WELCOME *To the*

2026 SYMPOSIUM

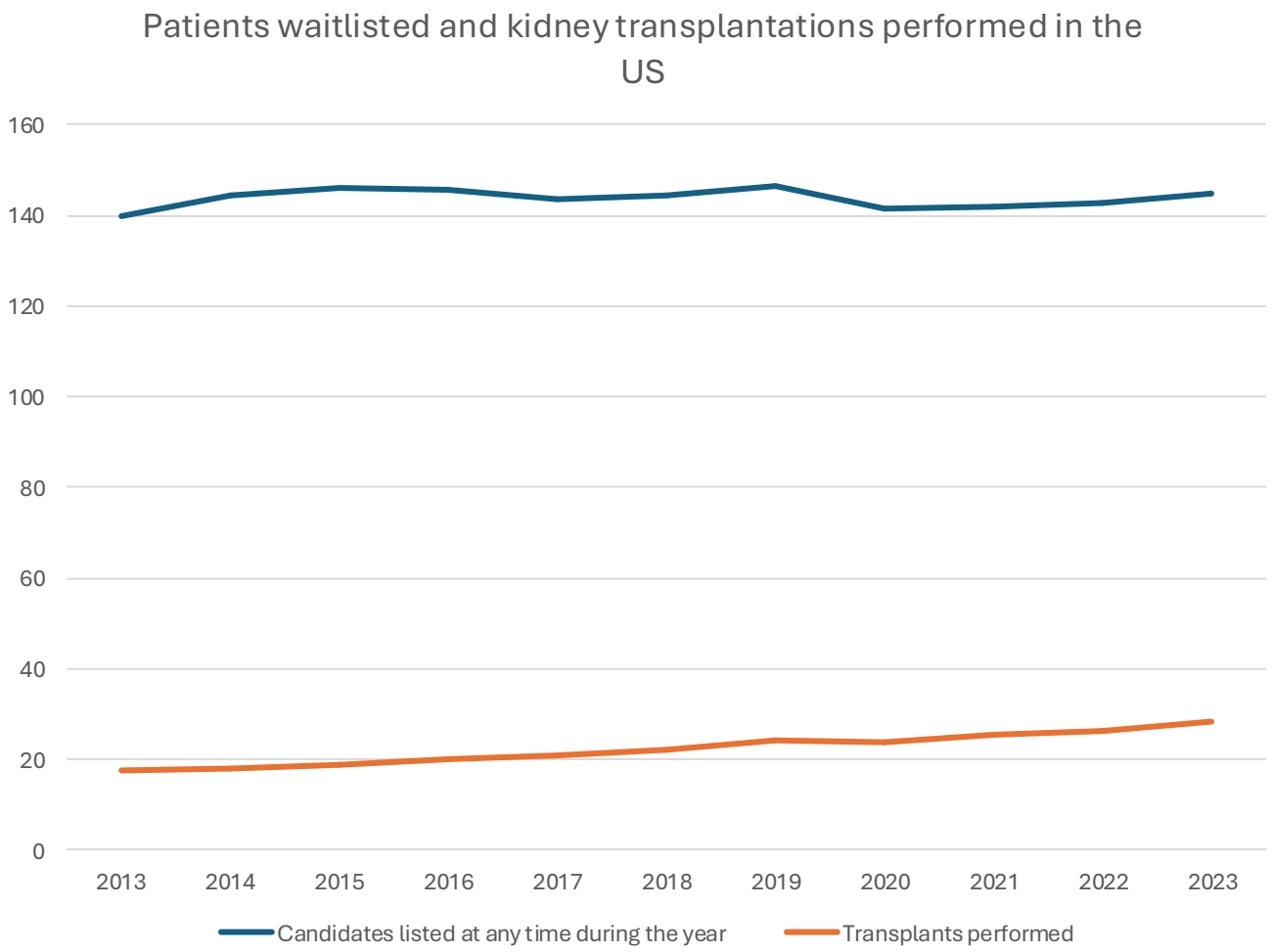
Toward and Unlimited Organ Supply

Translating Xenotransplantation to the Clinic

Ragnar Palsson, MD
Massachusetts General Hospital

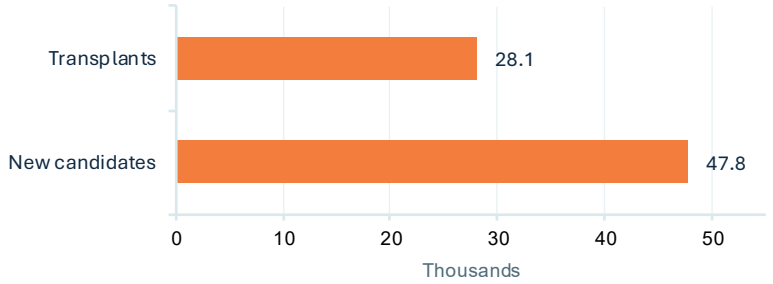
May 20th, 2026

Organ shortage is a major obstacle in transplantation



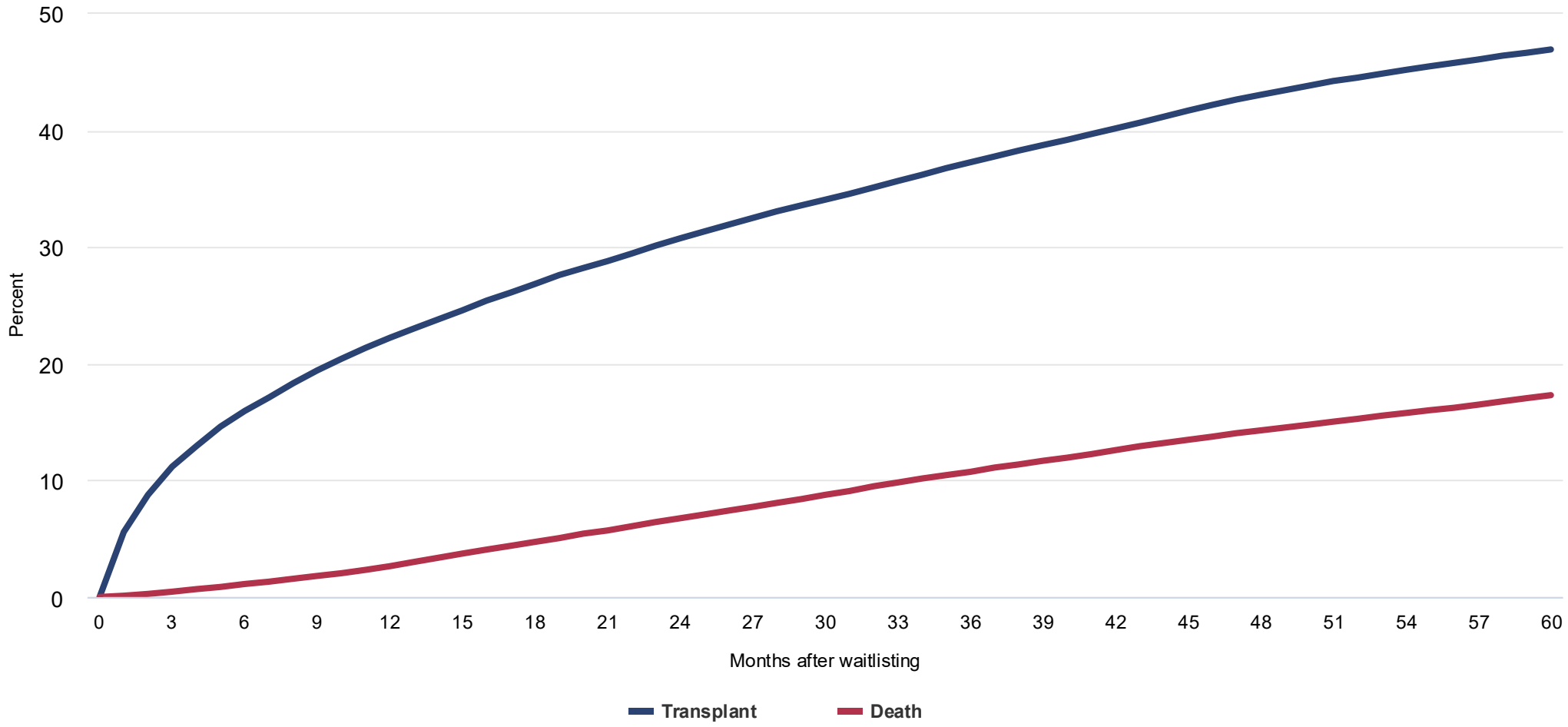
2023 snapshot

New kidney candidates exceeded transplants by 19.7k in 2023.



Data from the Organ Procurement and Transplantation Network (OPTN)

Mortality on the waitlist is high



2025 United States Renal Data System Annual Data Report

How can the organ shortage be ameliorated?

In practice: Transplant more of today's organs

- Minimize organ discards
  - Expedite organ placement
  - Machine perfusion
- Maximize donor pool
  - Living donation
