

A Porcine Vascularized Composite Allotransplantation Model For Assessing Early Prognostic Biomarkers Of Rejection



Department of Surgery
UNIVERSITY OF COLORADO
ANSCHUTZ MEDICAL CAMPUS

Caitlin Blades¹, Zari Dumanian¹, Paula Arrowsmith³, Zhaohui Wang¹, Yong Wang¹, Bing Li¹, Kia M. Washington¹, Julia B. Slade², Jason Yu¹, Mark Greyson¹, David W. Mathes¹, Evan Farkash³, Conor L. Evans², Nalu Navarro-Alvarez¹, Christene A. Huang¹

¹Department of Surgery, University of Colorado Denver Anschutz Medical Campus, Aurora, CO, USA.

²Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Charlestown, MA

³University of Michigan School of Medicine, Ann Arbor, MI, USA.



BACKGROUND

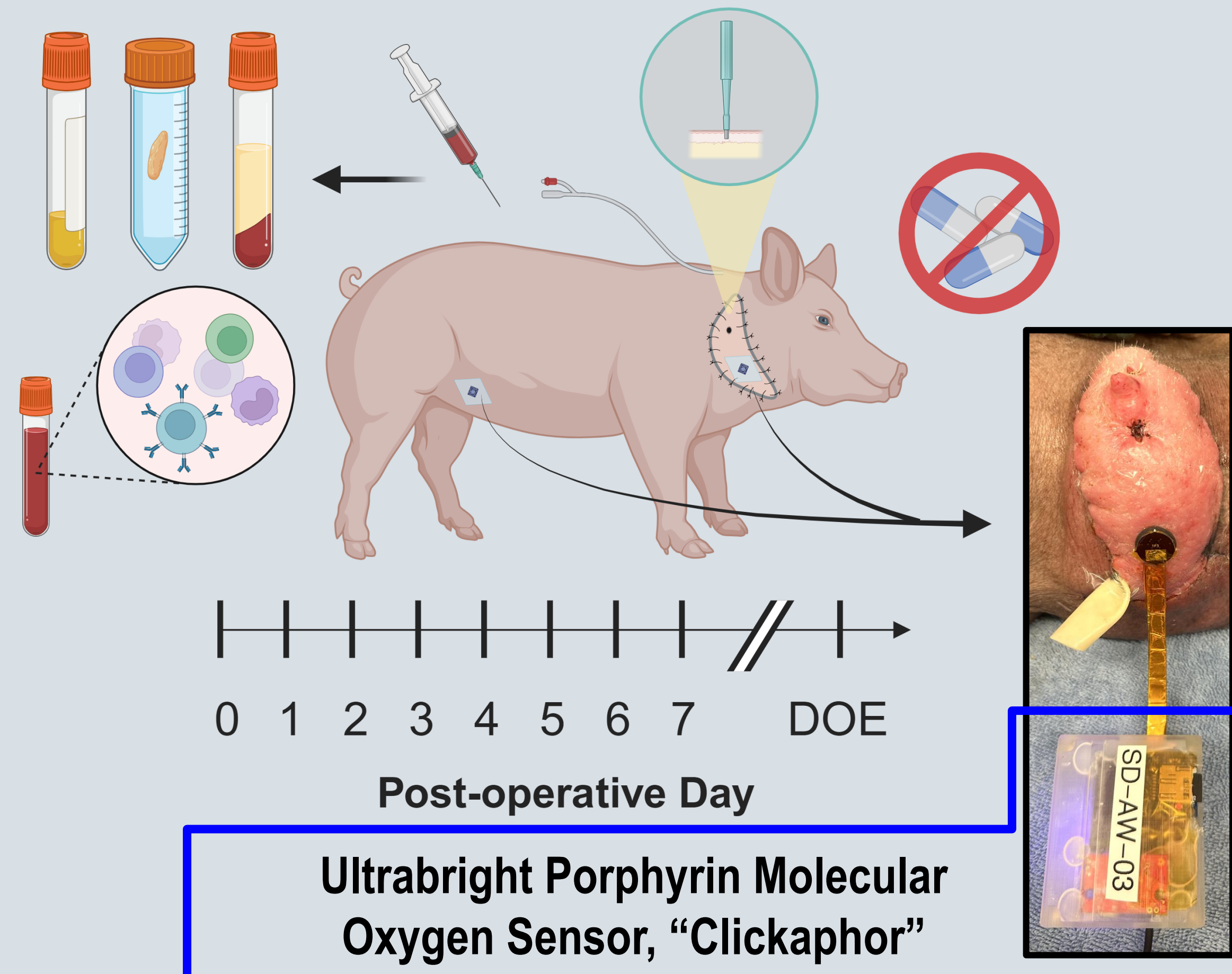
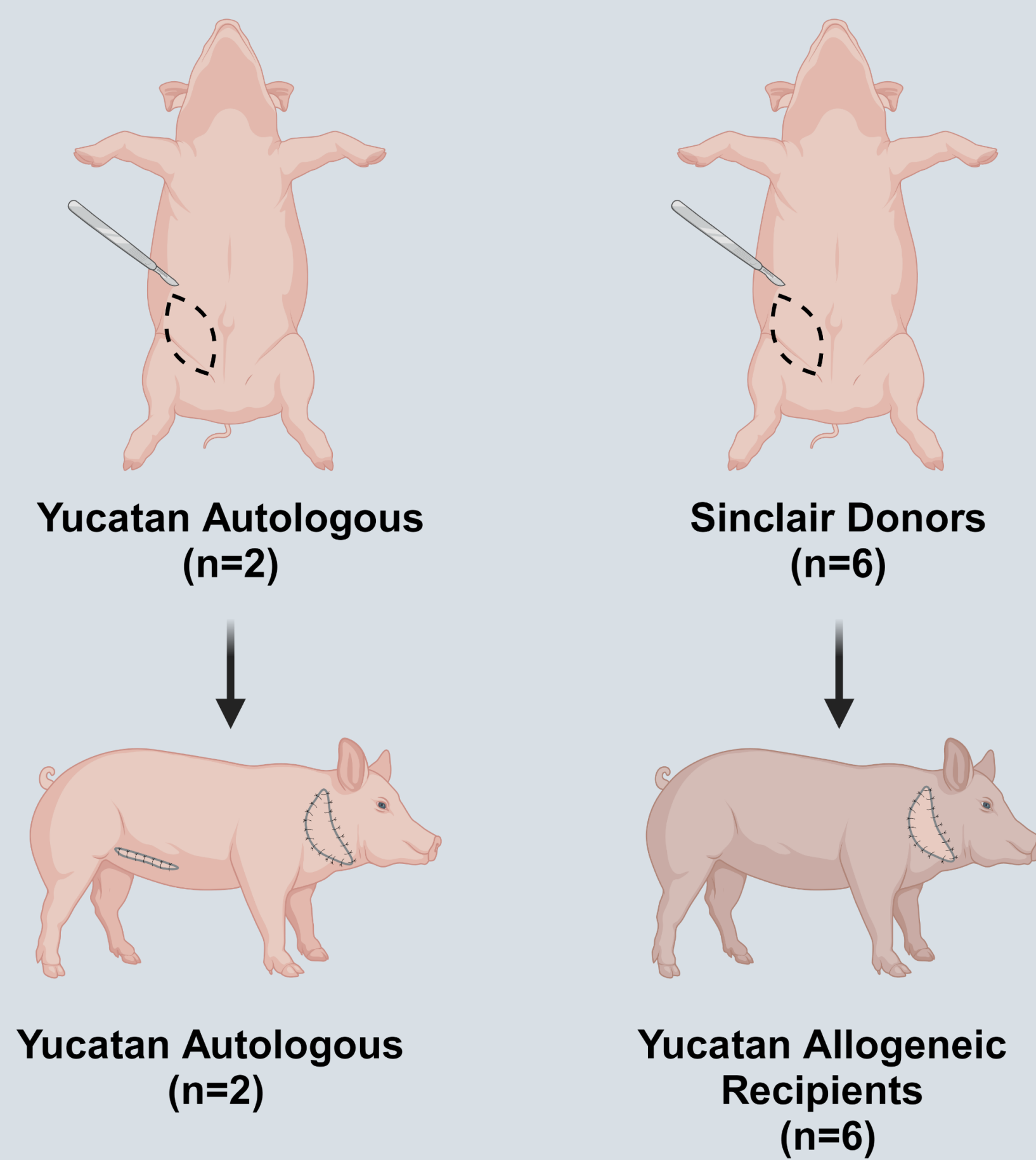
- Vascularized Composite Allotransplantation (VCA) has shown tremendous promise in restoring form and function in patients with large tissue defects
- VCA recipients require immunosuppressive therapy to prevent acute and chronic rejection
- Often at higher levels than for solid organ transplants
- Noninvasive biomarkers of rejection will allow for early detection of signs of rejection and tailored immunosuppression
- Swine models offer skin that is structurally, cellularly, and antigenically similar to humans

