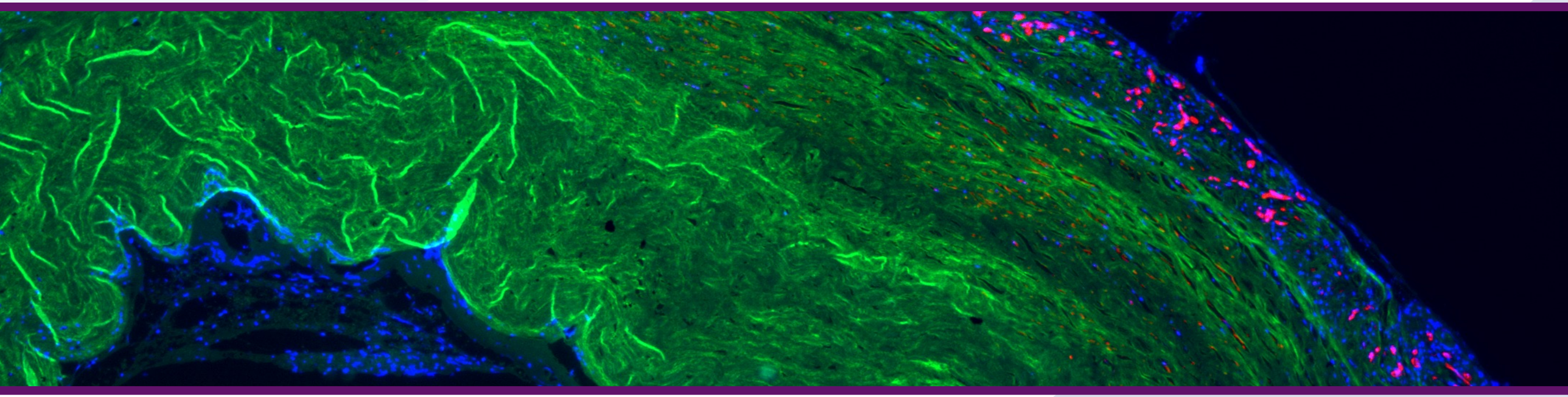

The Future of Engineered Tissues & Potential for Organ Transplantation

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DISCLOSURES

FINANCIAL DISCLOSURE:

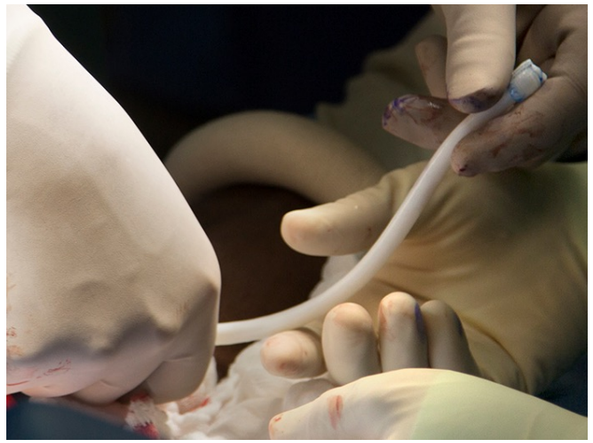
Chief Surgical Officer; Humacyte, Inc.
Dr. Lawson receives salary, and holds stock options, from Humacyte.

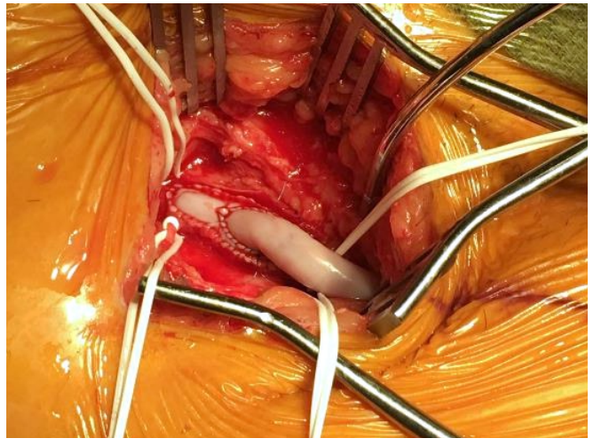
DISCLAIMER:

None of the data presented in this lecture is intended to be perceived as “claims” for the potential clinical use, efficacy, or safety of the vascular tissues discussed today.

The HAV is an investigational product that has not been approved by the FDA for any indication.

