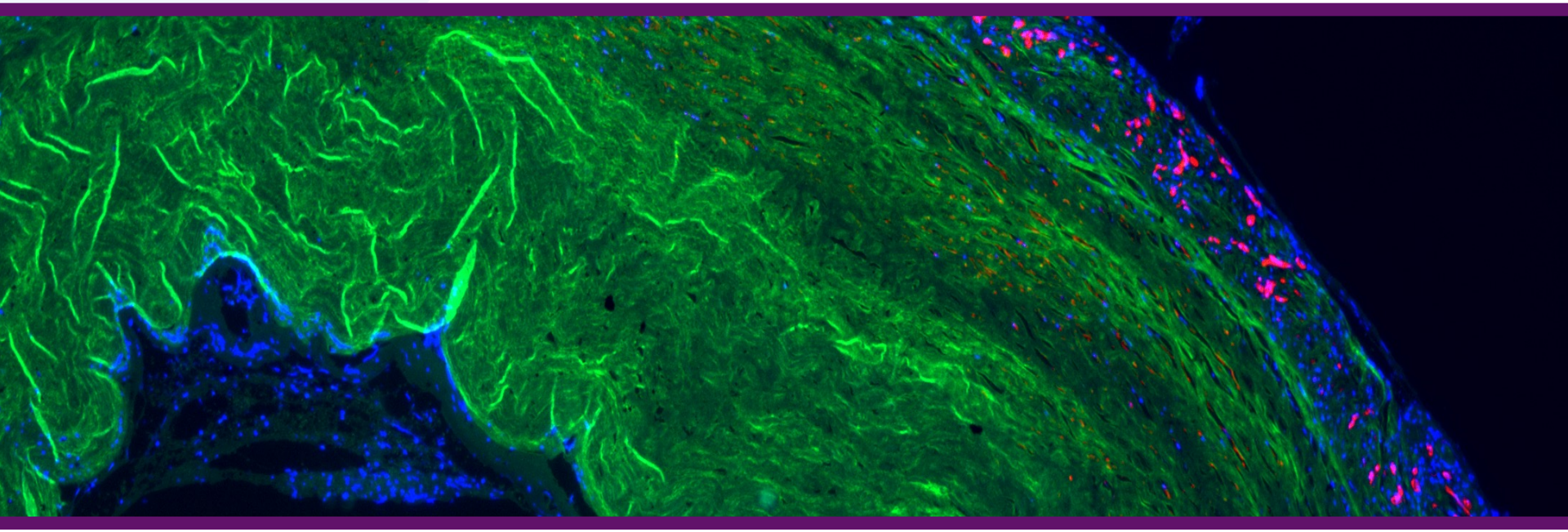

A Pancreatic Islet Transplantation Approach using an Acellular Vessel

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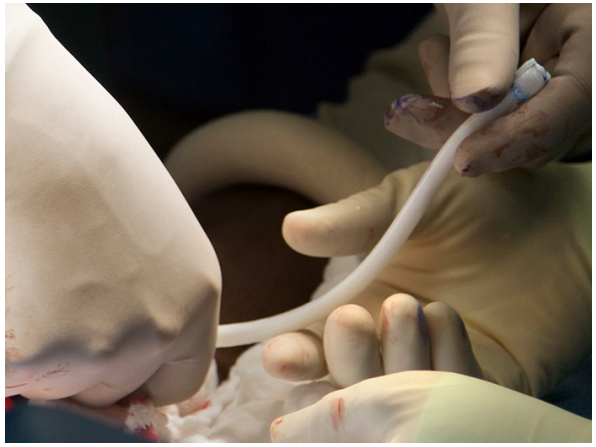
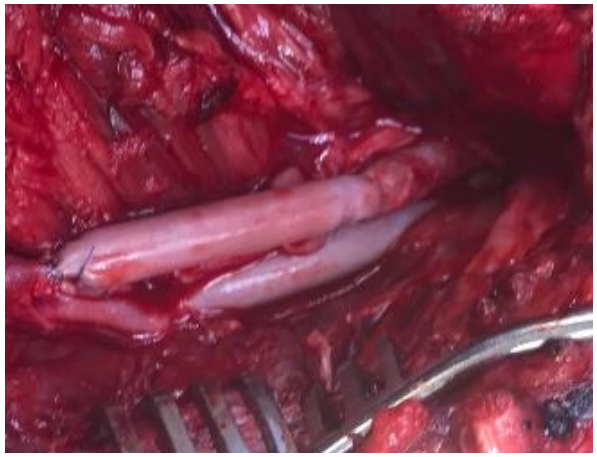
CONFLICTS OF INTEREST & DISCLOSURES

Dr. Lawson is the Chief Surgical Officer and a shareholder in Humacyte, Inc.

