Quantifying the Immune Response to Tissue Engineered Porcine Extracellular Matrix

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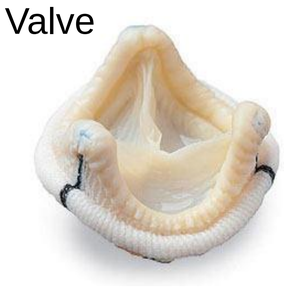
Background

Valvular heart disease is a relatively common condition with an estimated 2.5% of the worlds population having surgical valvular heart disease and approximately 250,000 heart valve replacements being performed every year. and is predicted to reach 850,000 by 2050. There are 3 main types of valve replacements, each with their own limitations.

Bioprosthetic (Tissue) Valve



Susceptible to structural valvular deterioration.
As high as 50% failure at 5 years in certain populations.

Mechanical Valve

Highly thrombogenic. Require lifelong anticoagulation with coumadin carrying a 2% per year risk of major bleeding.

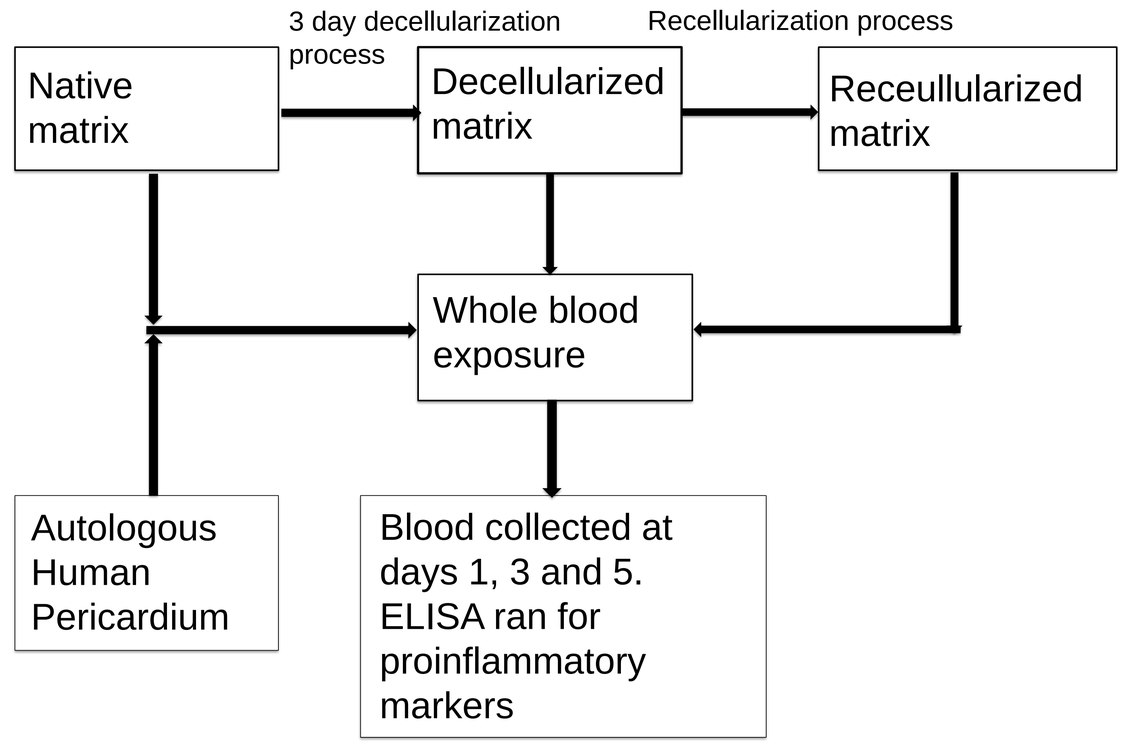
Allograft Valve

Limited availability.

Purpose

None of the current options are ideal and each of the shortfalls is significant. We look to create a superior prosthetic valve replacement. A durable, cost effective replacement that does not require anticoagulation.