METHODOLOGY

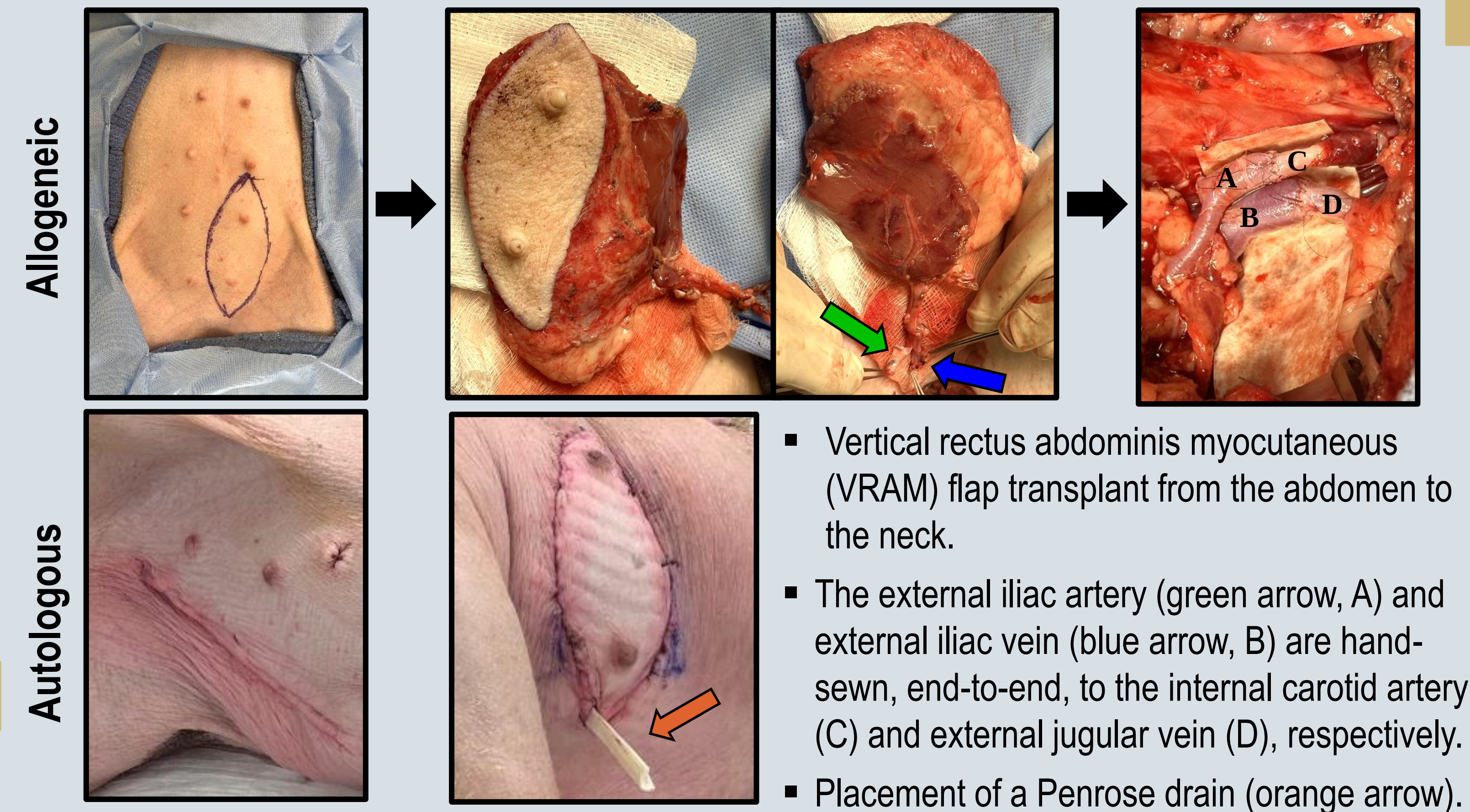
- Male and Female 3-4-month-old Yucatan pigs (11.4-18.5 kg) were used as recipients