None of the data presented in this lecture is intended to be construed as claims for the clinical use, efficacy, or safety of any medical product. The human accellular vessel (HAV) is an investigational product that has not been approved by FDA for any indication.

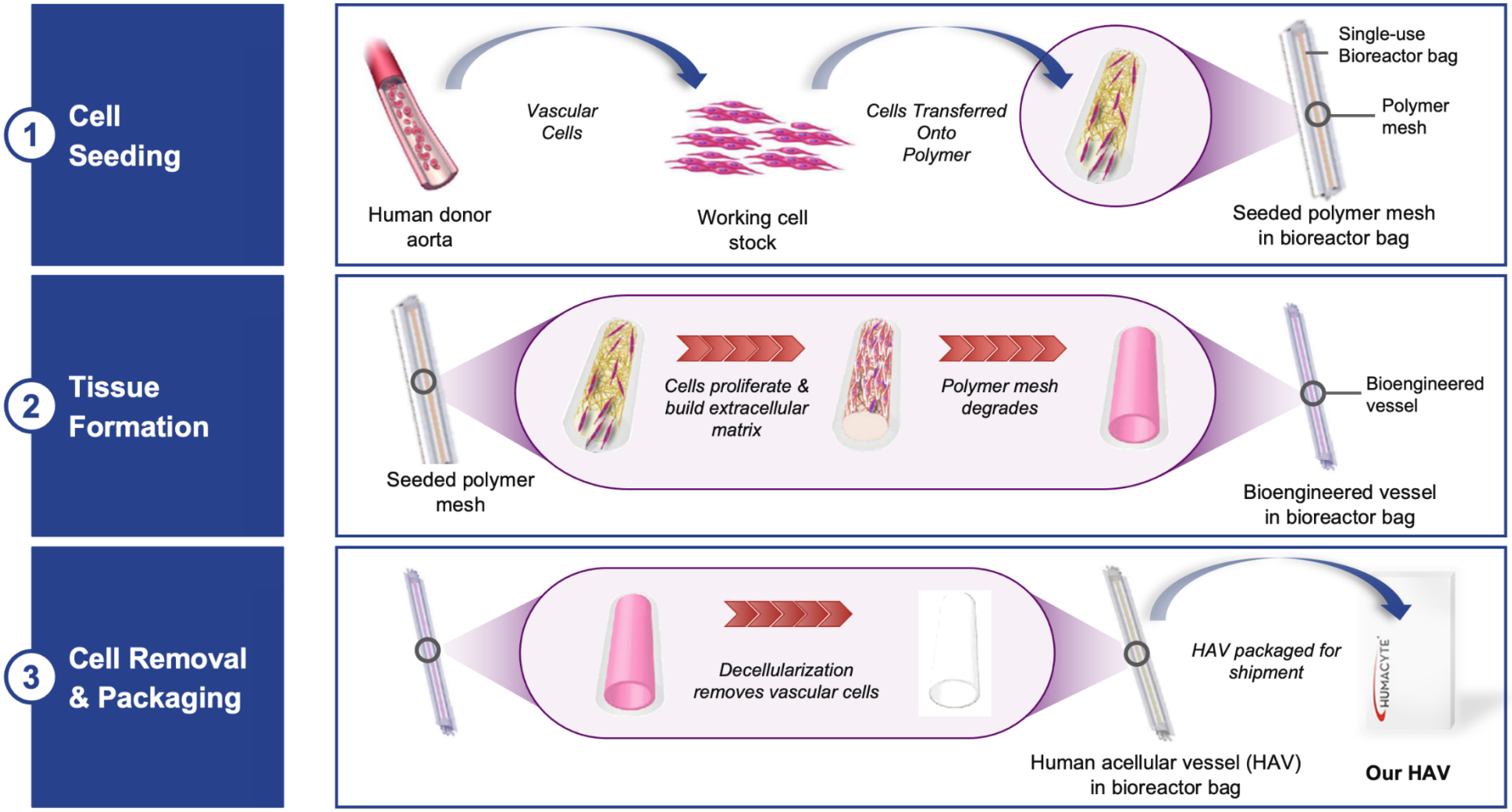
HUMAN ACELLULAR VESSEL (HAV) TECHNOLOGY
KEY EVIDENCE FROM CLINICAL TRIALS TO DATE





