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## **Pattern of porcine CMV detection and its association with recipient survival following renal xenotransplantation in non-human primate preclinical study**

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**Introduction:** With growing interest in xenotransplantation to resolve the worldwide organ shortage, a considerable progress in the prevention of immunological rejection has been made using genetic modifications of pig that is considered the best donor animal. However, a paucity of knowledge exists in the potential zoonotic transmission and its impact on clinical outcome. Notably, porcine cytomegalovirus (pCMV), also known as Roseolovirus, remains a major barrier to clinical application of xenotransplantation. pCMV is highly resistant to the traditional antiviral therapy and has been reported to negatively impact on the graft survival. This study was conducted to analyse the pattern of pCMV detection, and the association between presence of pCMV and survival of cynomolgus primate recipients following kidney xenotransplantation.

**Methods:** A retrospective review was performed in twenty-one pig-to-cynomolgus renal xenotransplants. Archived sections of various anatomical tissues and blood samples were analysed for the presence of pCMV, using real-time PCR, which is currently the gold standard modality for its detection. Genetically modified pigs with at least -1,3-galactosyltransferase knockout (GalT-KO) were used as a donor, and they were pre-operatively determined pCMV negative on routine husbandry practice.

**Results:** Despite negative pre-operative surveillance, five donor pigs were later found to be pCMV positive on PCR testing. Interestingly, the detection was not uniformly positive across the samples tested, indicating the significance of latency in pCMV and the need for multi-site testing. A marked difference was demonstrated in mean survival ( $p < 0.001$ ), with the pCMV negative kidney recipients ( $n = 17$ ) averaging 40.8 days and the pCMV positive recipients ( $n = 4$ ) only 8.0 days with rapid viral replication.

**Conclusion:** This study confirms that the presence of pCMV is associated with reduced survival following kidney xenotransplantation. Therefore, with no effective treatment available, thorough donor evaluation is warranted pre-operatively, remembering that pCMV is a latent infection.