after (D) 1 day of blood exposure; (E) 3 days of blood exposure; (F) 5 days of blood exposure (n = 6). HP: human pericardium; NPAV: native porcine aortic valve; DPAV: decellularized porcine aortic valve; aDAPV: alpha-gal cleaved decellularized porcine aortic valve; RPAV: recellularized porcine aortic valve; aRPAV: alpha-gal cleaved recellularized porcine aortic valve. * Indicates P = 0.005; *** indicates P < 0.0001; # indicates HP < RPAV, P < 0.05; ' indicates RPAV < HP, P <0.05.

Alberta Innovates Health Solutions (AIHS), University Hospital Foundation

P011
IMMUNOENGINEERING APPLICATION OF MXENE FOR PREVENTION OF TRANSPLANT VASCULOPATHY

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BACKGROUND: Cardiac allograft vasculopathy is an aggressive form of atherosclerosis and a major cause of mortality among patients with heart transplants. Blood vessel endothelial cells stimulate alloreactive T-lymphocytes to result in sustained inflammation. MXenes are an emerging class of nanomaterials that have significantly outperformed several existing biomaterials as anti-cancer agents, biosensors, and in anti-microbial therapies. Herein, we report the first application of titanium carbide ($Ti_3C_2T_x$) MXene nanosheets for prevention of allograft vasculopathy.

METHODS AND RESULTS: To infer mechanisms and to ensure reproducibility of results, detailed physicochemical characterization of $Ti_3C_2T_x$ MXene nanosheets was performed using scanning/transmission electron microscopy, x-ray diffraction, and x-ray photoelectron spectroscopy. In vitro studies were carried out using co-cultures of human umbilical vein endothelial cells (HUVECs) with allogeneic peripheral blood mononuclear cells, and immunomodulatory function was assessed using flow cytometry and RNA sequencing. A rat aortic transplantation model was used for in vivo validation of safety and immunomodulatory function. $Ti_3C_2T_x$ MXene nanosheets were 2 to 5 μm in size and enriched with biologically active surface groups, including carboxyl, hydroxyl, and fluorine. In vitro, MXene nanosheets interacted with