  - DCD organs
  - Normothermic regional perfusion
  - HCV positive donors

In 2025 U.S. kidney transplant volume was ~27,573, while >90,000 Americans were still waiting for a kidney

In theory: Create new kidney sources

- *Ex vivo* refurbishment of discarded kidneys?
- Bioartificial kidneys?
- Xenografts?

History of xenotransplantation

Jean-Baptiste Denys attempts xenotransfusion of sheep's blood to a 15-year-old boy in 1667



History of xenotransplantation

Animal-to-human skin grafts attempted in the 19th century

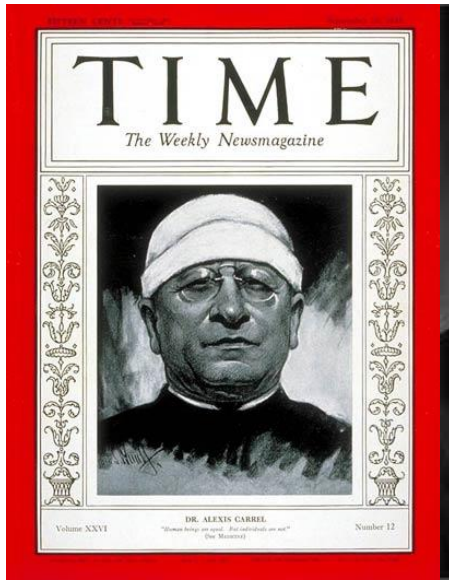
Porcine corneal xenotransplant performed in 1838

Testicular xenotransplantation from chimpanzees and baboons for "rejuvenation" performed in the early 20th century

Jabouley transplants one pig and one goat kidney to antecubital vessels of two women in 1906

