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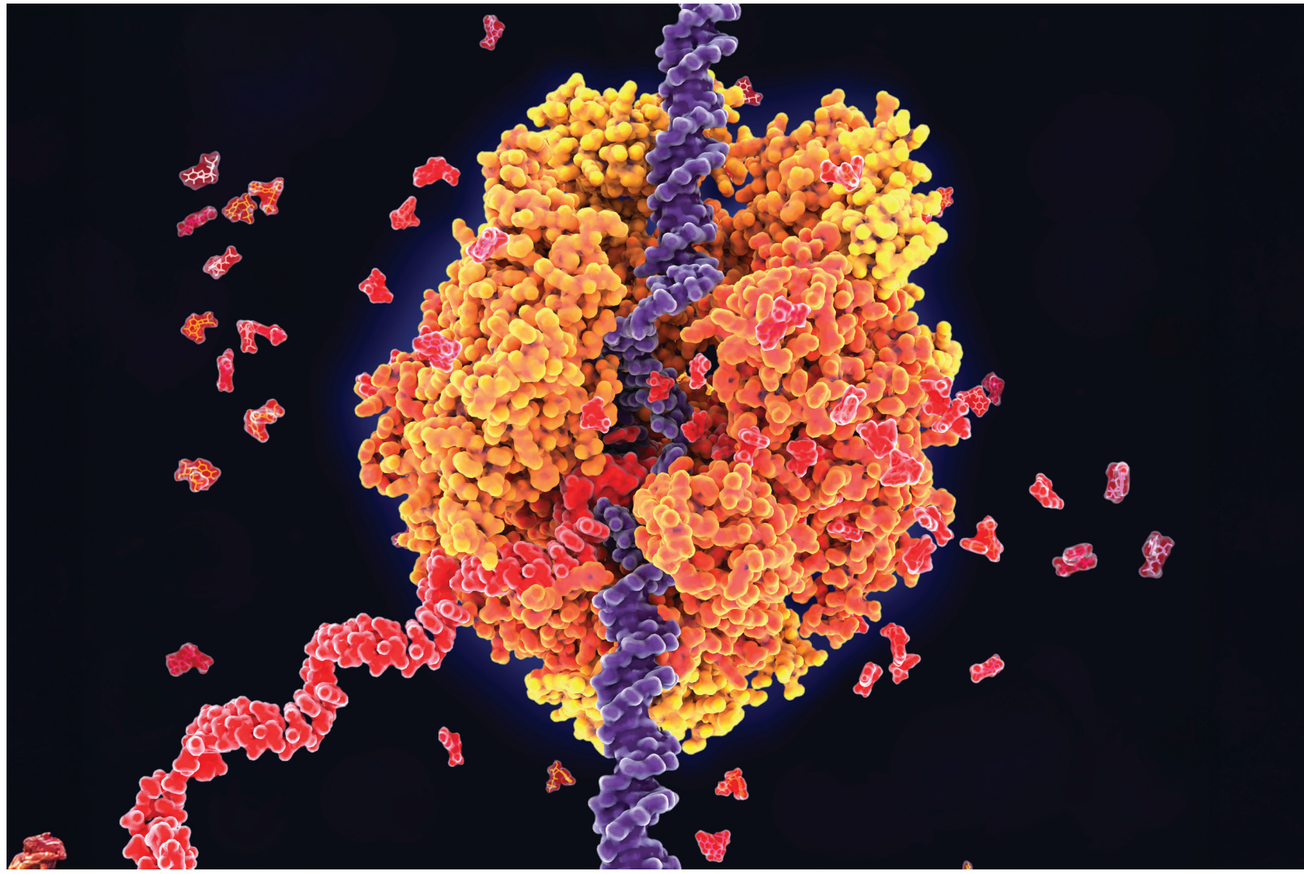