- Off-the-shelf, immediately available at time of need
- Repopulates with patient’s own cells and transforms into patient's own tissue
- HAV appears to be highly resistant to infection
- No evidence of immunogenicity detected
- 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

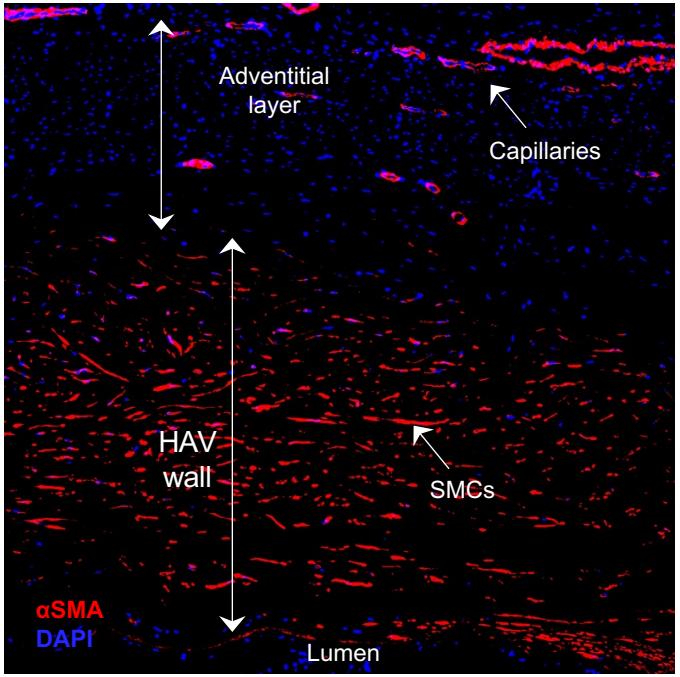
For patients awaiting a transplant, changes in PRA values are closely monitored and evaluated as part of the donor matching and organ allocation considerations

- Patients with increases in PRA levels are viewed as “sensitized” with >20% increase, or “highly sensitized” with >80% increase; and are challenged or less likely to be successfully matched to an immunologically compatible donor candidate [1, 2]

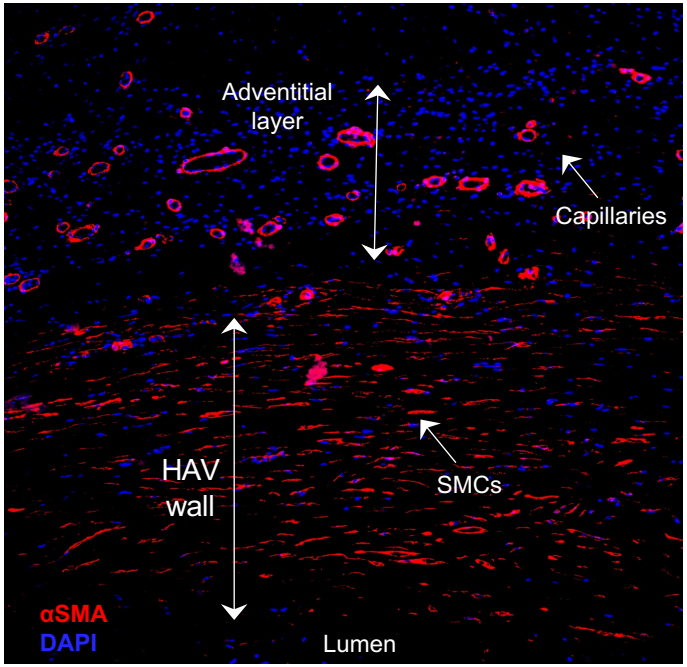
1) Hemodialysis International 2020; 24:36–42
2) Clinical Transplant 2011, Terasaki Foundation Laboratory, Los Angeles, California