Inconceivable that any attempts such as these were successful

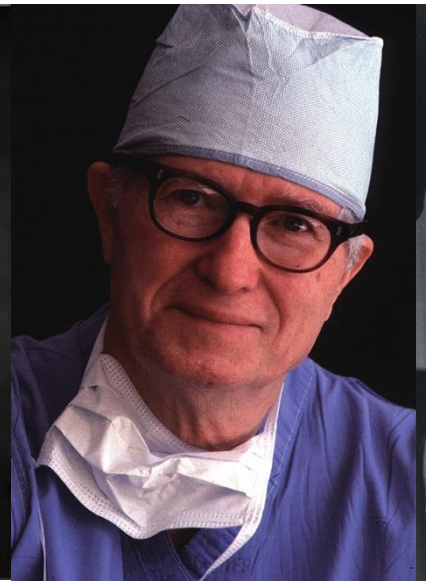
History of xenotransplantation



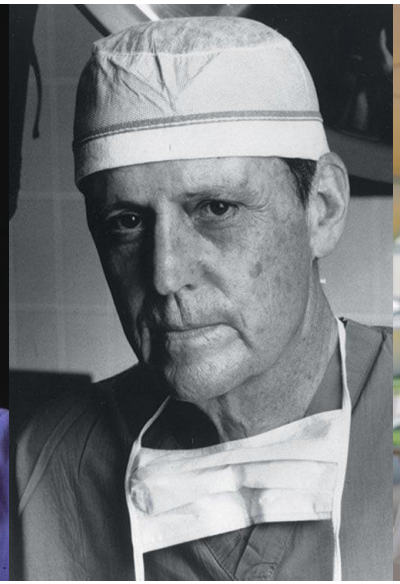
Alexis Carrell



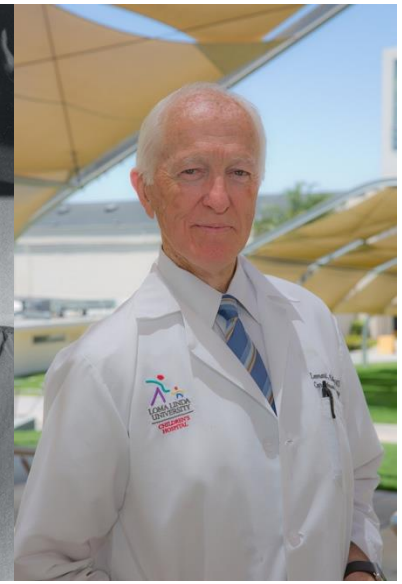
Keith Reetsma



James Hardy



Thomas Starzl



Leonard Bailey

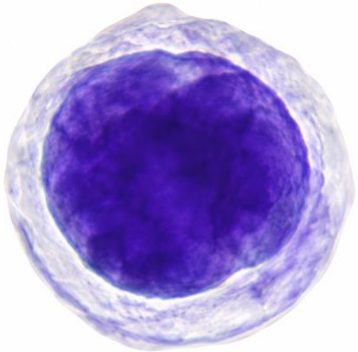
History of xenotransplantation

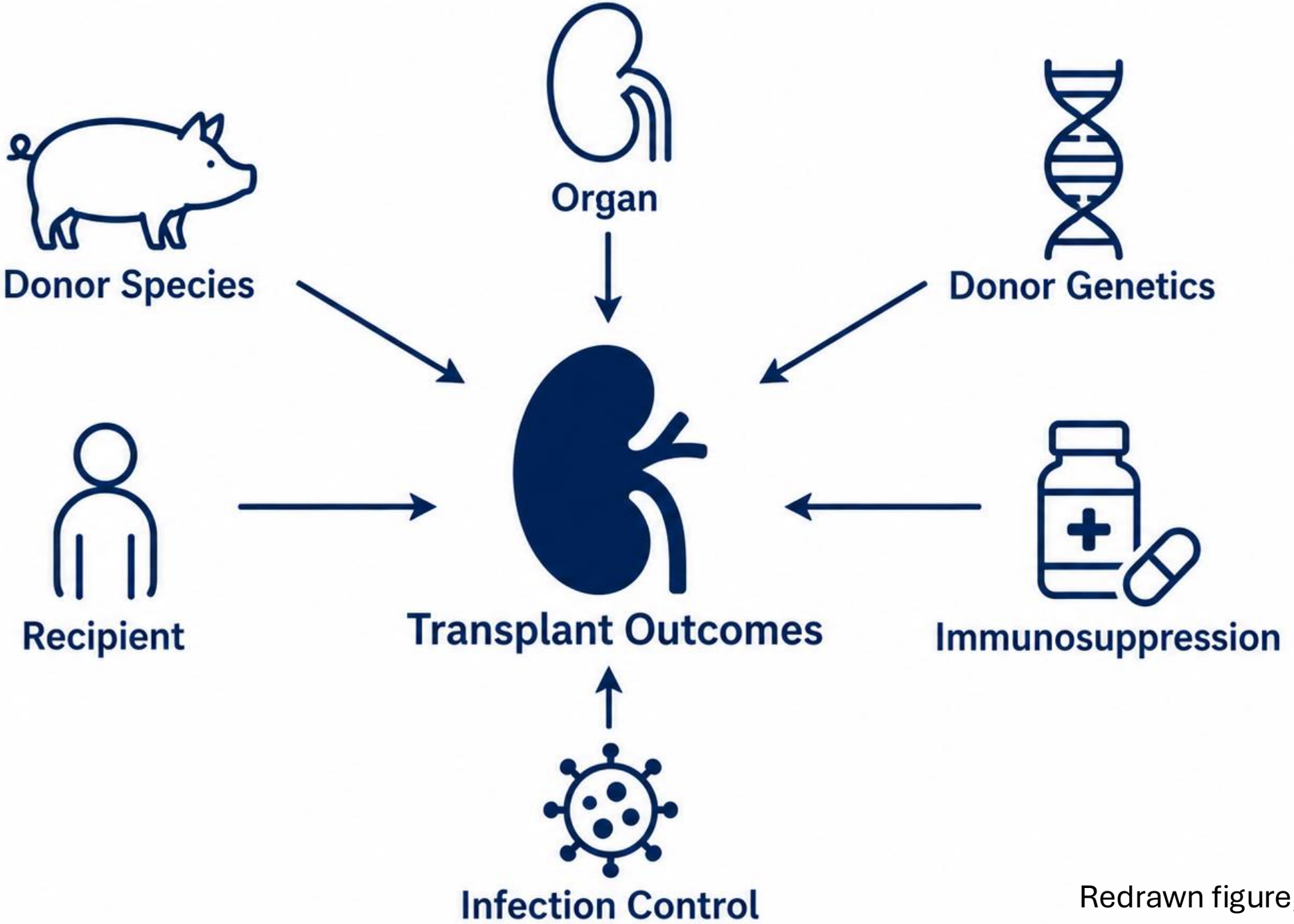
Baby Fae s/p baboon heart xenotransplantation in 1984



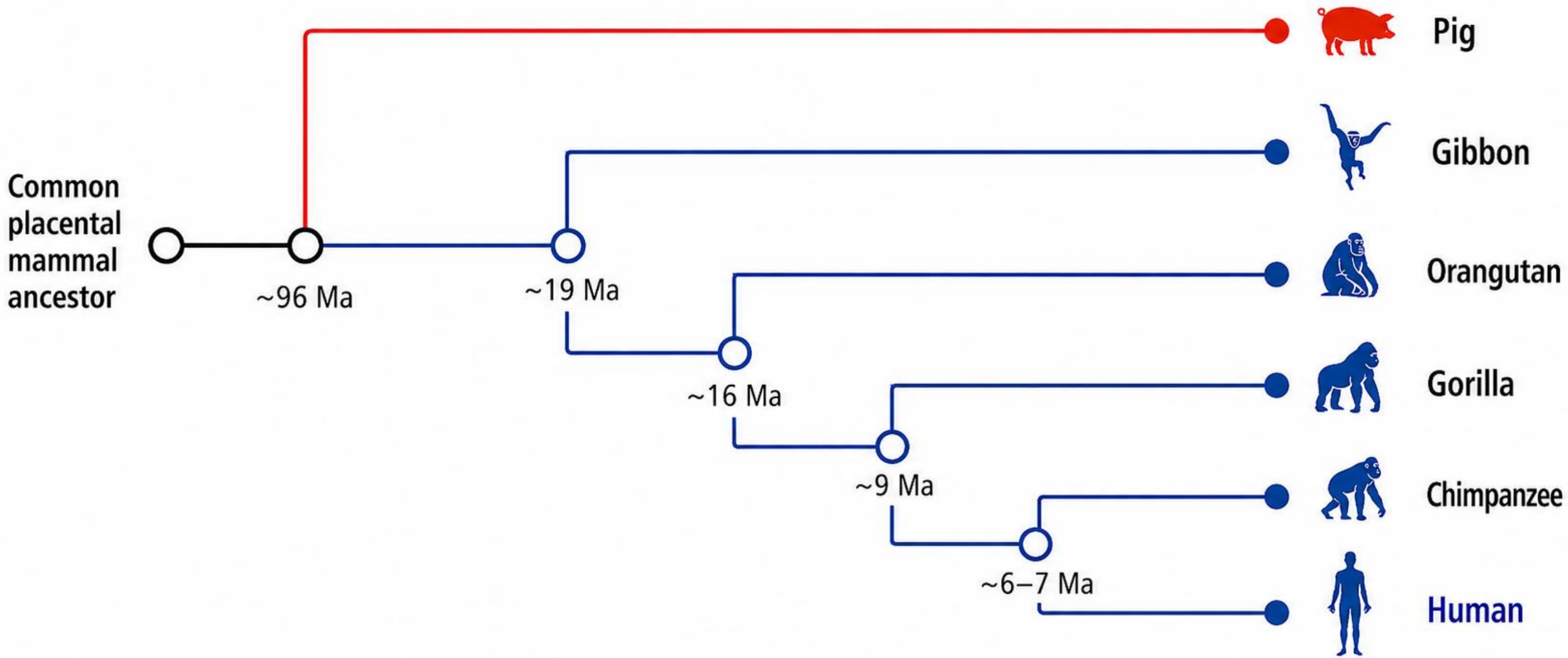
Why is clinical xenotransplantation resurfacing once again?