KEY FEATURES OF THE HUMAN ACELLULAR VESSEL (HAV) TECHNOLOGY

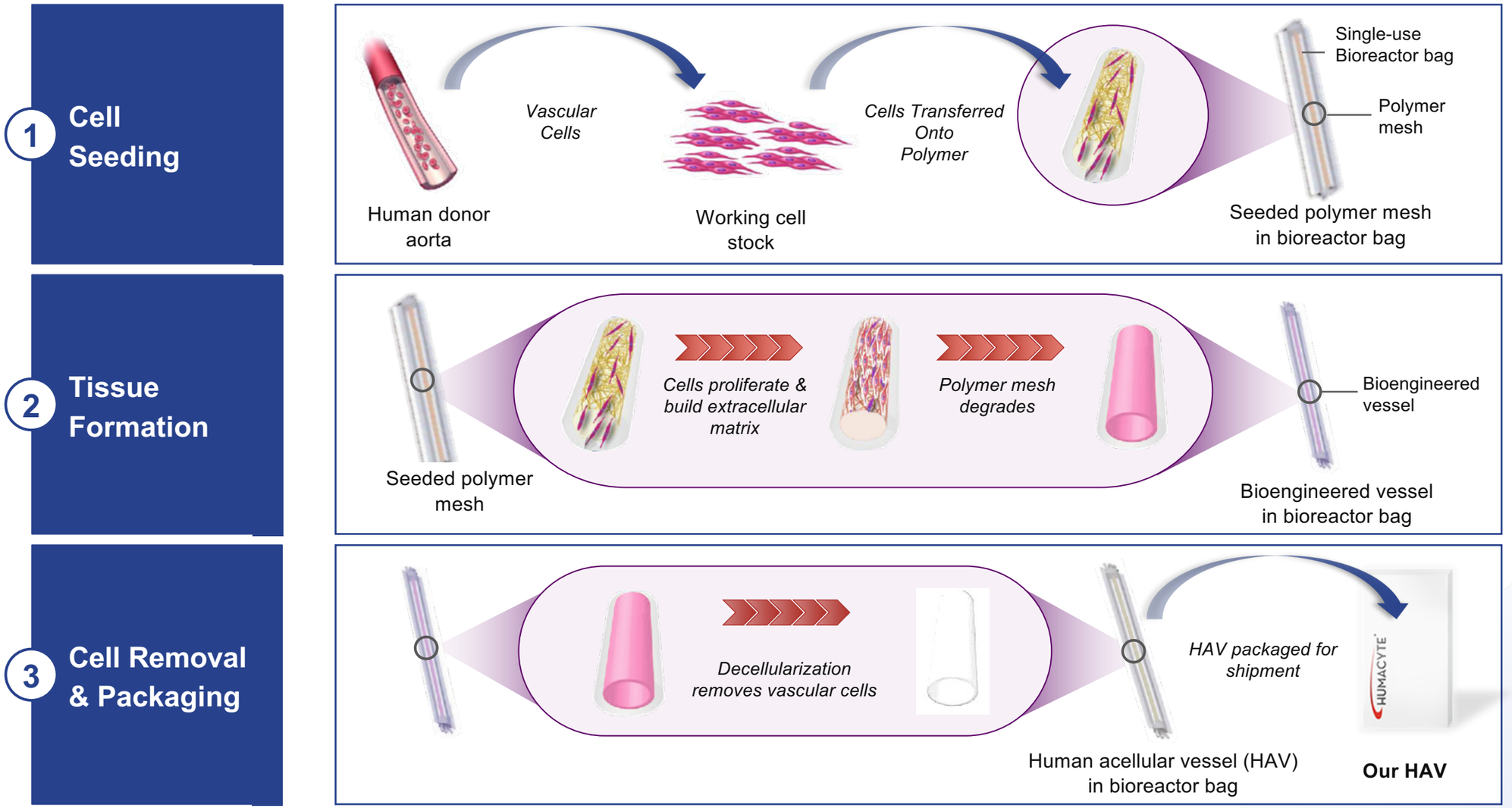




Potential benefits of HAV evaluated in completed and ongoing clinical trials include:

- Off-the-shelf, immediately available
- Repopulates with cells and thereby transforms into patient's own tissue
- HAV appears to be highly resistant to infection
- HAV has no evidence of immunogenicity
- Usable for dialysis access within one month after implantation
- Potential for decreased catheter contact time as compared to patients awaiting fistula maturation
- Long-term durability in ongoing studies.

BIOENGINEERED HUMAN ACELLULAR VESSELS (HAVs)



THE HAV DOES NOT STIMULATE INCREASES IN PANEL REACTIVE ANTIBODIES

There have been no reported instances of clinical HAV rejection observed in any patient with more than 430 patients evaluated overall.

Calculated Panel Reactive Antibodies (cPRA) have been measured in many HAV clinical studies to determine potential sensitization, with more than 250 patients evaluated to date.

- Less than 4% of HAV patients reported an increase over baseline values
- Less than 2% of patents reported an increase of more than 20% over baseline

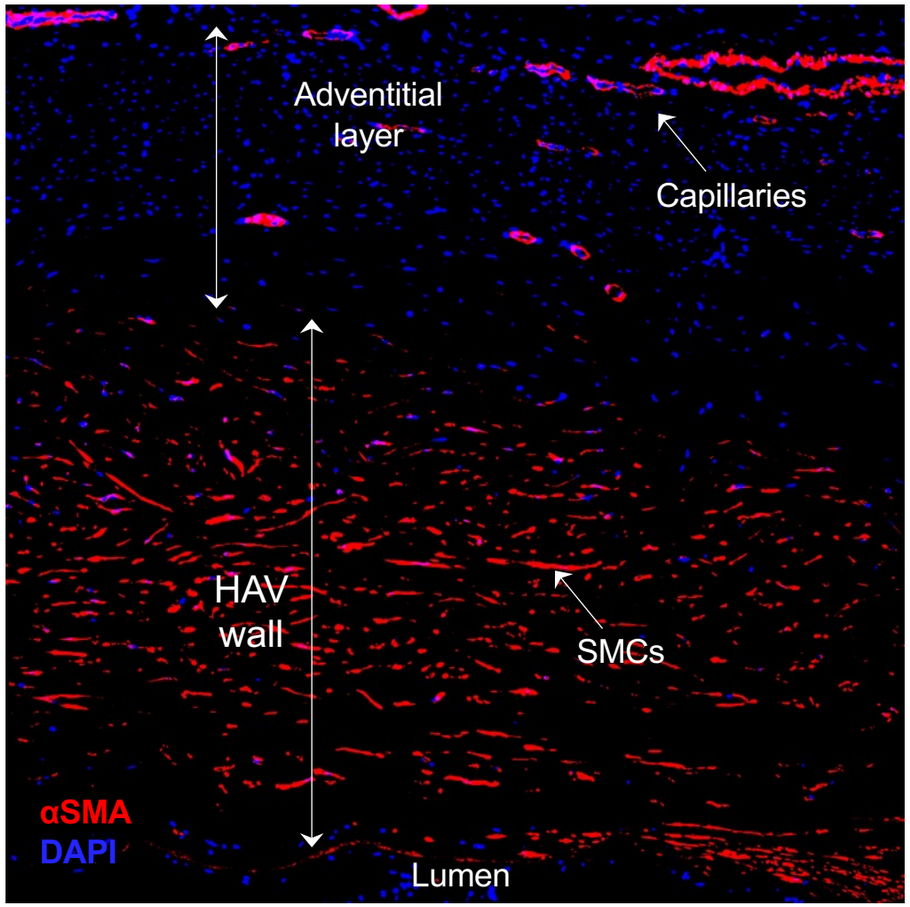
For patients awaiting a transplant, changes in PRA values are closely monitored and evaluated as part of the organ matching and allocation considerations