REMODELING OF THE HAV IS CONSISTENT AND ANGIOGENIC

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



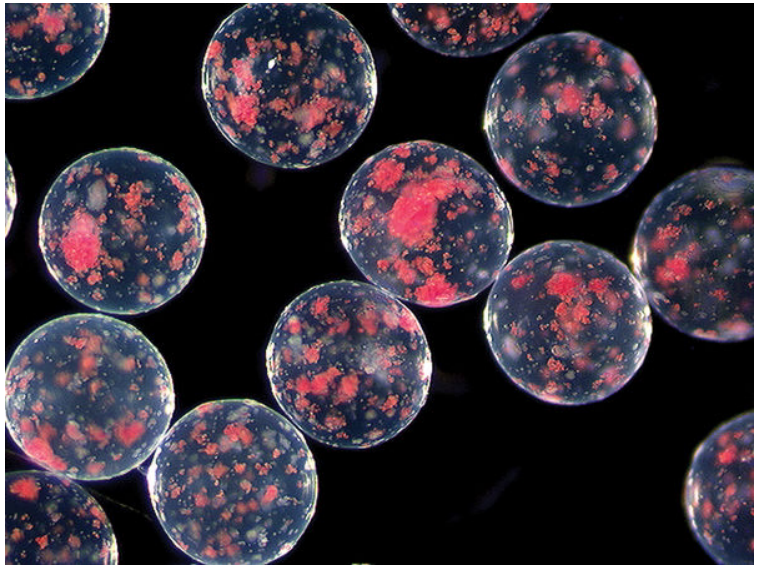
Subject 1006-001-V006, male, 83 years old.
66 weeks post-implantation of HAV



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

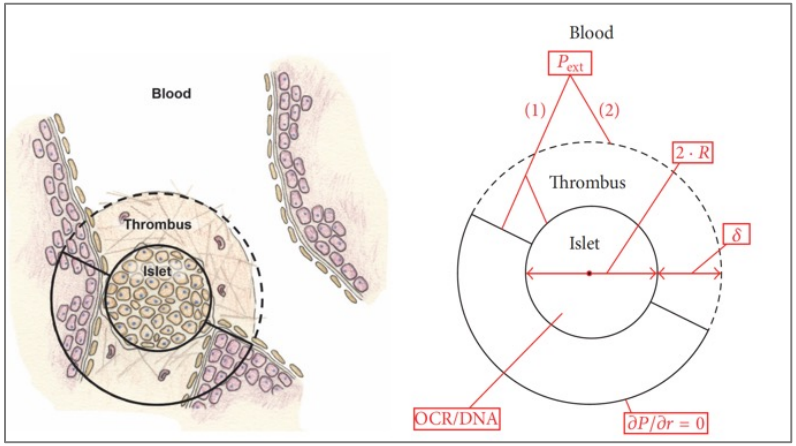
DEVELOPMENT OF ISLET & INSULIN MANAGEMENT THERAPIES
ISLET TRANSPLANTATION LEADS TO SIGNIFICANT ISLET HYPOXIA