- Advances in
  - Understanding of immunology
  - Immunosuppressive treatment
  - Genetic engineering of potential donor animals
  - Outcomes in animal models of xenotransplantation





Redrawn figure, courtesy of
Dr. Leonardo Riella

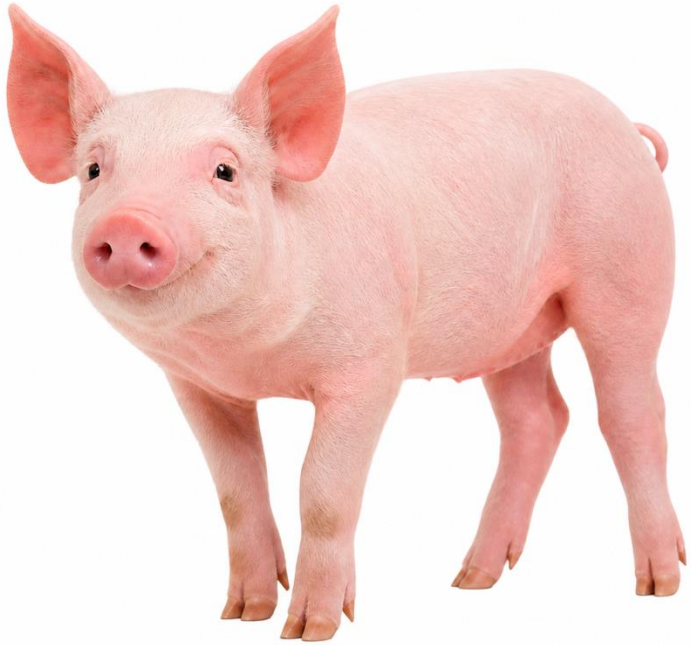


Ma, million years ago

Data based on Kumar et al, Molecular Biology and Evolution, 2022. Timetree.org

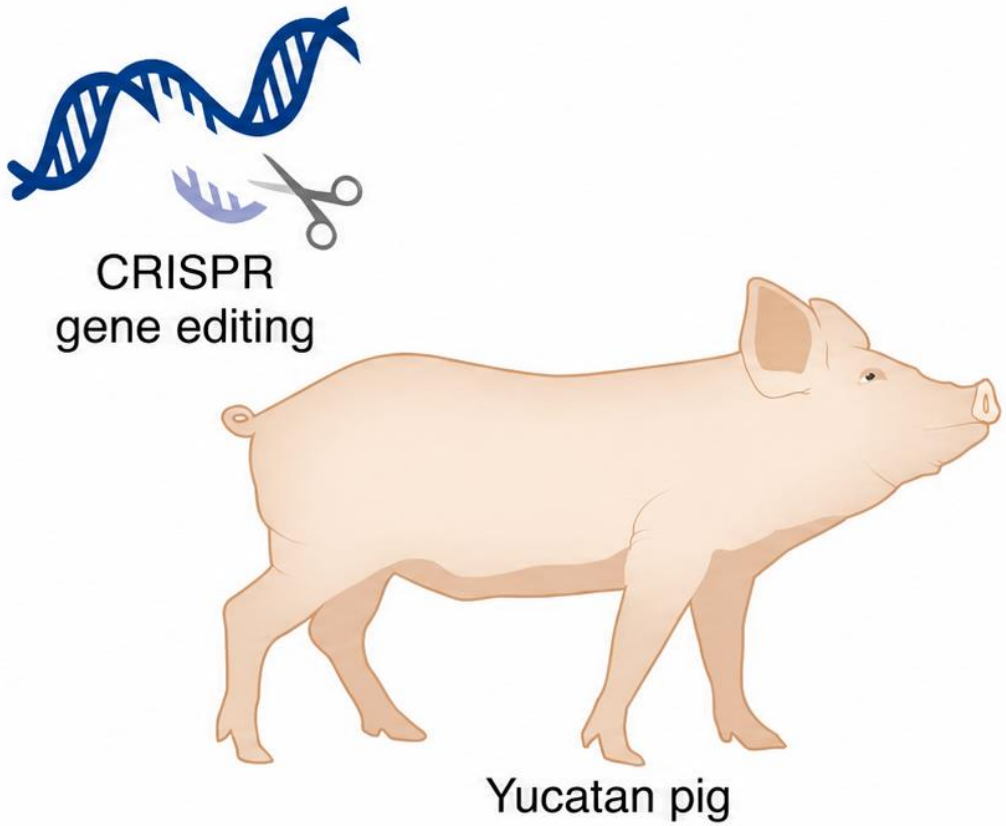
Why pigs rather than non-human primates?

- Shorter reproductive maturity
- Larger litter
- Shorter growth time
- Extensive breeding experience
- Appropriately sized organs
- Lower risk of zoonotic infection
- Possibly more acceptable to the public



Pig Genes Removed

- Pig carbohydrates (αGal, Sd(a), Neu5Gc)
- Pig endogenous retrovirus inactivation



Human Genes Added

- Complement inhibitors (hCD46, hCD55)
- Anticoagulants (hTHBD, hPROCR)
- Immune regulators (hCD47, hHMOX1, hTNFAIP3)