Methods



Hypothesis

Tissue engineering by decellularizing tissue and reseeding with autologous progenitor cells will attenuate the humoral and cell mediated immune response to valve material exposed to whole blood increasing the durability and longevity of a bioprosthetic valve.

Results

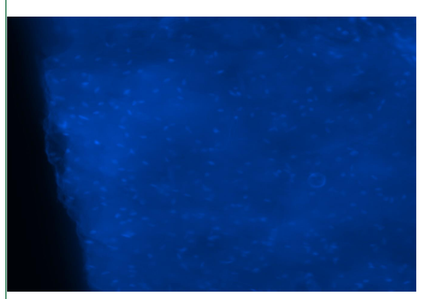


Figure 1. DAPI stain of native porcine matrix showing nuclei.

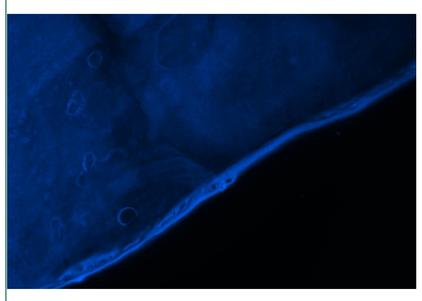


Figure 2. DAPI stain of decellularized porcine matrix showing absence of nuclei.

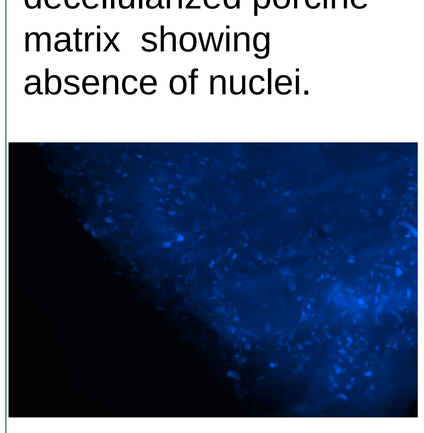


Figure 3. DAPI stain of recellularized porcine matrix showing human nuclei.

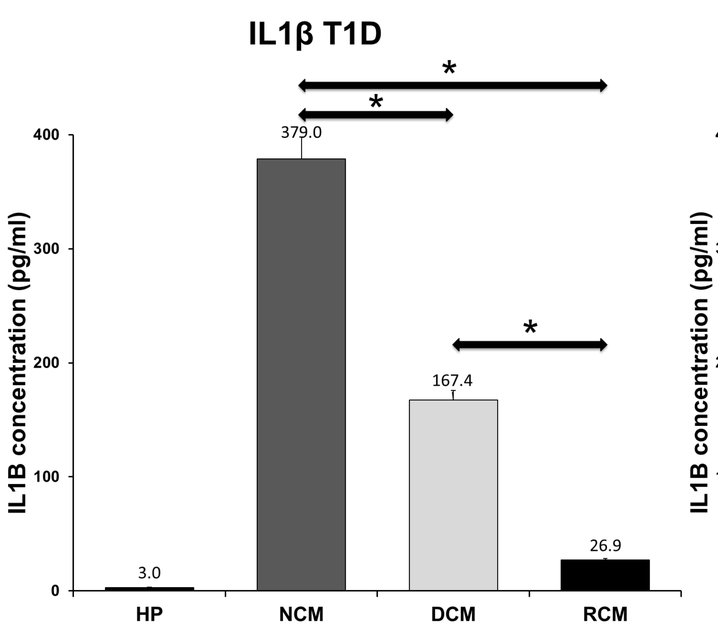


Figure 4. IL1β cytokine concentration at 1 day of whole blood exposure. NCM: Native matrix, DCM: Decellularized matrix, RCM: Recellularized matrix, HP: Autologous Human Pericardium.
Unpaired T Test NCM:DCM *P=0.00026, NCM:RCM P=0.00024, DCM:RCM P=0.0034.*

