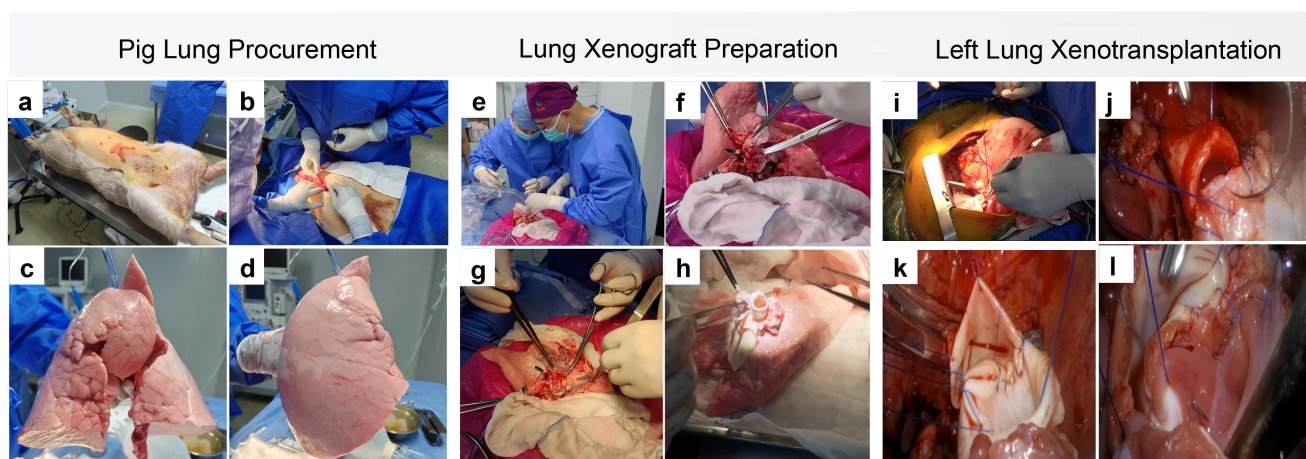