Riella, JASN 2024

nature

Article

Design and testing of a humanized porcine donor for xenotransplantation

https://doi.org/10.1038/s41586-023-06594-4

Received: 2 December 2022

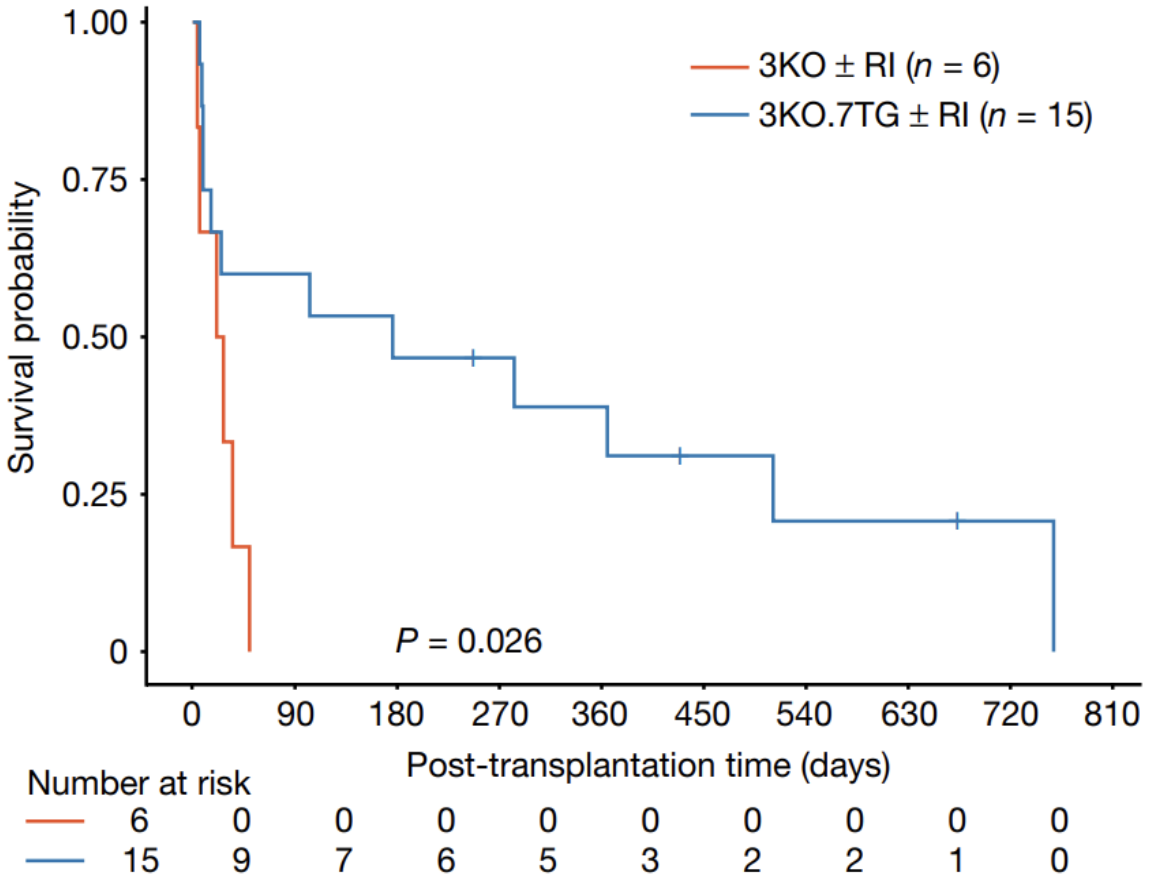
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Ranjith P. Anand[1,10], Jacob V. Layer[1,10], David Heja[1,10], Takayuki Hirose[2,10], Grace Lassiter[2,10], Daniel J. Firl[1,2,10], Violette B. Paragas[1], Adam Akkad[1], Sagar Chhangawala[1], Robert B. Colvin[3], Russell J. Ernst[1], Nicholas Esch[1], Kristen Getchell[1], Alexandra K. Griffin[1], Xiaoyun Guo[1], Katherine C. Hall[1], Paula Hamilton[1], Lokesh A. Kalekar[1], Yinan Kan[1], Ahmad Karadagi[2], Feng Li[1], Susan C. Low[1], Rudy Matheson[2], Claudia Nehring[1], Ryo Otsuka[2], Matthew Pandelakis[1], Robert A. Policastro[1], Rebecca Pols[1], Luis Queiroz[1], Ivy A. Rosales[3], William T. Serkin[1], Kathryn Stiede[1], Toshihide Tomosugi[2], Yongqiang Xue[1], Gabriel E. Zentner[1], David Angeles-Albores[1], J. Chris Chao[1], Juliet N. Crabtree[1], Sierra Harken[1], Nicole Hinkle[1], Tania Lemos[1], Mailin Li[1], Lorena Pantano[1], Denise Stevens[1], Omar D. Subedar[1], Xiaoqing Tan[1], Shiyi Yin[1], Imran J. Anwar[4], David Aufhauser[5], Saverio Capuano[6], Dixon B. Kaufman[5], Stuart J. Knechtle[4], Jean Kwun[4], Dhanansayan Shanmuganayagam[7], James F. Markmann[2], George M. Church[8,9], Mike Curtis[1], Tatsuo Kawai[2,11], Michele E. Youd[1,11]✉ & Wenning Qin[1,11]✉



Anand et al, Nature 2023

The New York Times

In a First, Surgeons Attached a Pig Kidney to a Human, and It Worked

A kidney grown in a genetically altered pig functions normally, scientists reported. The procedure may open the door to a renewable source of desperately needed organs.

Share full article 564



Dr. Robert Montgomery is director of the N.Y.U. Langone Transplant Institute in Manhattan. Genetically engineered pigs "could potentially be a sustainable, renewable source of organs," he said. Amir Hamja for The New York Times



Genetically modified pig kidney transplanted to a brain-dead recipient in September 2021

nature

Article

Physiology
human dece

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man

Personal Viewpoint

The decedent model: A new paradigm for de-risking high stakes clinical trials like xenotransplantation



Robert A. Montgomery [1,*], Adam D. Griesemer [1], Dorry L. Segev [1], Philip Sommer [1,2]

[1] NYU Langone Transplant Institute, New York, NY, USA
[2] NYU Department of Anesthesiology, Perioperative Care and Pain Medicine, New York, NY, USA