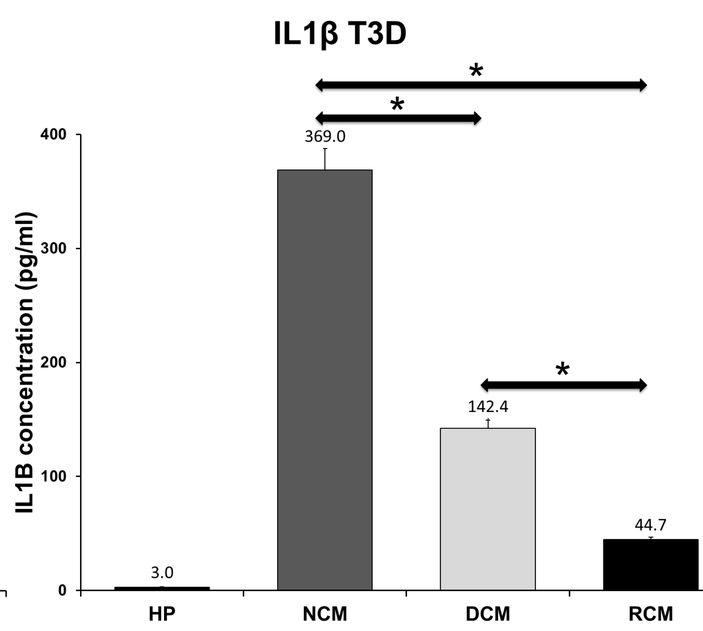


Figure 5. IL1β cytokine concentration at 3 days of whole blood exposure. NCM: Native matrix, DCM: Decellularized matrix, RCM: Recellularized matrix, HP: Autologous Human Pericardium.
Unpaired T Test NCM:DCM *P=0.0011, NCM:RCM P=0.00095, DCM:RCM P=0.047.*

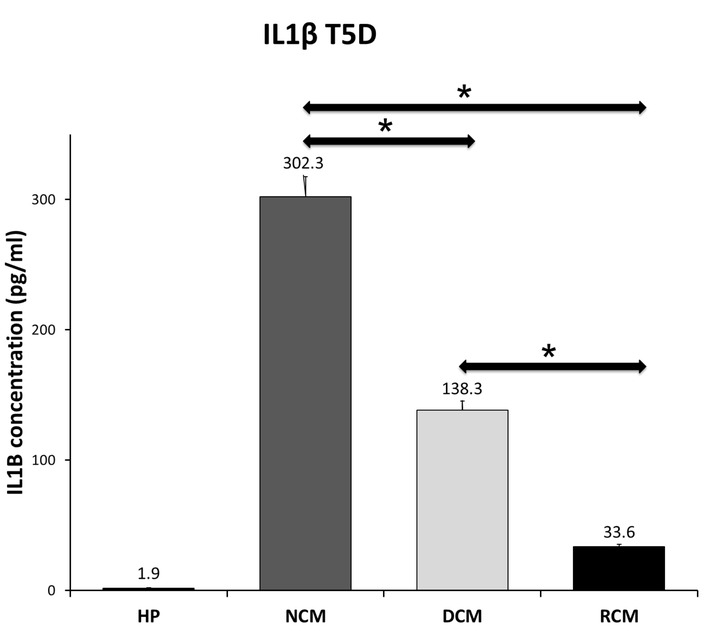


Figure 6. IL1β cytokine concentration at 5 days of whole blood exposure. NCM: Native matrix, DCM: Decellularized matrix, RCM: Recellularized matrix, HP: Autologous Human Pericardium.
Unpaired T Test NCM:DCM *P=0.0085, NCM:RCM P=0.0018, DCM:RCM P=0.017*