- Patients with increases in PRA over 20% are viewed as “highly sensitized”, are less likely to be successfully matched to an immunologically compatible donor candidate [1]
- Published literature on kidney transplants considers a patient with a cPRA of >20% to be highly sensitized [2]

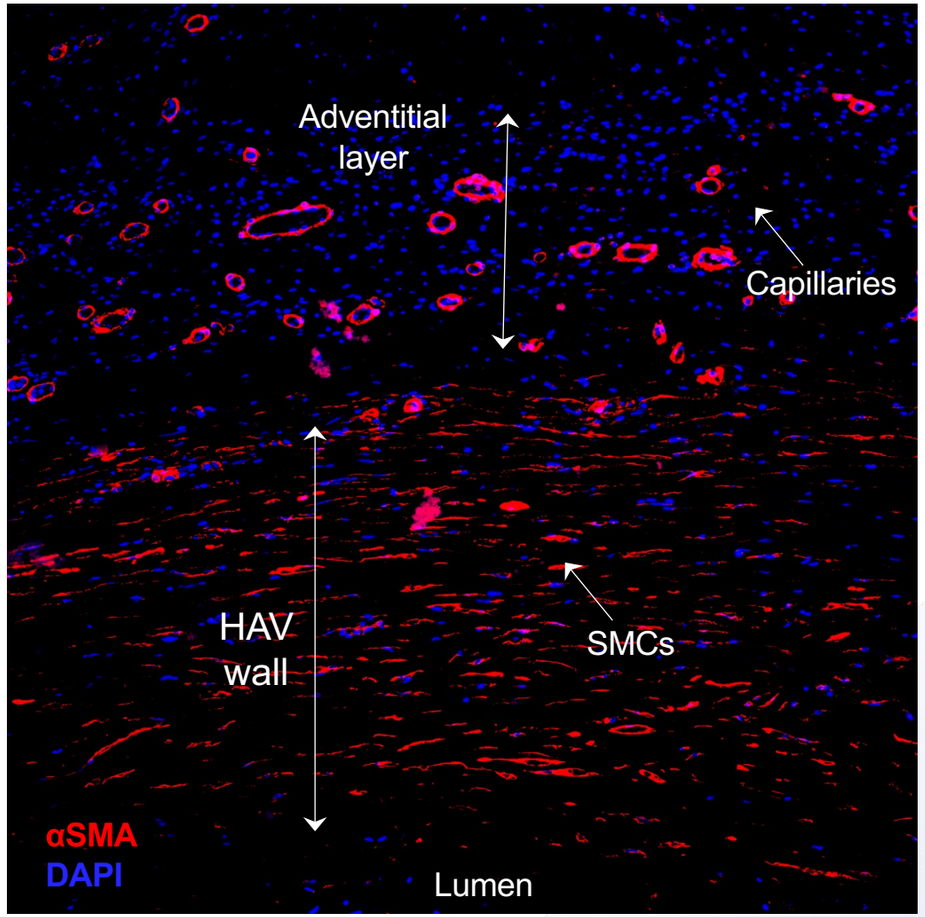
[1] Hemodialysis International 2020; 24:36–42
[2] Clinical Transplant 2011, Terasaki Foundation Laboratory, Los Angeles, California

REMODELING OF THE HAV IS CONSISTENT and STRONGLY ANGIOGENIC

Subject 3079-012-V006, male, 26 years old.
67 weeks post-implantation of HAV



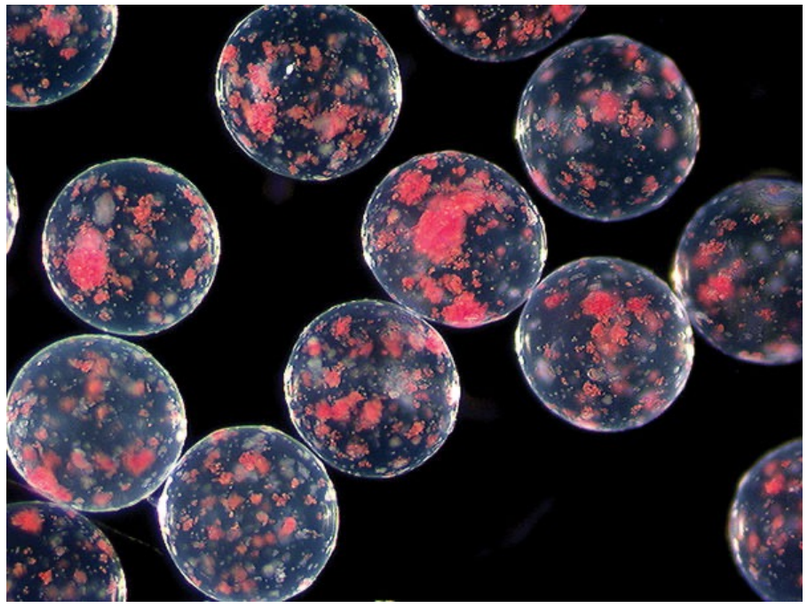
Subject 1006-001-V006, male, 83 years old.
66 weeks post-implantation of HAV