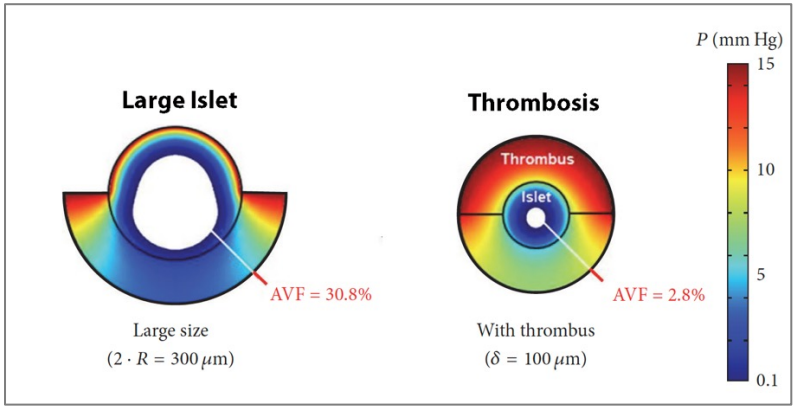
Microencapsulation



Tomei 2016

Edmonton Protocol – Portal Vein Injection

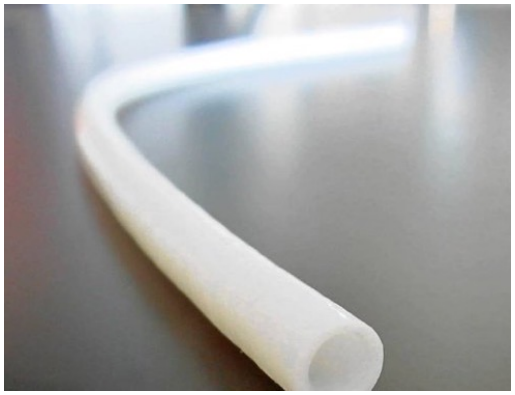




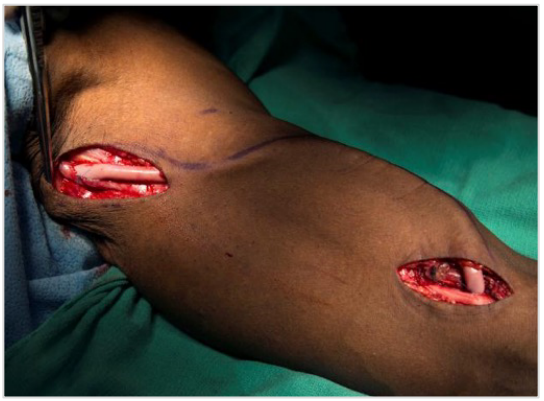
Suszynski T.M. et al Journal Diabetes Research 2016.

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

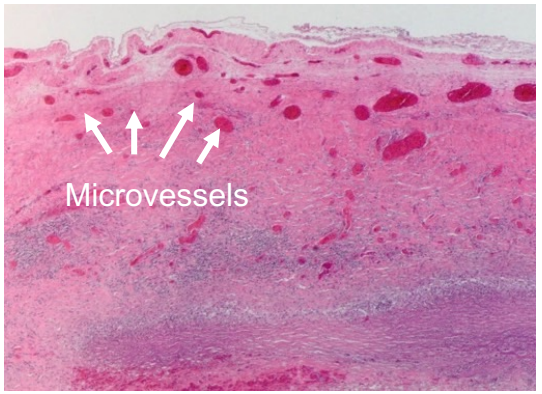
HAV



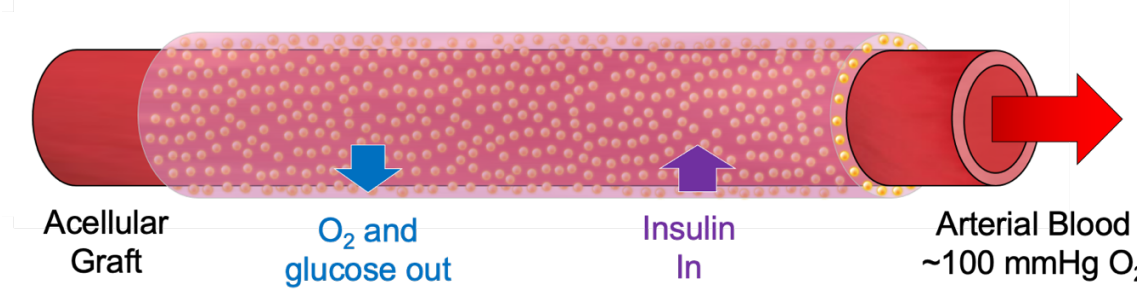
Arteriovenous HAV Conduit
Arterial Blood Flow ~ 1L/min