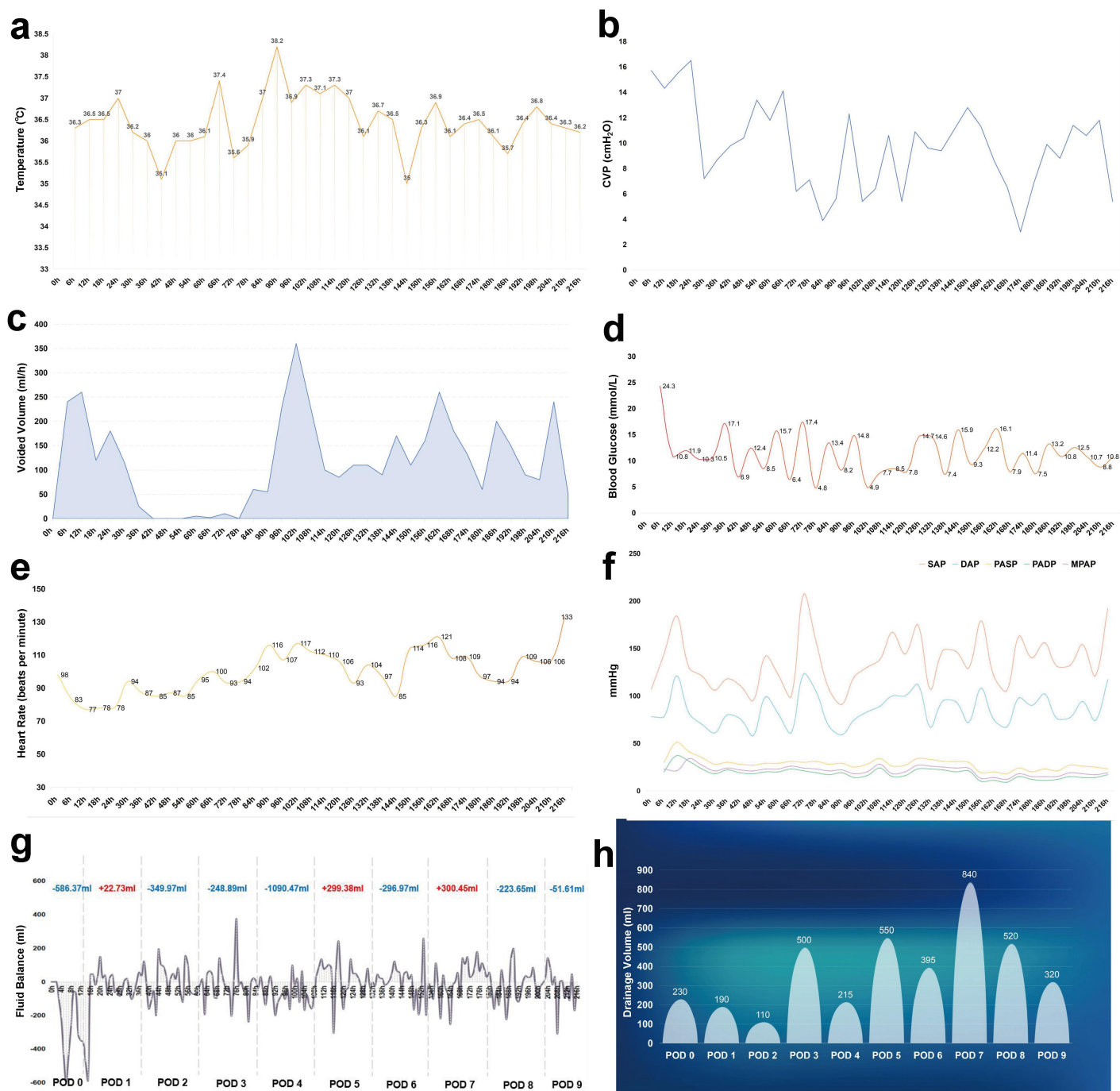