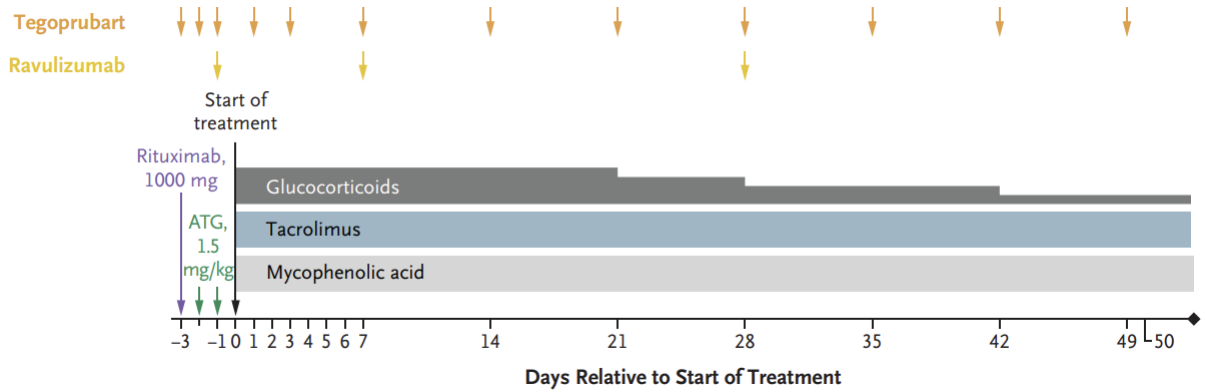
aedeh Mohebnasab[4], in Bombardi[7], Ian Jaffe[1,5], Darragh P. O'Brien[8], sca Zanoni[1,5,10], Jon Albay[11], Vikman[1,5], Diana Argibay[1,5], ng[13], Loren Gragert[14], azova[13], Brendan R. Camellato[13], Ali[15], Alawi H. Habara[16], otter[5], Scott C. Thomas[17], driana Heguy[20], Ali Crawford[7], el V. Holmes[21], Anita S. Chong[22], es[25], Marc Lorber[26], a S. Tatapudi[1,5], Ryan Taft[7], ern[1,5], Adam Griesemer[1,5], rendan J. Keating[1,5,13]

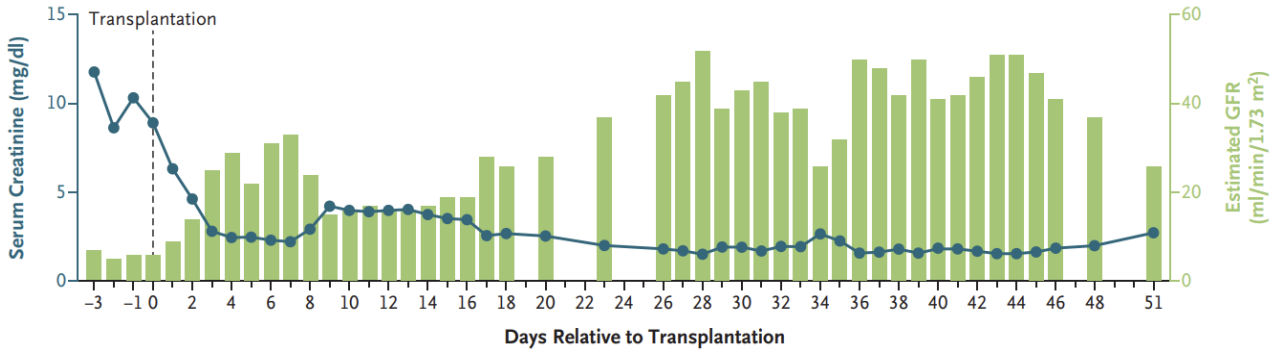
The NEW ENGLAND JOURNAL of MEDICINE

BRIEF REPORT

Xenotransplantation of a Porcine Kidney for End-Stage Kidney Disease

Tatsuo Kawai, M.D., Ph.D.,[1,4] Winfred W. Williams, M.D.,[1,4] Nahel Elias, M.D.,[1,4] Jay A. Fishman, M.D.,[1,4] Kerry Crisalli, R.N.,[1,4] Alban Longchamp, M.D.,[1,4] Ivy A. Rosales, M.D.,[2,4] Michael Duggan, D.M.D.,[3,4] Shoko Kimura, M.D., Ph.D.,[1,4] Leela Morena, M.D.,[1,4] Thiago J. Borges, Ph.D.,[1,4] Toshihide Tomosugi, M.D., Ph.D.,[1,4] Ahmad Karadagi, M.D., Ph.D.,[1,4] Tsukasa Nakamura, M.D., Ph.D.,[1,4] Kassem Safa, M.D.,[1,4] Alessia Giarraputo, Ph.D.,[2,4] Claire T. Avillach, M.D.,[2,4] Eva D. Patalas, M.D.,[2,4] R. Neal Smith, M.D., Ph.D.,[2,4] David H. Sachs, M.D.,[1,4] A. Benedict Cosimi, M.D.,[1,4] Joren C. Madsen, M.D., D.Phil.,[1,4] David K.C. Cooper, M.D.,[1,4] Richard Pierson, M.D.,[1,4] Steve Perrin, Ph.D.,[5] Ranjith P. Anand, Ph.D.,[6] Sagar Chhangawala, Ph.D.,[6] Matthew Coscarella, M.S.,[6] Alexandre Daigneault, B.S.,[6] Feng Li, Ph.D.,[6] Owen Pearce, B.S.,[6] Wenning Qin, Ph.D.,[6] William T. Serkin, B.S.,[6] Vincent Yeung, Ph.D.,[6] Kristen Getchell, M.A.,[6] Susan C. Low, Ph.D.,[6] Michael Curtis, Ph.D.,[6] Robert B. Colvin, M.D.,[2,4] and Leonardo V. Riella, M.D., Ph.D.[1,4]





MGH kidney xenotransplantation program

- After the initial xenotransplant, a subsequent 3 patient pilot study was approved by the FDA

- This has now been completed, with a larger trial underway

www.mghxenotransplant.org

Massachusetts General Hospital
Founding Member, Mass General Brigham

egenesis

HARVARD MEDICAL SCHOOL

FDA

nature medicine

Article

https://doi.org/10.1038/s41591-025-04053-3

Immune profiling in a living human recipient of a gene-edited pig kidney

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American Journal of Transplantation



Case Report

Infectious disease s
clinical xenotranspla
human porcine kidn

Jay A. Fishman [1,2,*], Josepl
Leonardo V. Riella [3,5], Nahel
Dean Hashimoto [6], Sivan Be
Gayathri Balasundaram [7], K
Sagar Chhangawala [8], Ama