Microvascularization of Peri-HAV Tissue



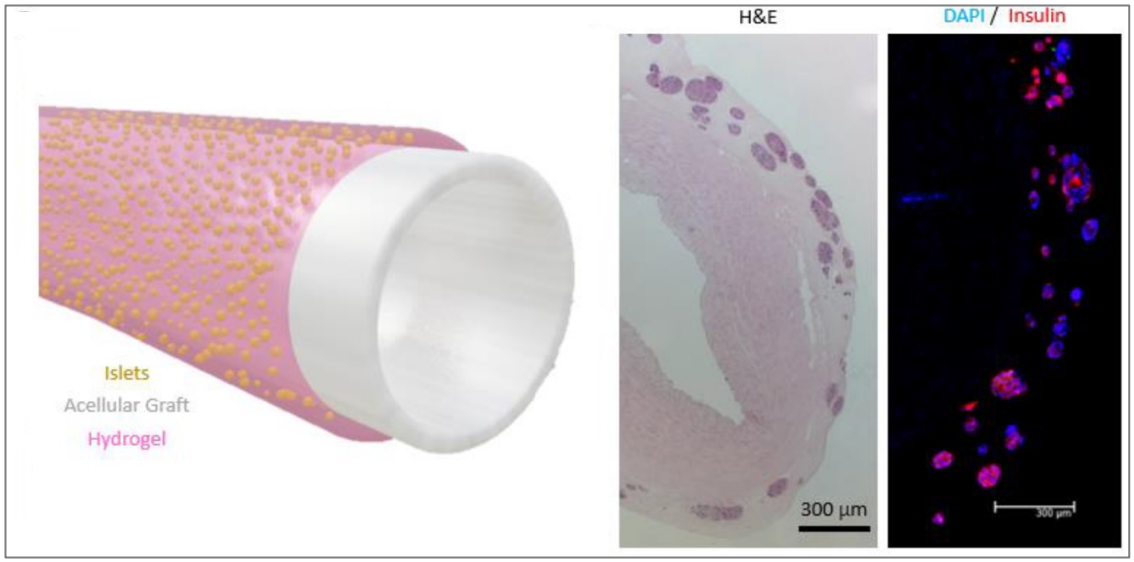
BioVascular Pancreas
Islets in Hydrogel Coating

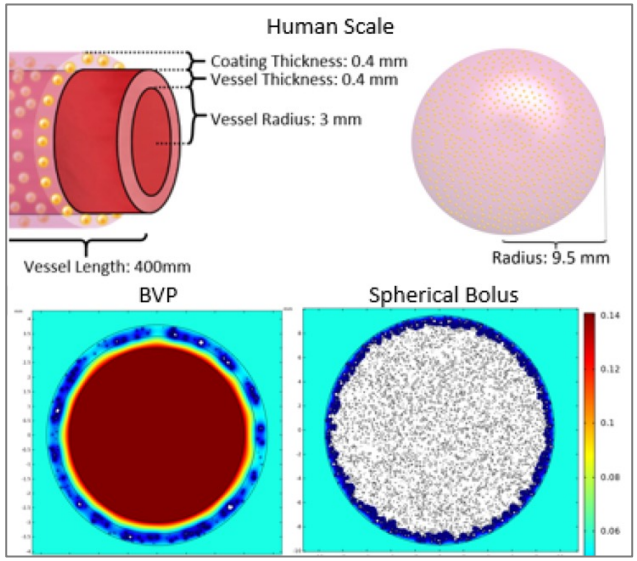


THE HAV COULD DELIVER ISLETS *IN VIVO*

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

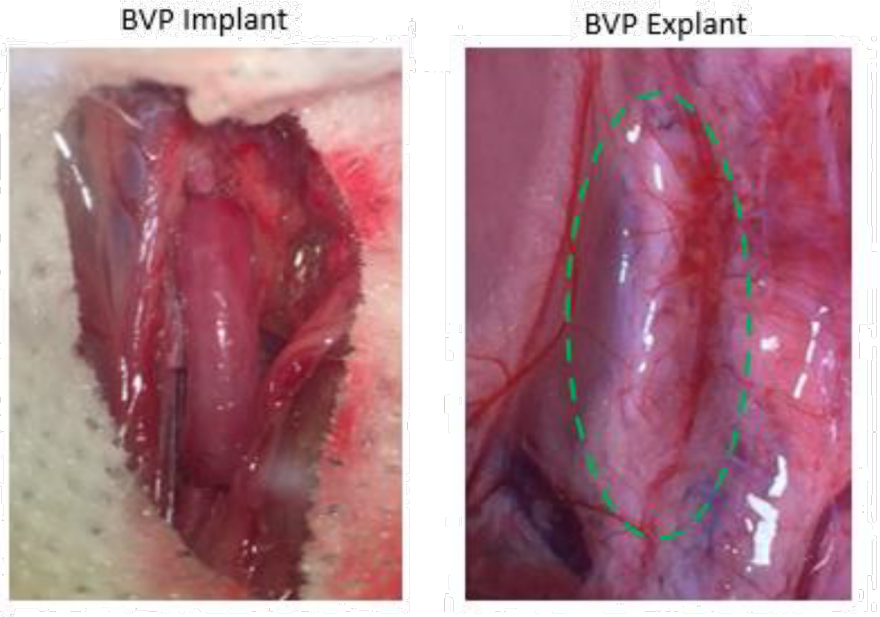
Islets can oxygenate as a sheet.
As a sphere → severe hypoxia.