# Monitoring Survival and Function of Gene-Edited Porcine Grafts in Cynomolgus Monkeys

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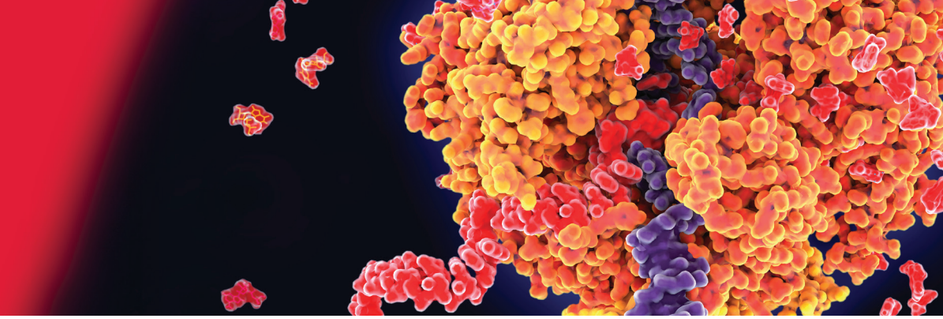

## INTRODUCTION

Xenotransplantation using gene-edited porcine kidneys represents a promising strategy to address the shortage of donor organs. Noninvasive methods for early and continuous assessment of graft function are essential in pig-to-nonhuman primate (NHP) transplant models. In these studies, EGEN-2784 porcine kidneys were transplanted into cynomolgus macaques. These kidneys had intentional genomic alterations, carrying specific edits intended to mitigate the risk of zoonotic disease transmission, eliminate acute rejection, and improve the compatibility of the porcine kidney with human recipients.

Xenograft performance was evaluated with a comprehensive multimodal monitoring approach, which incorporated ultrasonography, clinical pathology, and urine output.

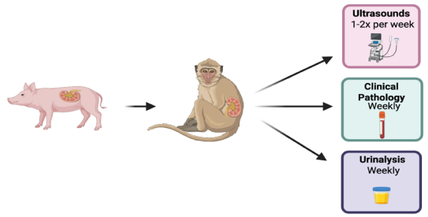


**Figure 1:** Schematic workflow of studies to evaluate EGEN-2784 gene-edited porcine kidneys xenotransplanted into NHPs

## RESULTS - ULTRASOUND IMAGING

Graft perfusion and size are critical for immediate and sustained renal function. Ultrasound imaging enables real-time assessment of vascular patency and microcirculatory integrity by evaluating the arterial and venous blood flows, resistive indices, and cortical perfusion of the porcine kidney xenografts (Figure 2a).

Any changes in these parameters may indicate compromised graft function before any detectable structural abnormalities or biochemical dysfunction. Abnormalities such as hydronephrosis can be detected early and can cause compression of the kidney tissue and reduced blood flow, leading to back pressure and potential impairment of renal filtration (Figure 2b).

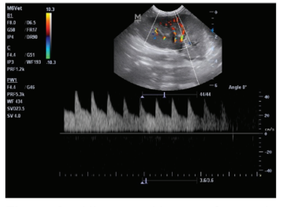

**Figure 2a:** Ultrasound image of normal graft function 21 days post transplant in NHP Subject 2 showing normal blood flow and perfusion

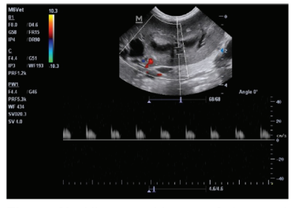

**Figure 2b:** Ultrasound image of abnormal graft function 21 days post transplant in NHP Subject 3 showing decreased perfusion and hydronephrosis.

## RESULTS - CLINICAL PATHOLOGY

Clinical pathology parameters including but not limited to serum creatinine, blood urea nitrogen (BUN), total protein, and albumin provide biochemical insights into renal filtration capacity and function.