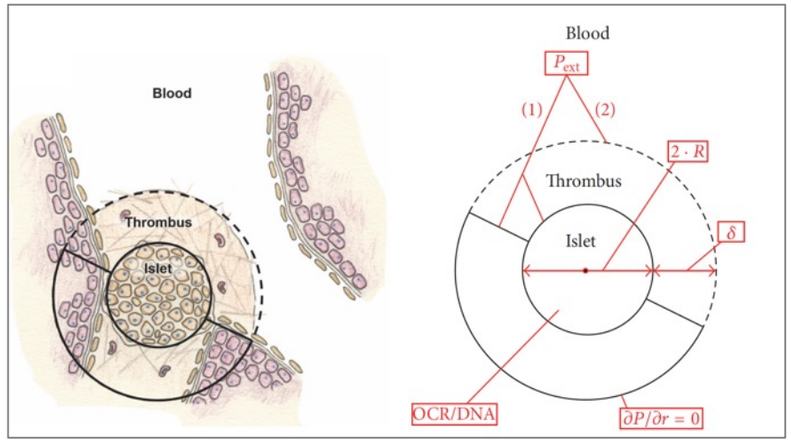
Patient cells remodel the HAV across a wide range of patient ages.
Repopulation with vascular cells is combined with robust peri-HAV angiogenesis.

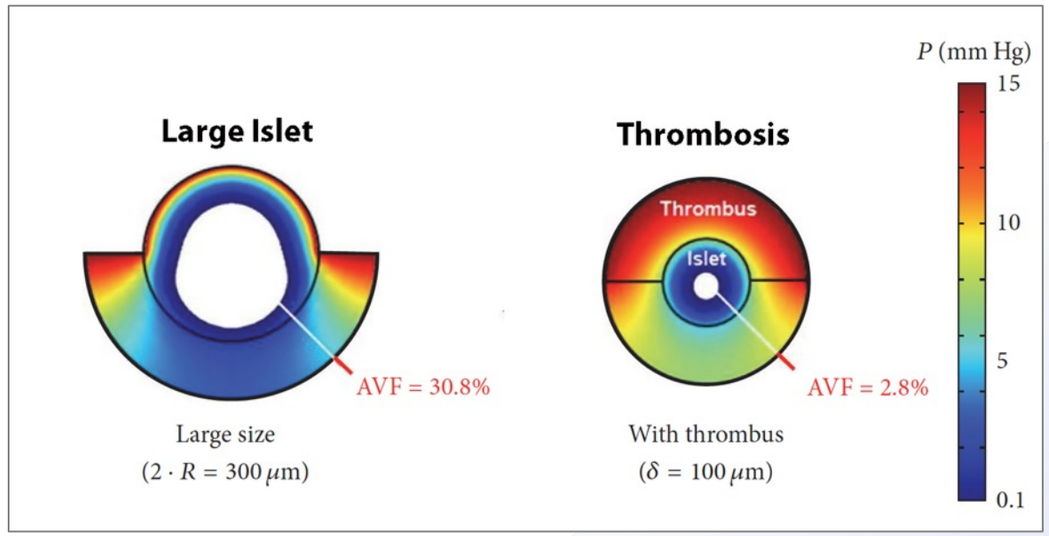
DEVELOPMENT OF ISLET & INSULIN MANAGEMENT THERAPIES
ISLET TRANSPLANTATION LEADS TO SIGNIFICANT ISLET HYPOXIA

Microencapsulation [1]



Edmonton Protocol – Portal Vein Injection [2]



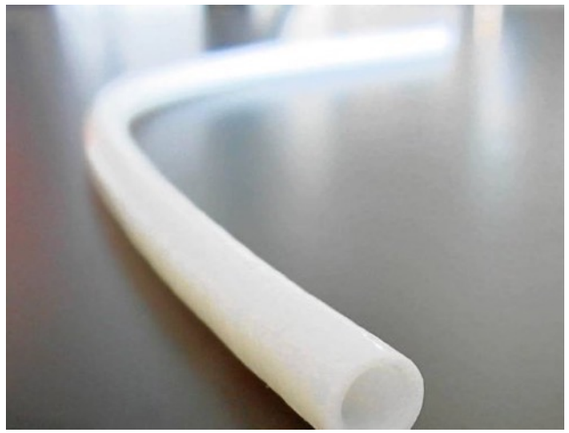


[1] Tomei 2016
[2] Suszynski T.M. et al Journal Diabetes Research 2016.

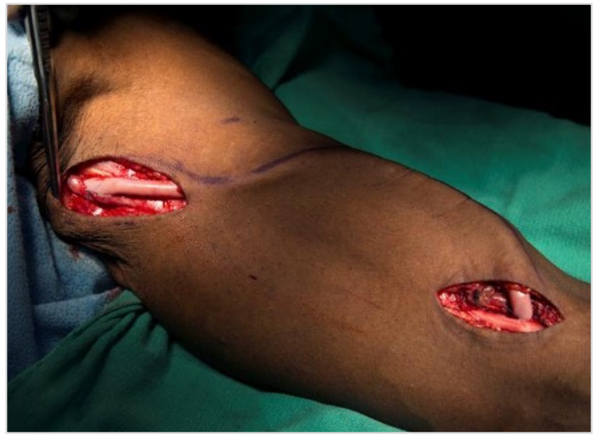
CAN WE USE THE HAV TO TRANSPLANT THERAPEUTIC CELLS?
BIOVASCULAR PANCREAS DESIGN MAY REDUCE ISLET HYPOXIA