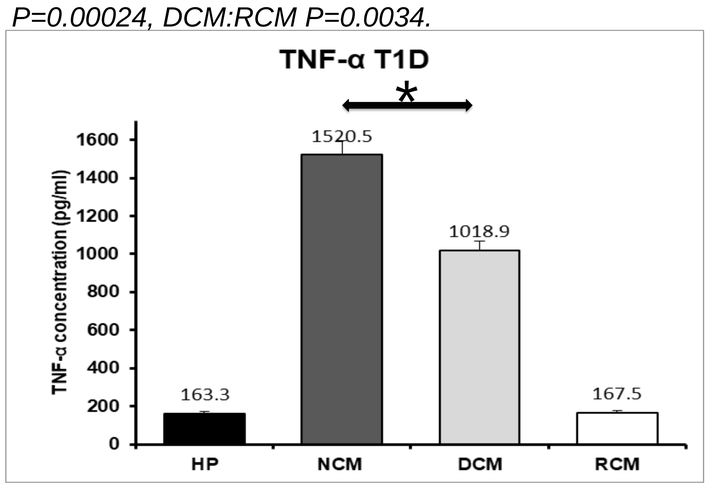


Figure 7. TNF-α cytokine concentration at 1 day of whole blood exposure. NCM: Native matrix, DCM: Decellularized matrix, RCM: Recellularized matrix, HP: Autologous Human Pericardium.
Paired T Test NCM:DCM, *P=.007.*

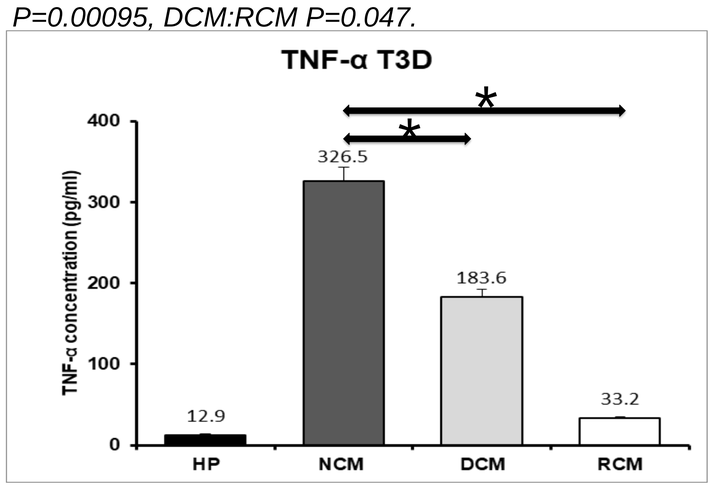


Figure 8. TNF-α cytokine concentration at 3 days of whole blood exposure. NCM: Native matrix, DCM: Decellularized matrix, RCM: Recellularized matrix, HP: Autologous Human Pericardium.
Unpaired T Test NCM:DCM, *P=.01. P*aired T Test NCM:RCM, *P=.02*

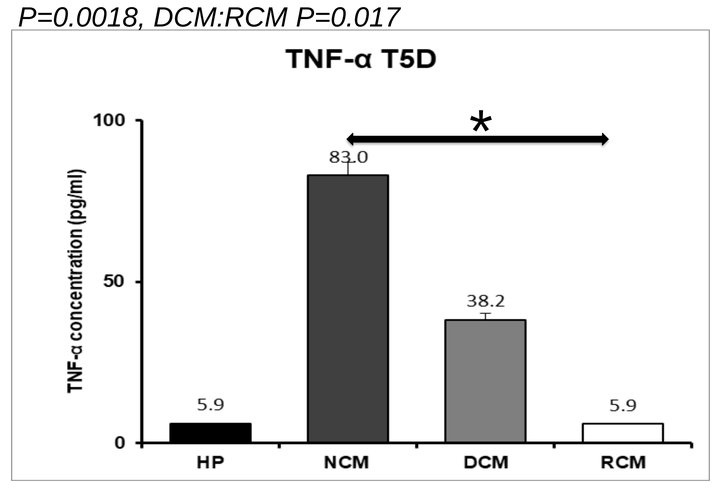


Figure 9. TNF-α cytokine concentration at 5 days of whole blood exposure. NCM: Native matrix, DCM: Decellularized matrix, RCM: Recellularized matrix, HP: Autologous Human Pericardium.
Paired T Test NCM:RCM, *P=.03*

Conclusion

Absence of original cells and presence of autologous cells along with reduced proinflammatory immune cytokines suggests tissue engineering a porcine extracellular matrix effectively and significantly attenuates the inflammatory immune response indicating that it may be an effective scaffold for bioprosthetic heart valve replacements.

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