nature communications

Article

https://doi.org/10.1038/s41467-025-63153-3

Physiologic Homeostasis in a Living Human after Pig Kidney Xenotransplantation

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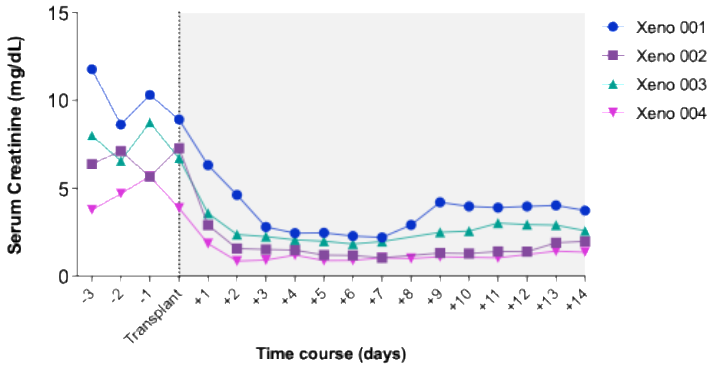
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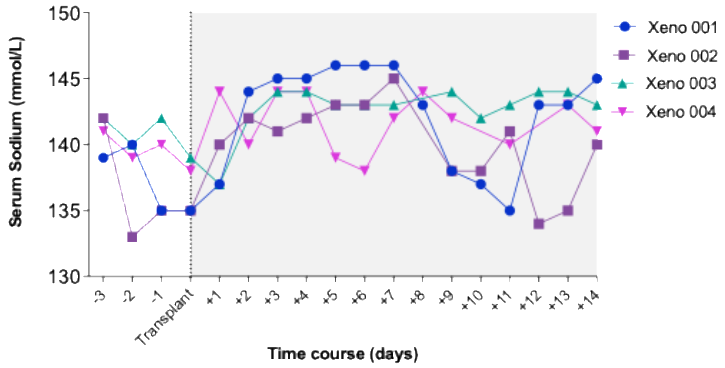
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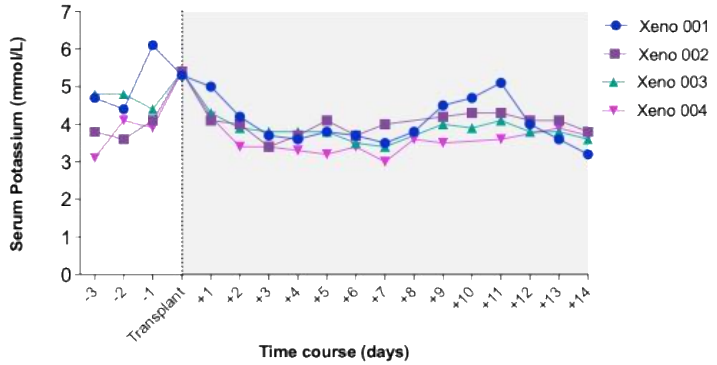
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Sul A Lee [1,2], Marie-Camille Lafargue [2,3], Winfred W. Williams[1,4], Kassem Safa[1,4], Ragnar Palsson[1,4], Ayman Al Jurdi[1,2,4], Abraham Cohen-Bucay [1,4], Pitchaphon Nissaisorakarn [1,4], Hannah Gilligan[1,4], Harald Jüeppner[4], Leela Morena[2], Thiago J. Borges [2,4], Mariesa A. Le [5], Kayla F. Joyal[5], Eugene P. Rhee [1,4], Ivy Rosales [4,6], Thomas Brannon[7], Jan Wysocki[7], Daniel Batlle[7], Tatsuo Kawai [2,4] & Leonardo V. Riella [1,2,4]