HUMACYTE®

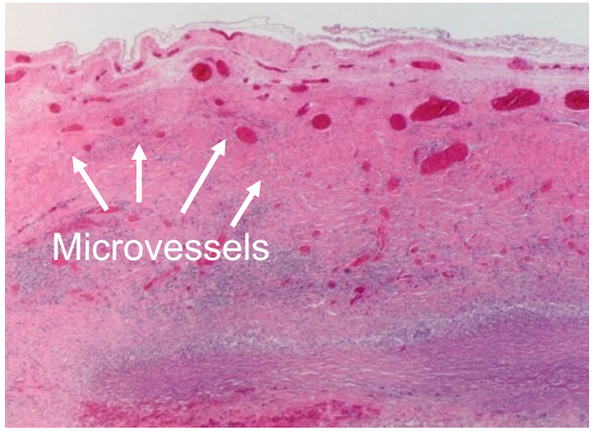
HAV



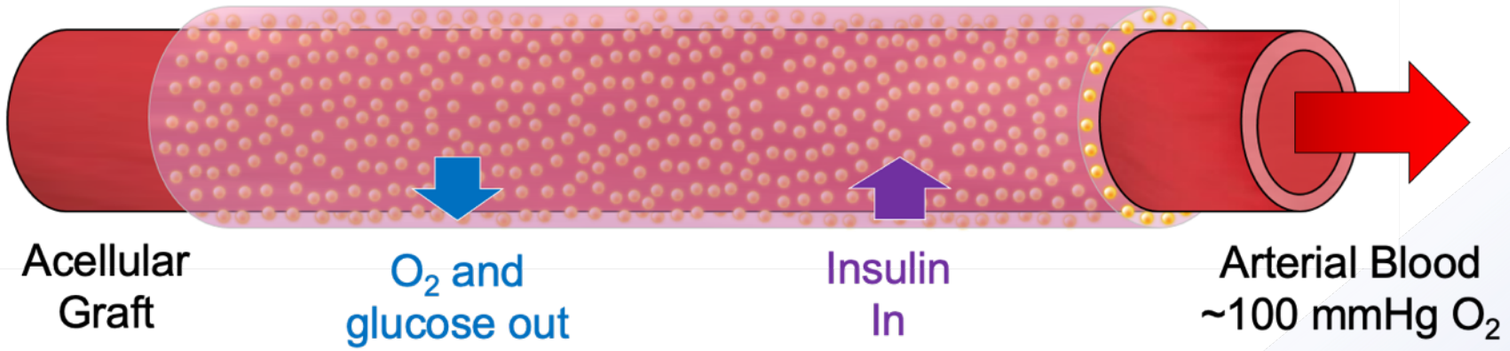
Arteriovenous HAV Conduit
Arterial Blood Flow ~ 1L/min



Microvascularization of Peri-HAV Tissue



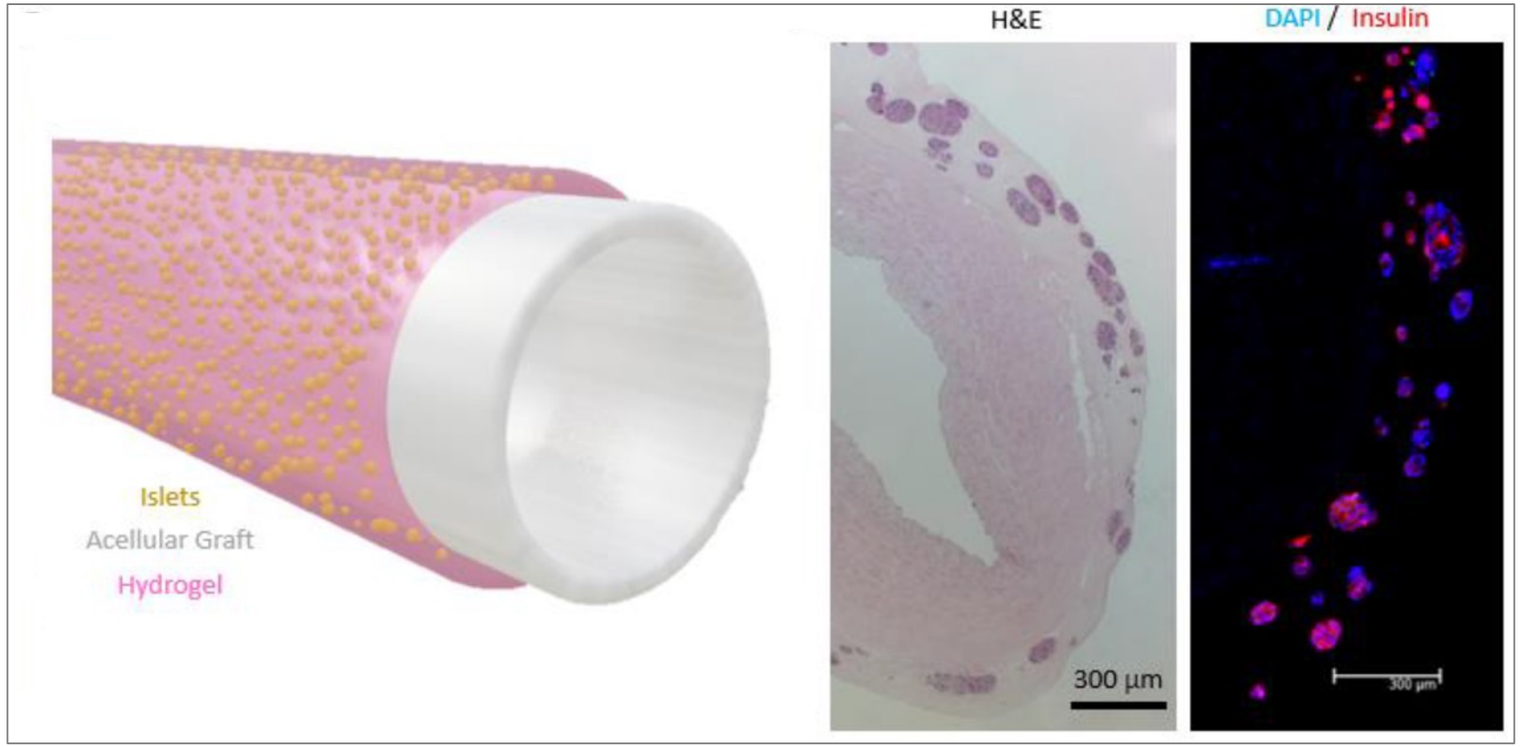
BioVascular Pancreas
Islets in Hydrogel Coating