Pig-to-human lung xenotransplantation into a brain-dead recipient

In the format provided by the
authors and unedited

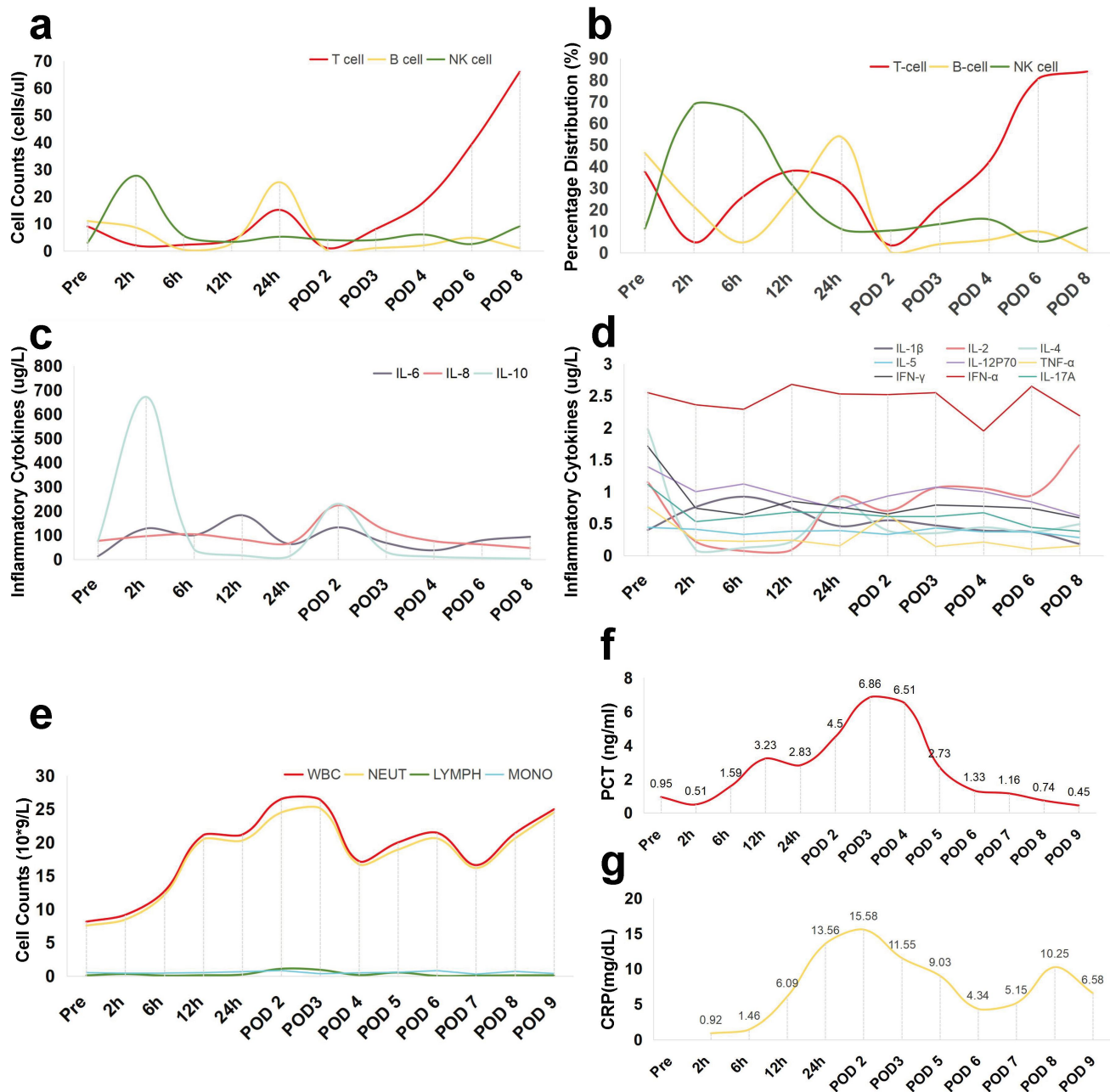


Supplementary Figure 1 The surgical procedure for pig-to-human lung xenotransplantation. Pig Lung Procurement (**a–d**): The donor pig undergoes preoperative preparation and disinfection (**a**), followed by lung retrieval via median sternotomy (**b**). The procured lungs are displayed (**c, d**). Lung Xenograft Preparation (**e–h**): Ex vivo modifications are performed to optimize the donor lung, including pericardial trimming (**e**), dissection of surrounding tissues from the trachea (**f**), and vascular trimming of the left pulmonary vein (**g**) and artery (**h**). Left Lung Xenotransplantation (**i–l**): The recipient undergoes surgical incision (**i**), followed by sequential anastomoses of the trachea (**j**), left pulmonary artery (**k**), and left pulmonary vein (**l**), ensuring proper vascular and airway integration for successful xenotransplantation.