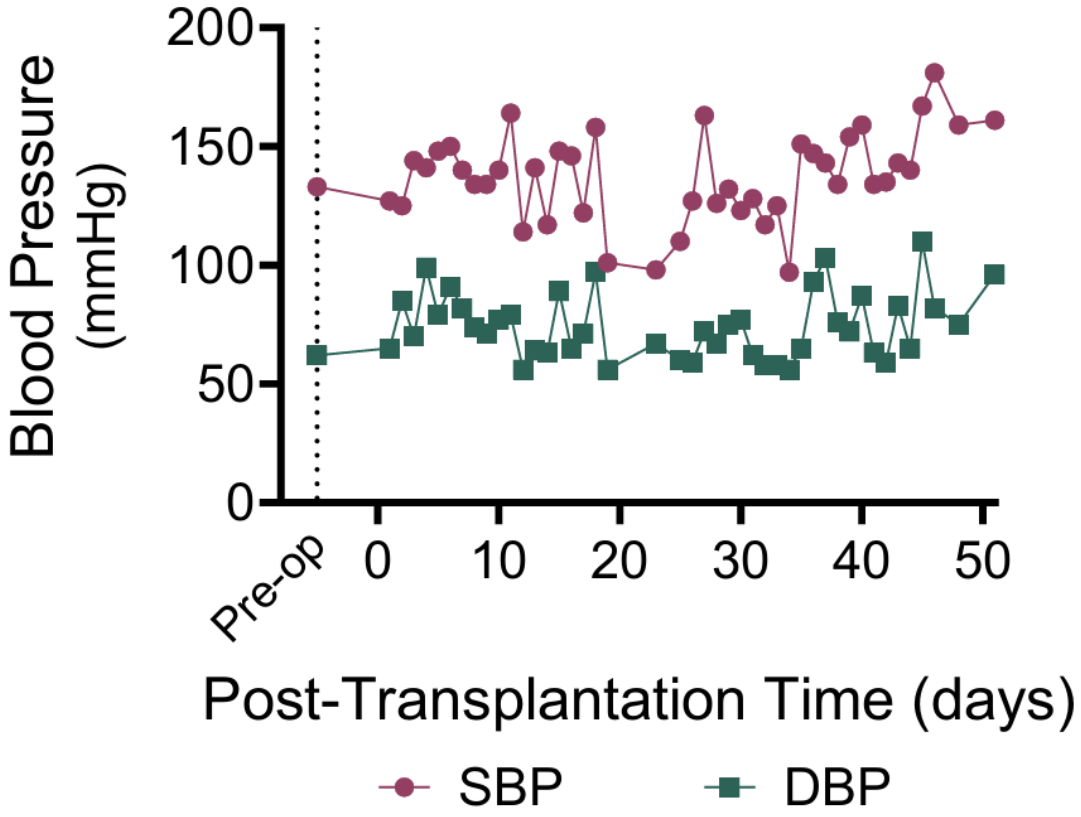
Function of pig xenografts



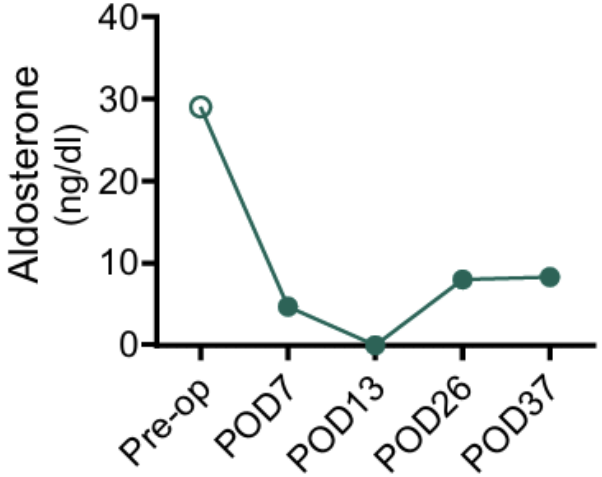


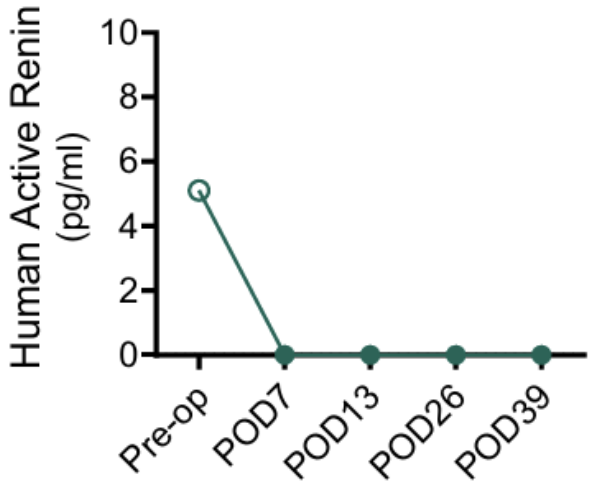


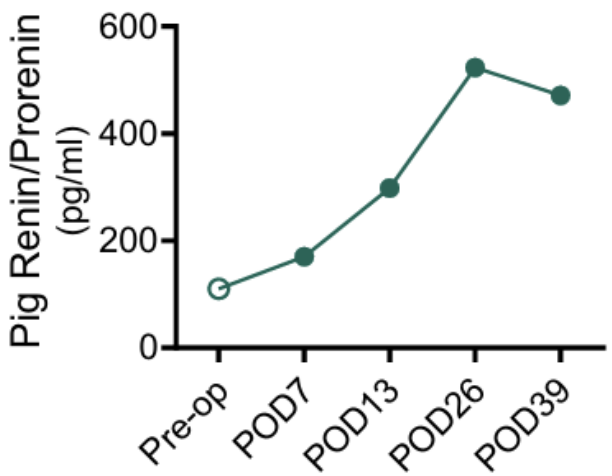
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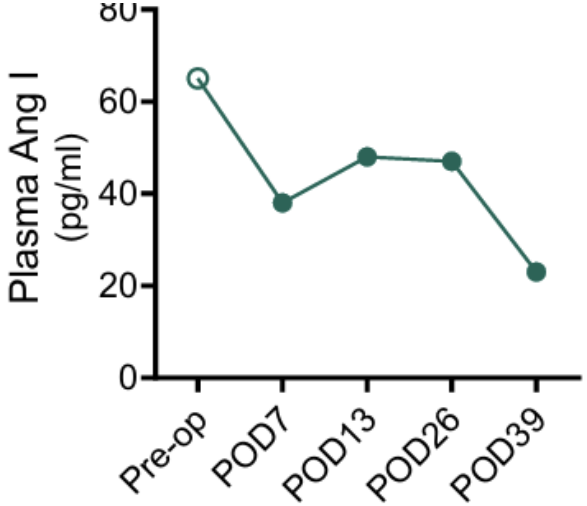


Lee et al, Nat Commun, 2025

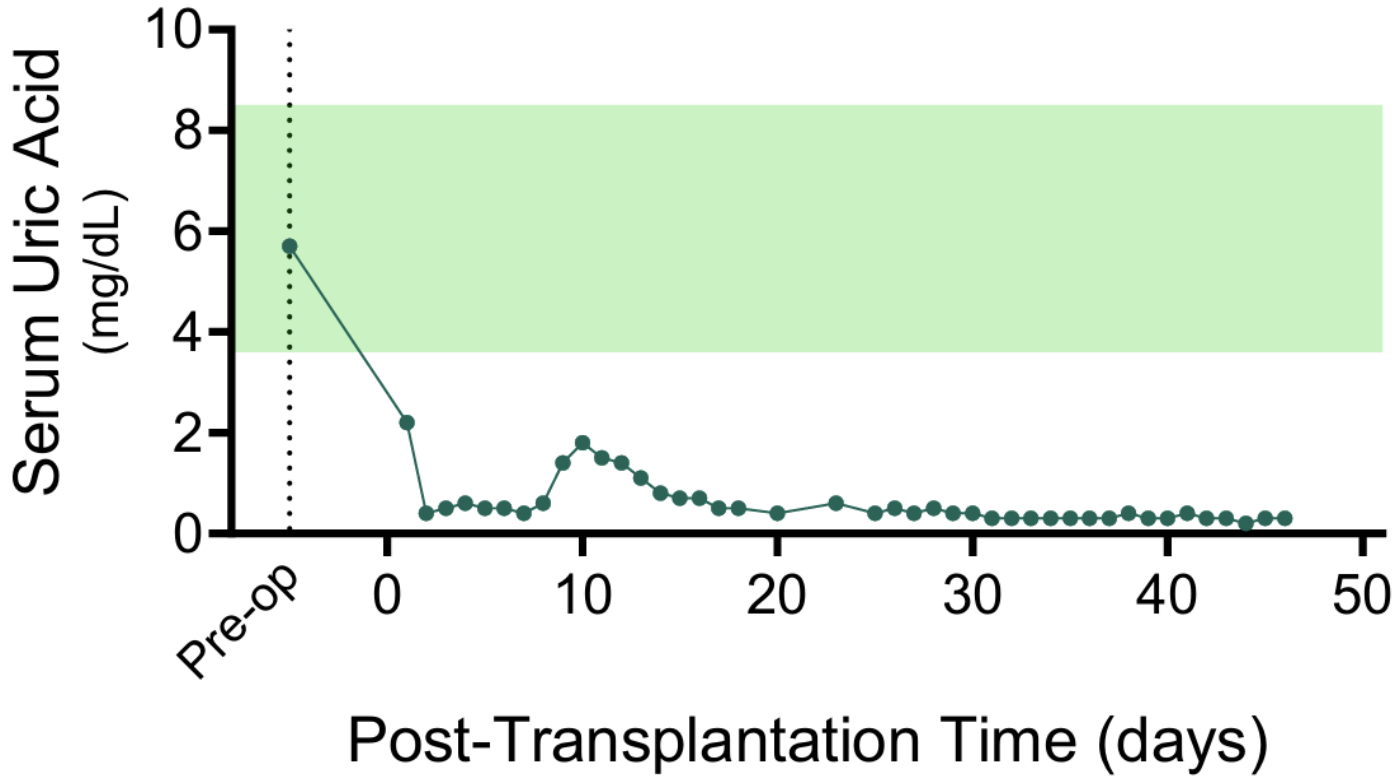








Lee et al, Nat Commun, 2025



Lee et al, Nat Commun, 2025






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