- Serum creatinine is one of the most widely used indicators of renal function. It is a byproduct of muscle metabolism that is normally filtered out of the blood by the kidneys. When kidney filtration declines, creatinine accumulates in the bloodstream as seen in Subjects 1 and 3 (Figure 3).
- Blood urea nitrogen (BUN) measures the amount of nitrogen in the blood in the form of urea, a waste product generated from protein metabolism in the liver. Like creatinine, urea is excreted by the kidneys, so increased BUN levels can indicate impaired kidney function in Subjects 1 and 3 (Figure 4).
- Total protein reflects the overall concentration of proteins in the blood, including albumin and globulins. In kidney disease, particularly conditions that damage the glomeruli, proteins may be lost into the urine (proteinuria), leading to decreased levels in the blood. Monitoring total protein helps identify systemic effects of kidney dysfunction and protein loss as seen in Subjects 1 and 3 (Figure 5).
- Albumin plays a crucial role in maintaining oncotic pressure and transporting substances in the blood. Healthy kidneys prevent albumin from passing into the urine. Low serum albumin levels can indicate significant protein loss due to kidney damage or impaired protein synthesis. In combination with urinary findings, albumin levels help assess the severity of kidney injury and the integrity of the filtration barrier (Figure 5; Subject 1 and 3).

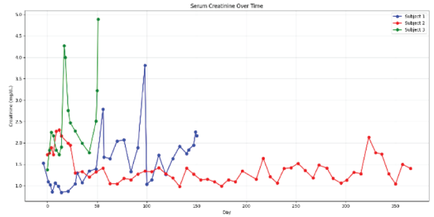


**Figure 3.** Creatinine (CRE) accumulation over time (up to 365 days) in the blood of three subjects: S1, S2 and S3.

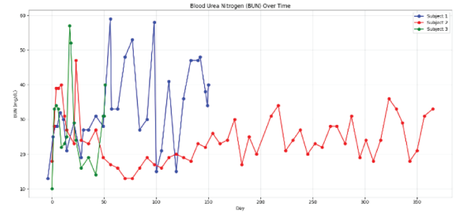


**Figure 4.** Blood urea nitrogen (BUN) accumulation over time (up to 365 days) in three subjects: S1, S2 and S3.

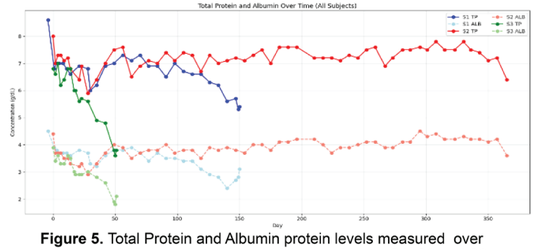


**Figure 5.** Total Protein and Albumin protein levels measured over time (up to 365 days) in the blood of three subjects: S1, S2 and S3.

## URINE VOLUME/PROTEIN EXCRETION

Monitoring urine volume and urinary protein excretion is essential in recently xeno-transplanted animals because it provides early, noninvasive insights into graft function and overall physiological stability.

- Urine output is a direct indicator of renal perfusion and filtration capacity; reductions may signal acute rejection, vascular complications, or ischemic injury. Conversely, adequate and stable urine production suggests proper integration and function of the transplanted organ (average urine rate of 2.6 mL/hr seen in Subject 2).
- Measurement of protein in the urine (proteinuria) is equally important, as it reflects the integrity of the glomerular filtration barrier. Elevated protein levels can indicate immune-mediated damage, inflammation, or early signs of graft dysfunction that may not yet be apparent through other clinical markers. In xenotransplantation, where immunological incompatibilities are a major concern, detecting subtle changes in protein excretion can help guide timely interventions.

## CONCLUSION

In conclusion, pig-to-nonhuman primate kidney xenotransplantation models are important for assessing gene-edited porcine kidney function. Noninvasive monitoring is essential for understanding graft performance and ensuring the welfare of the transplanted animals.

In this study, 3 NHP Subjects were evaluated using a multi-modal strategy combining ultrasonography, clinical pathology, and urine output. This strategy is imperative for early detection of dysfunction and precise evaluation of graft health and strengthen the translational potential of xenotransplantation to support its progression toward clinical applications.

## CONTACT

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