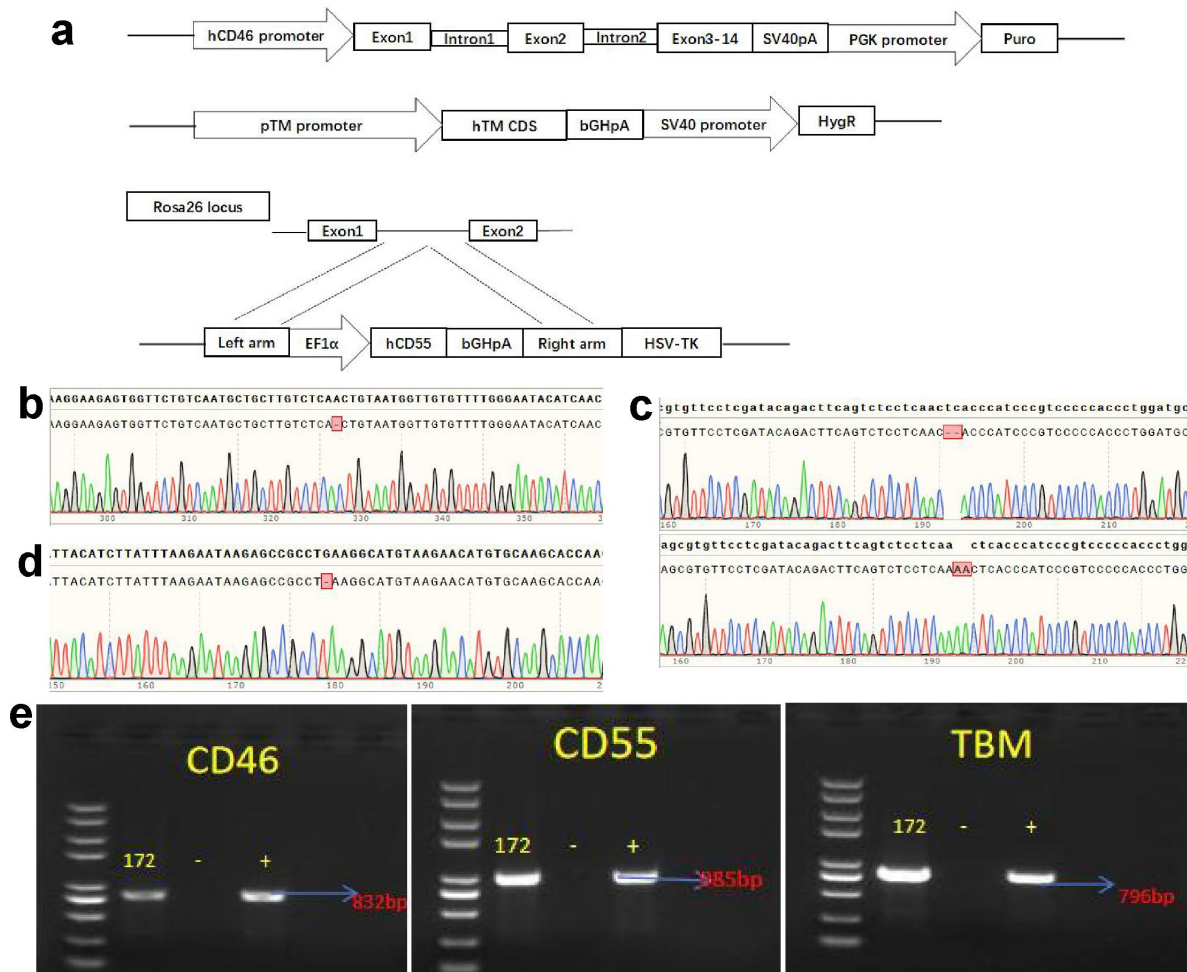
Supplementary Figure 2 Postoperative physiological parameters were continuously monitored to assess recipient stability. **a**, Body temperature fluctuations throughout the postoperative period. **b**, CVP monitoring. **c**, Hourly voided urine volume, reflecting renal function. **d**, Blood glucose levels over time. **e**, Heart rate variations post-transplantation. **f**, Continuous monitoring of arterial and pulmonary artery pressures, including SAP, DAP, PASP, PADP, and MPAP. **g**, Fluid balance measurements for each POD. **h**, Drainage volume exhibited a peak on POD 7,

with subsequent gradual reduction. These data indicate overall physiological stability throughout the observation period. CVP, central venous pressure; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; PASP, pulmonary artery systolic pressure; PADP, pulmonary artery diastolic pressure; MPAP, mean pulmonary artery pressure; POD, postoperative day.