- Male and Female 7-8-month-old Sinclair pigs (10.9-17.9 kg) were used as donors

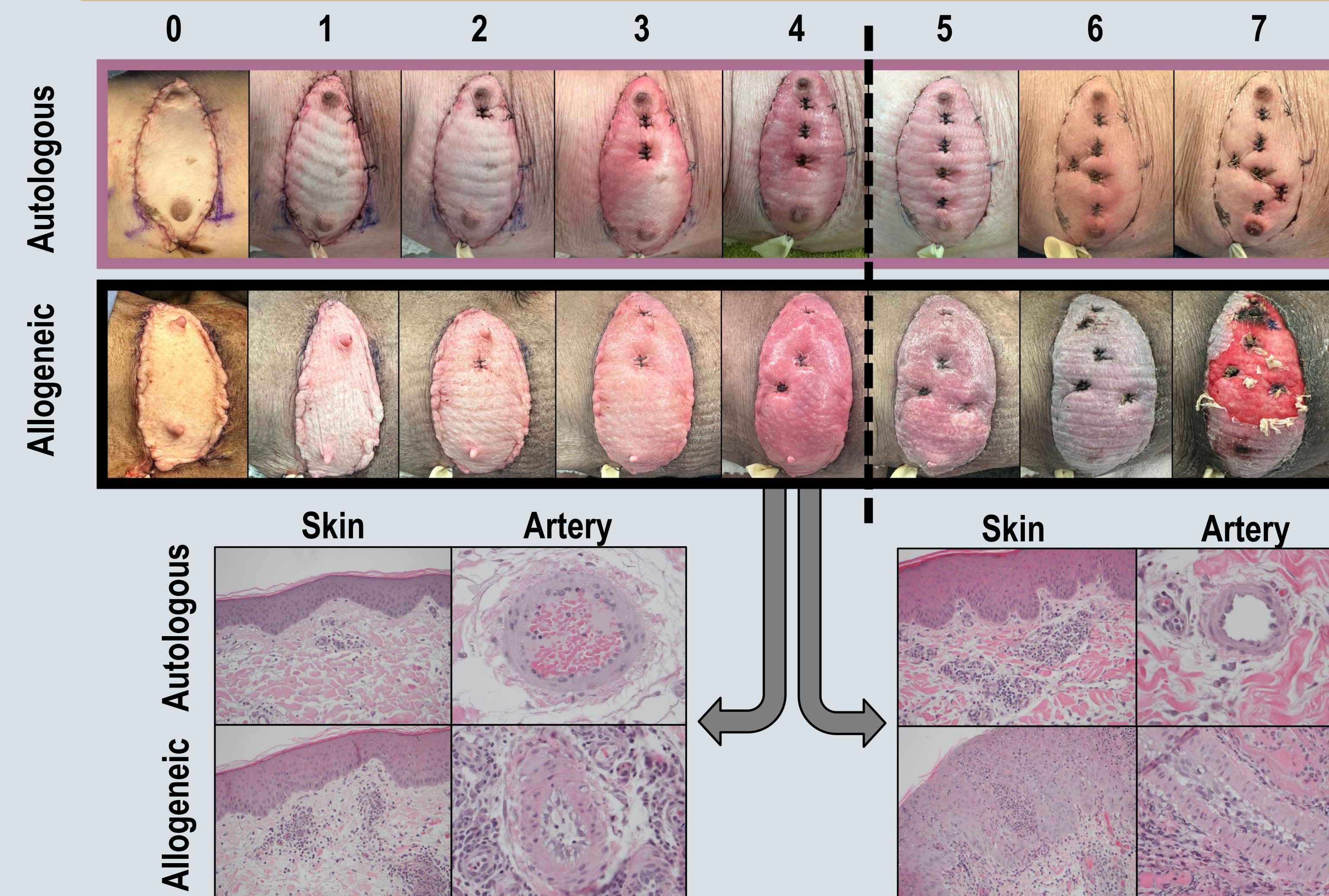
- All pigs were non-inbred



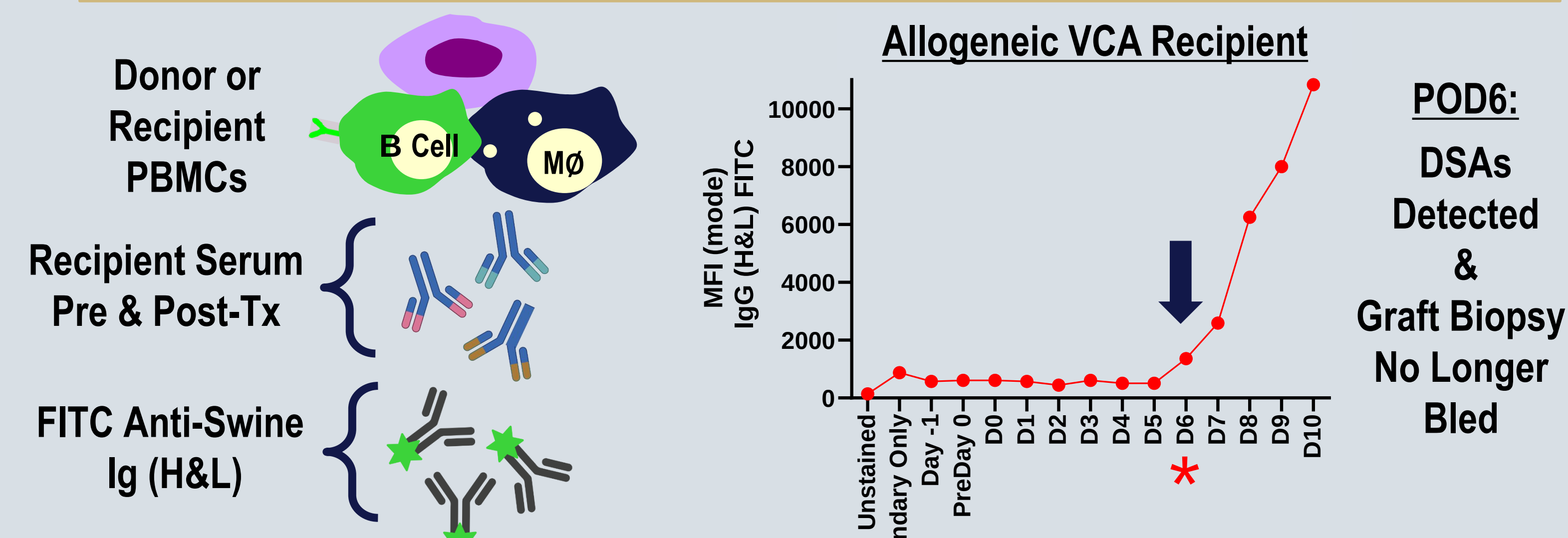
SURGICAL MODEL



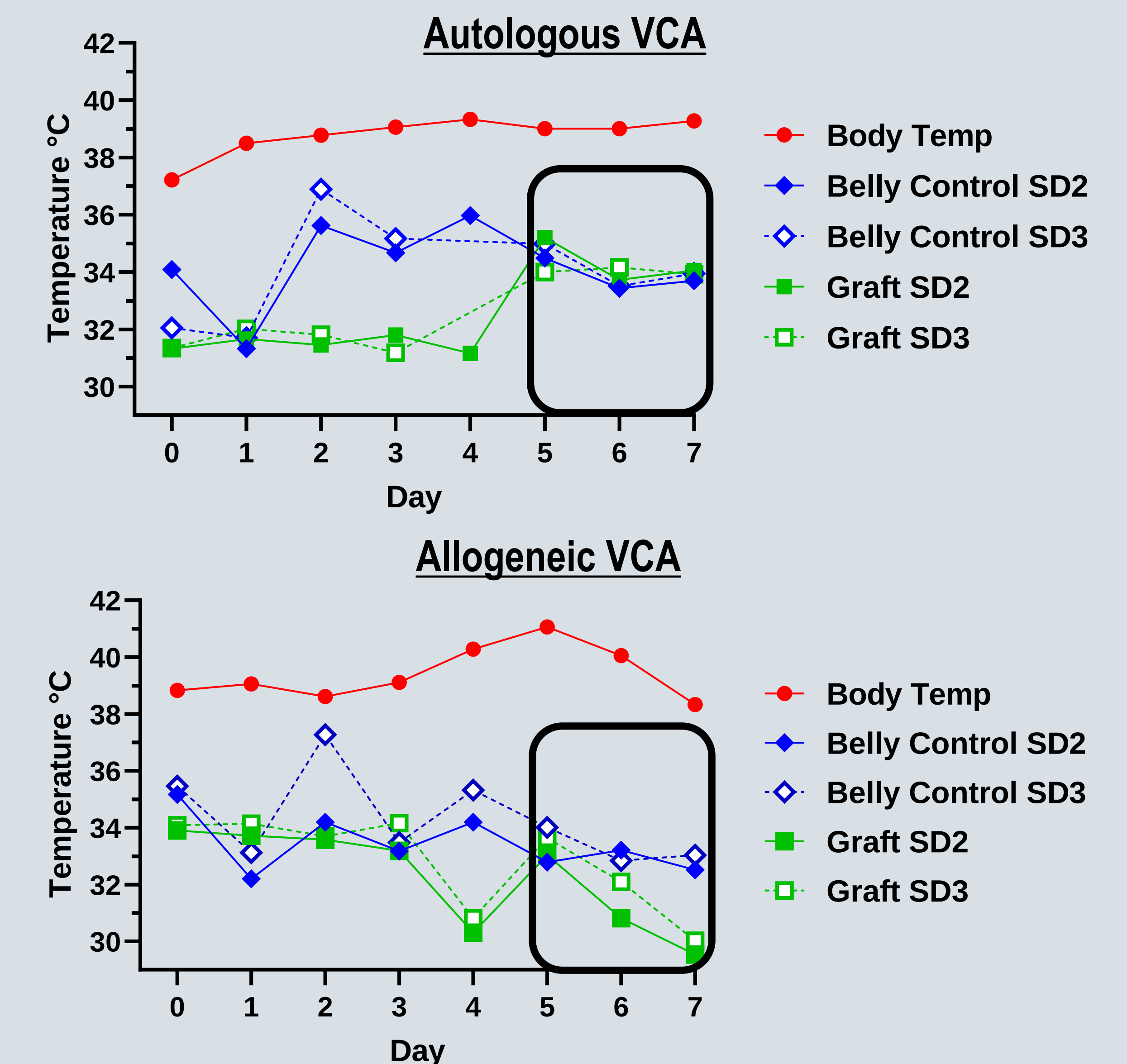
RESULTS: GRADE 3 REJECTION IN ALLOGRAFTS BY POD4



FLOW CYTOMETRY: DONOR SPECIFIC ANTIBODIES (DSAs) ON POD6



TRANSCUTANEOUS TEMPERATURE DECREASE PARALLELS ALLOGENEIC VCA REJECTION



CONCLUSIONS

- We have successfully validated a reproducible allogeneic and autologous porcine VCA model
- Allogeneic flaps rejected early in the setting of no immunosuppression
- Graft temperatures correlated well with graft status
- Galectin-3 levels and transcutaneous tissue oxygen levels are currently being analyzed
- Next cohort will be given immunosuppressive therapy until the graft heals, to better assess biomarkers specific for rejection
- Future studies to analyze biomarkers include transcriptomic, proteomic, and metabolomic analyses

ACKNOWLEDGMENTS



CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.