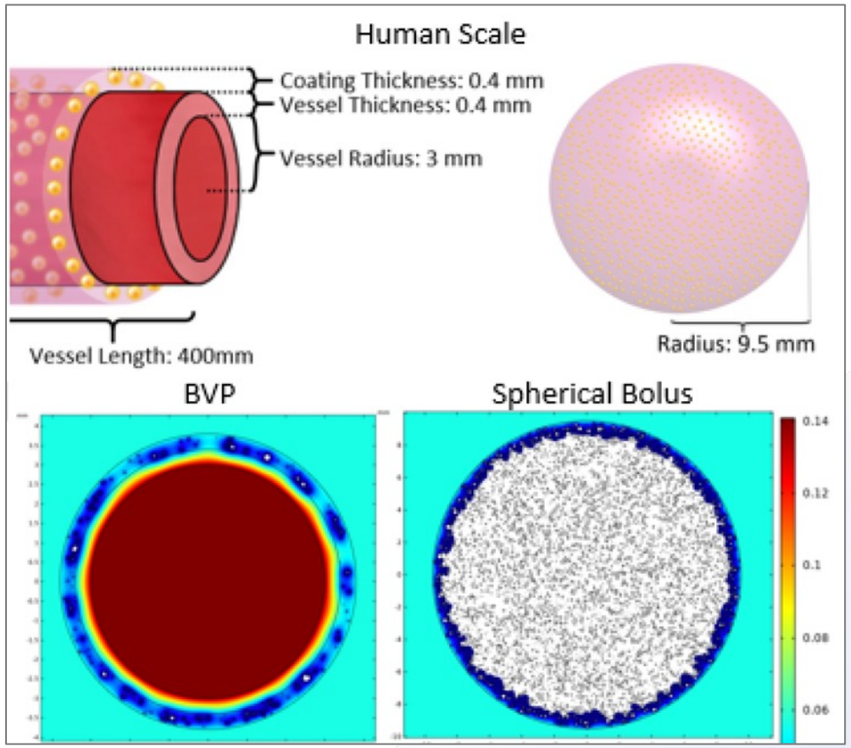


HUMAN ACELLULAR VESSELS COULD DELIVER ISLETS *IN VIVO*

42-cm x 6mm diameter HAV can accommodate ~ 800,000 islets
(approximately the total islet complement of a human pancreas)

Islets can oxygenate as a sheet.
As a sphere → severe hypoxia.

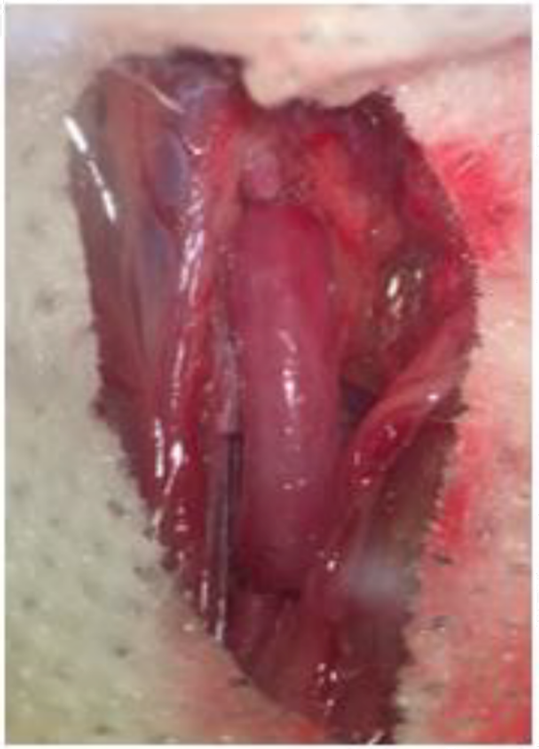




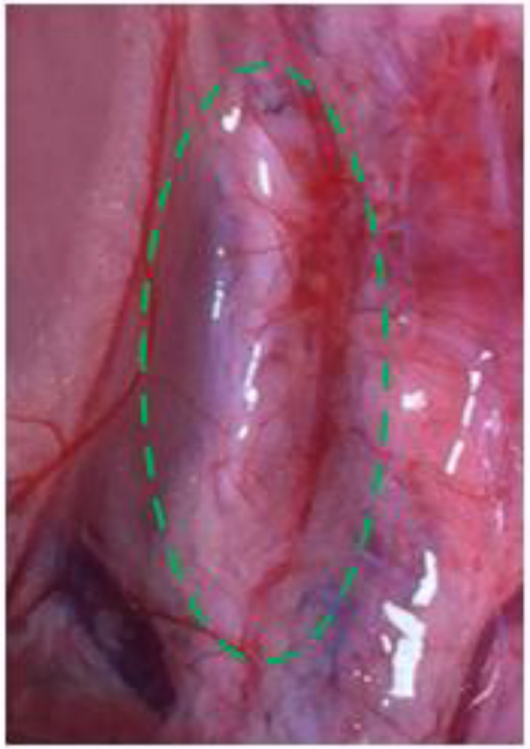
The acellular vessel may provide oxygenation and mass transfer to a therapeutic number of human islets.