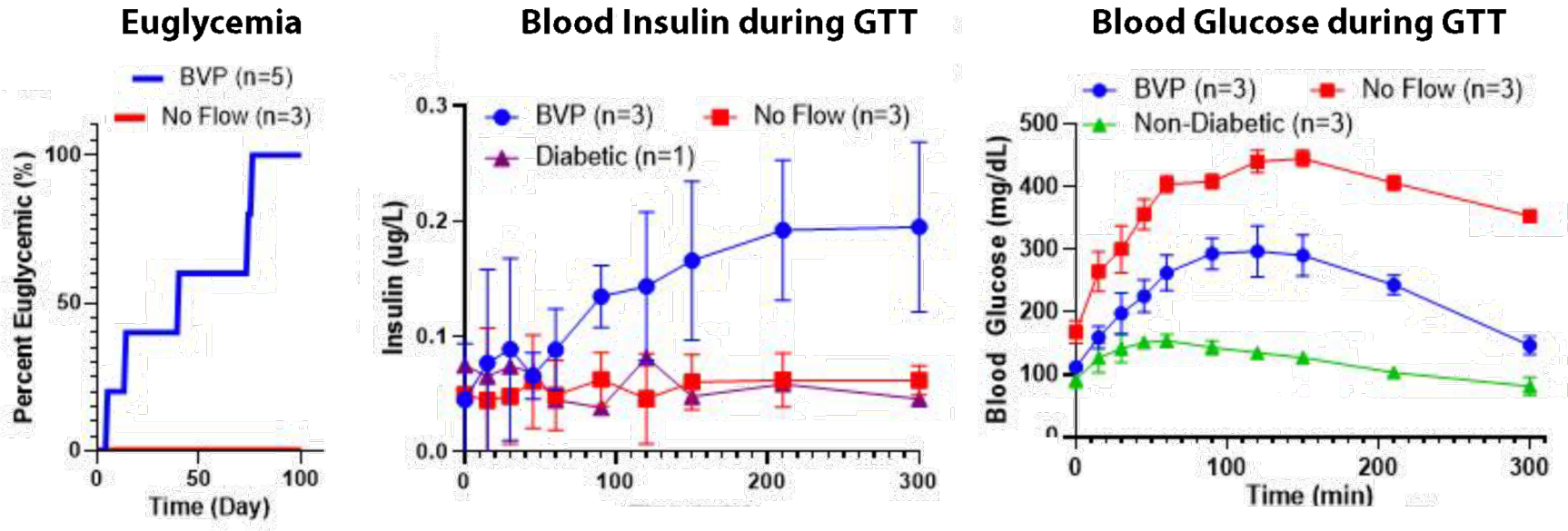
The acellular vessel may provide oxygenation and mass transfer to a therapeutic number of human islets.

BVP IN A DIABETIC SMALL ANIMAL MODEL NORMALIZES BLOOD GLUCOSE



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.

PRELIMINARY STUDIES RECENTLY PUBLISHED

Original Article

Development of a Bioartificial Vascular Pancreas

Edward X Han[1], Juan Wang[2,3], Mehmet Kural[2,3], Bo Jiang[4,5], Katherine L Leiby[1], Nazar Chowdhury[6], George Tellides[2,4,7], Richard G Kibbey[8,9], Jeffrey H Lawson[10,11] and Laura E Niklason[1,2,3,11]

Journal of Tissue Engineering
Volume 12: 1–18

DOI: 10.1177/20417314211027714
journals.sagepub.com/home/tej
SAGE

Collectively, these data support the potential of a biovascular pancreas to provide an effective method for transplanting pancreatic islets that produce insulin for the treatment of type 1 diabetes.