Supplementary Figure 3 Inflammatory markers and cytokine responses. a, Dynamic changes in T cell, B cell, and NK cell counts over time. **b,** Percentage distribution of T cells, B cells, and NK cells. **c,** Levels of IL-6, IL-8, and IL-10

post-transplantation. **d**, Profiles of pro-inflammatory cytokines, including IL-1 β , IL-2, IL-4, IL-5, IL-12p70, IFN- γ , IFN- α , TNF- α , and IL-17A. **e**, Trends in WBC, NEUT, LYMPH, and MONO counts. **f**, Changes in serum PCT levels. **g**, CRP levels over time. NK, natural killer cell; IL, interleukin; CRP, C-reactive protein; TNF- α , tumor necrosis factor-alpha; IFN- γ , interferon-gamma; IFN- α , interferon-alpha; WBC, white blood cell; NEUT, neutrophil; LYMPH, lymphocyte; MONO, monocyte; PCT, procalcitonin.



Supplementary Figure 4 Detailed Information on the Genetically Modified Pig (Pig 172 *GTKO/SdaKO/CMAHKO/CD46/CD55/TBM*). **a**, The design of the expression vectors. **b**, Identification of GGTA1 gene, target: exon 4 of *GGTA1* gene. The target site editing type for Pig 172 is (-1/-1). **c**, *SdaKO* identification, target: *B4GALNT2* exon 2 pig 172, target editing type: (-2/+2). **d**, *CMAH* identification, target: *CMAH* exon 1 pig 172 target site editing type: (-1/-1). **e**, PCR-based validation

of human transgene insertions (hCD46, hCD55, hTBM). Amplicon sizes: hCD46 (832 bp), hCD55 (985 bp), hTBM (796 bp). Lane "172" represents the six-gene-edited pig, while "+" and "—" indicate positive and negative controls, respectively.

Supplementary Table 1 Porcine pathogen detection by metagenomics and meta-transcriptomics

Pathogens	Porcine peripheral blood (pretransplant, reads)	Porcine lung (pretransplant, reads)	Recipient peripheral blood (POD 9, reads)	Xenograft lung (POD 9, reads)
Pathogens in metagenomics				
Porcine endogenous retrovirus C (PERV-C)	Negative	Negative	Negative	Negative
Porcine lymphotropic herpesvirus 1 (PLHV-1)	16	53	1	Negative
Porcine lymphotropic herpesvirus 3 (PLHV-3)	276	19	Negative	Negative
Suid betaherpesvirus 2 (porcine CMV)	3	Negative	Negative	Negative
Porcine circovirus 1	Negative	Negative	Negative	Negative
<i>Staphylococcus equorum</i>	32,157	Negative	Negative	Negative
<i>Corynebacterium camporealensis</i>	17,450	Negative	Negative	Negative
<i>Corynebacterium stationis</i>	8,671	Negative	Negative	Negative
<i>Moraxella porci</i>	6,727	Negative	Negative	Negative
<i>Aerococcus suis</i>	2,216	Negative	Negative	Negative
<i>Streptococcus suis</i>	921	Negative	Negative	Negative
<i>Actinobaculum suis</i>	605	Negative	Negative	Negative
Pathogens in meta-transcriptomics				
Suid gammaherpesvirus 5	42	Not tested	Negative	Negative
<i>Streptococcus suis</i>	4	Not tested	Negative	Negative
Porcine endogenous retrovirus C (PERV-C)	Negative	Not tested	Negative	Negative
Porcine circovirus 1	Negative	Not tested	3	Negative

Supplementary Table 2 Baseline Monitoring of specific pathogenic microorganisms.

Pathogens	Donor Pig
African Swine Fever Virus	Negative
Classical Swine Fever Virus	Negative
Foot-and-Mouth Disease Virus	Negative
Porcine Reproductive and Respiratory Syndrome Virus	Negative
Japanese Encephalitis Virus	Negative
Streptococcus suis Type II	Negative
Mycoplasma hyopneumoniae	Negative
Pseudorabies Virus	Negative
Brucella	Negative
Pig Leptospira	Negative