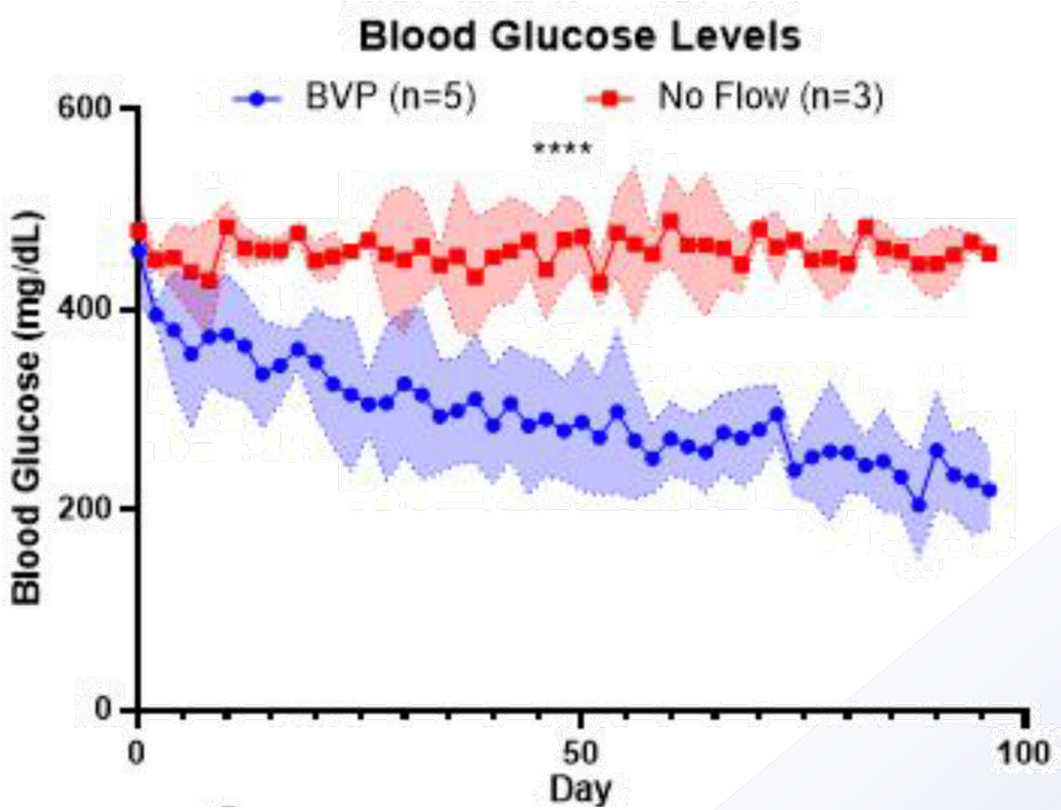
BVP IN A DIABETIC SMALL ANIMAL MODEL NORMALIZES BLOOD GLUCOSE

BVP Implant



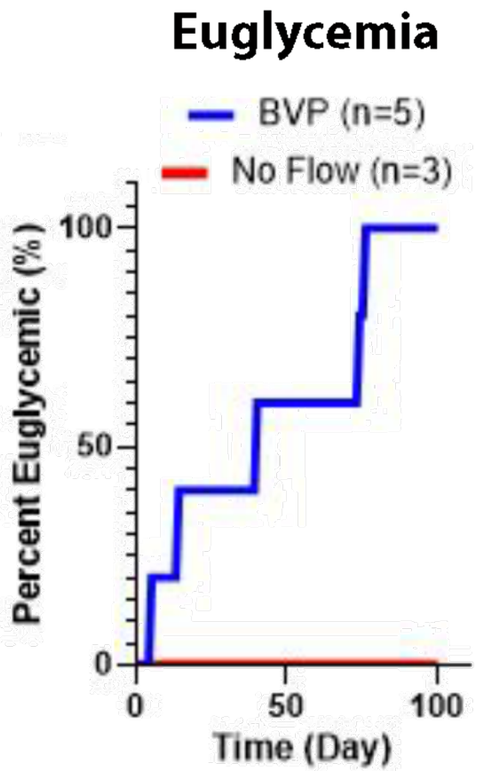
BVP Explant

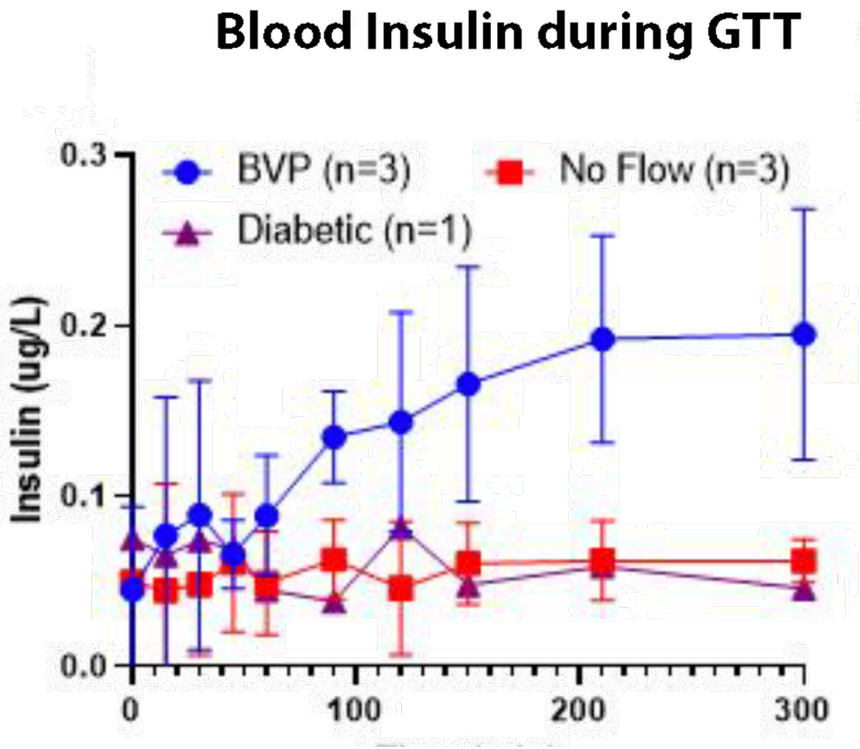


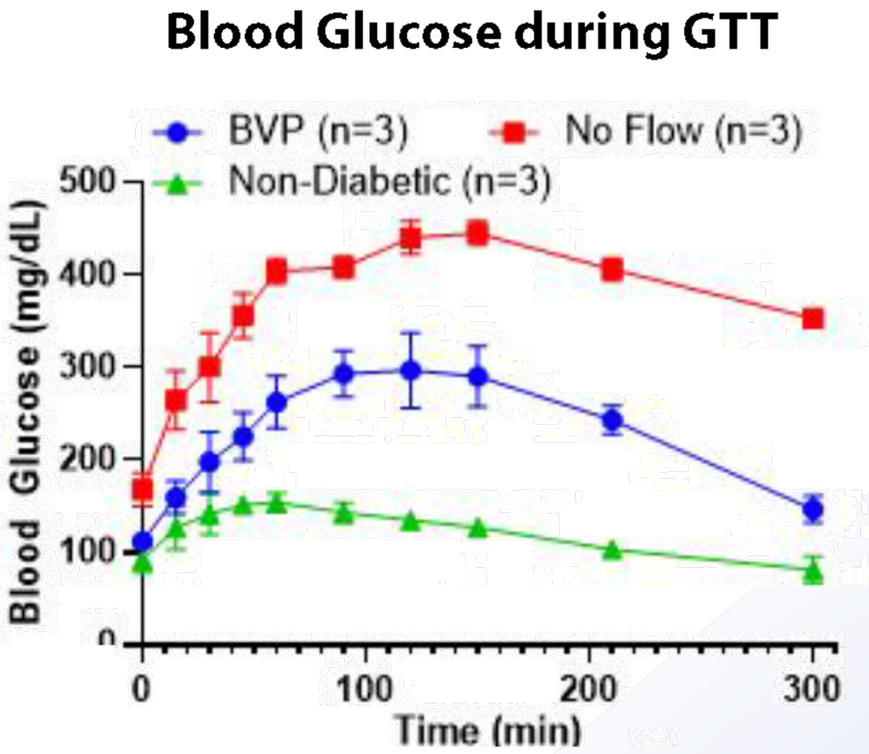


Luminal arterial blood flow supports islets at time of implantation.
Angiogenesis, visible at 8 weeks, supports microvascularization of implanted islets.

BVPs PRODUCE EUGLYCEMIA AND IMPROVE GLUCOSE TOLERANCE TESTS



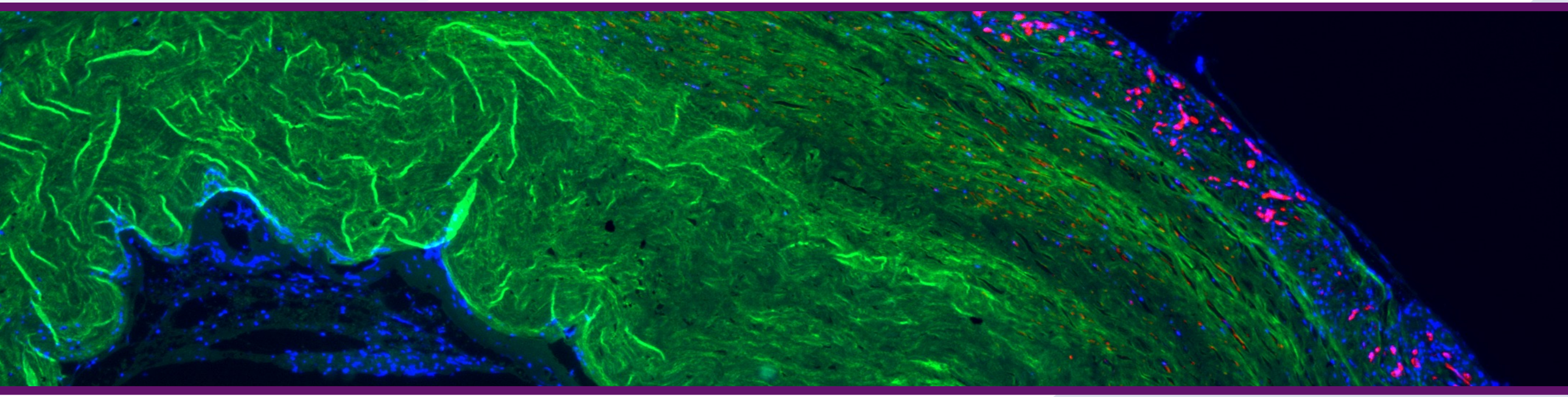




BVPs implanted into the arterial system of small animals improved Glucose Tolerance Tests (GTTs); whereas BVPs implanted adjacent to the aorta (“No Flow”) had no therapeutic effect.

CONCLUSIONS

- Humacyte's Human Acellular Vessel (HAV) is an engineered human tissue comprised of human extracellular matrix proteins.
- The HAV can be produced at commercial scale in controlled bioreactor systems.
- The HAV shows no evidence of stimulation of adaptive immunity, as measured by PRA values.
- HAV appears to be durable, with prolonged implantation times, evidence of host cell repopulation, and stimulation of extensive local angiogenesis after implantation.
- Based on the properties of the HAV, it may potentially represent an ideal way to transplant therapeutic cells into proximity of the bloodstream, to support islet graft oxygenation and vascularization.
- Rodent studies show that the BioVascular Pancreas, or BVP, can normalize blood glucose in a type I diabetic model, and scaling to human islet delivery should be feasible.
- Humacyte is working with potential partners to bring a human BVP into clinical testing.
- This is just the start of bioengineered tissues and organs for patients in need.



Engineered Blood Vessels as Transplants

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