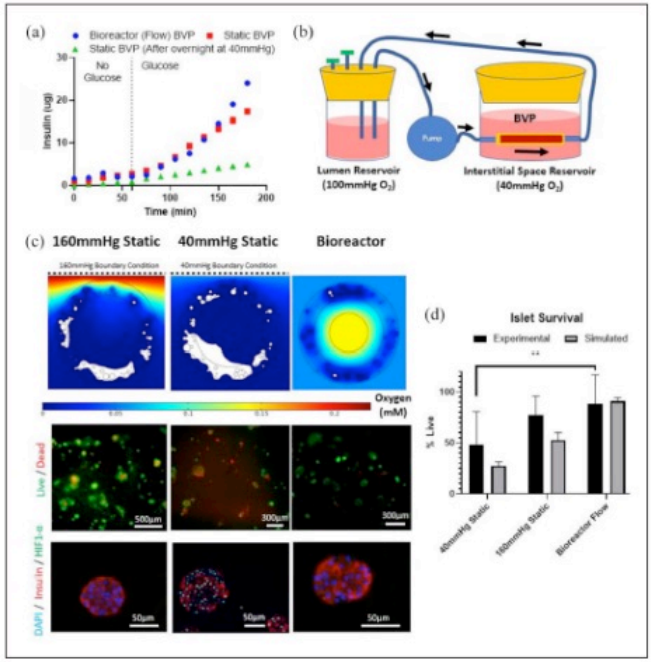
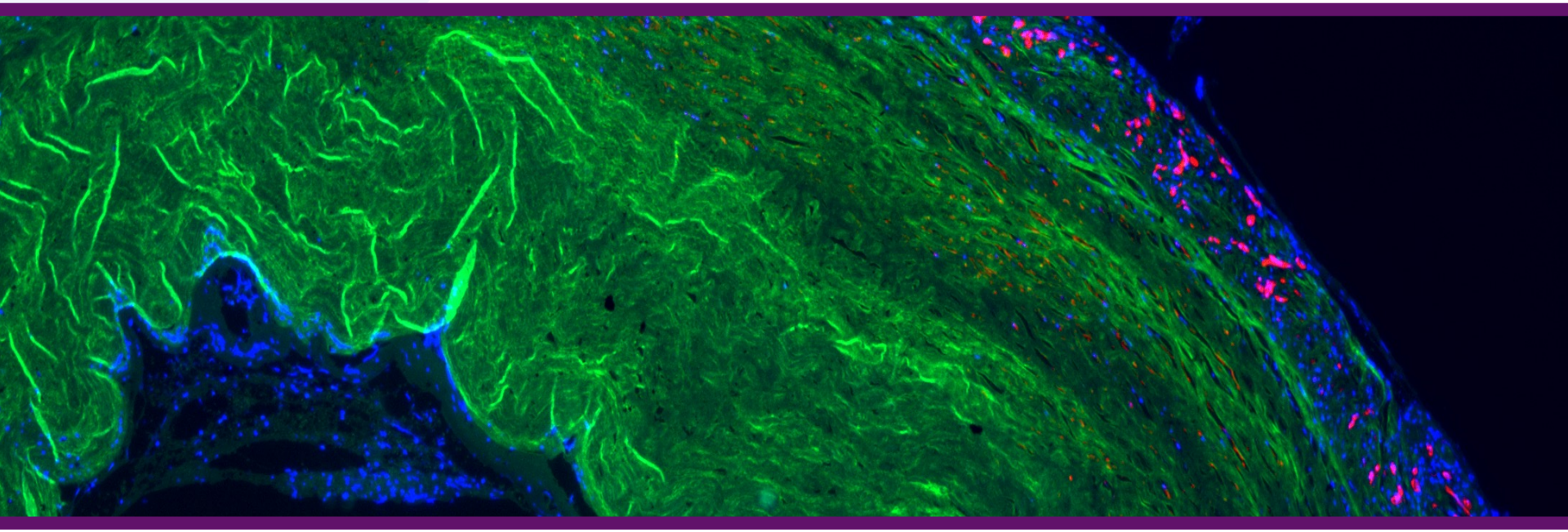


Figure 3. Insulin release and survival percentages in BVPs tested in vitro. (a) Glucose tolerance test performed on BVPs exposed to luminal flow or on static BVPs either immediately after creation, or after overnight incubation at 40 mmHg O_2. (b) Flow bioreactor setup for the BVP designed to mimic in vivo conditions. (c) Simulations (top), in vitro live/dead staining (middle) and HIF1-α staining (bottom) of BVPs statically incubated at 160 mmHg O_2, statically incubated at 40 mmHg O_2, or in the bioreactor setup shown in (b). (d) Quantification of survival percentages for simulations and in vitro live dead staining shown in (c). Statistical significance between experimental 40 mmHg Static and experimental bioreactor group determined using unpaired, two-tailed t-test (**$p = 0.0072$) ($n = 3$).

CONCLUSIONS

- Humacyte's Human Acellular Vessel (HAV) is an investigational 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.



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