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Invited Editorial

Commentary on "Indicators of impending pig kidney and heart xenograft failure: Relevance to clinical organ xenotransplantation" (Int J Surg 2019;Aug 21. Pii: S1743-9191(19)30215-8. doi:10.1016/j.ijsu.2019.08.024. [Epub ahead of print])

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Dear Editor,

End-stage organ failure is one of the most important public health concerns in the Unites States and around the world. Not only is there a shortage of human organ donors for people on waiting lists, there have been recent articles that highlight the fact that thousands of donated organs such as heart, kidney, lung, pancreas and liver are not being utilized because of conservative acceptance criteria [1]. Even if the number of accepted donated organs were increased, it would still not be enough to transplant everyone needing organ replacement. Some ways to relieve this shortage would either be to extend the life of the recipient by applying a short-term life saving artificial organ or bioreactor until a suitable donor is found or to find an alternative source for the donor organ.

Xenotransplantation has been proposed for many years as a way of filling the void of human organ donors. Although the roadblocks facing animal to human xenotransplantation are formidable, recent advances in the pre-clinical field are bringing us closer to making this a reality. The majority of the work has been focused on pigs as donors due to several reasons such as similar anatomy and physiology to humans. However, perhaps the greatest reason to focus on pigs is the valuable experience that has been accrued in genetically engineering pigs to be more compatible with the human immune system. Compatibility has advanced even further with the event of the CRISPER/Cas9 system (replacing such techniques as somatic cell nuclear transfer) that offers a high degree of specificity in construct design and results in pigs with multiple genetic alterations [2]. The available alterations, including complement and coagulation regulatory proteins, the blockade of costimulatory molecules and mTOR inhibition have resulted in longer-term function of xenografts [3,4].

Needless to say, developing and generating these potential donors is costly but the potential benefit will be to prolong human life that is now lost due to organ donor shortages. With the prospect of clinical trials not far off, every advantage needs to be taken to protect a functioning graft before it proceeds to a point that failure is imminent and rescue is not possible. The report by Iwase et al. outlines a way to predict an impending graft failure 2–3 days before conventional indicators such as a rise in serum creatinine or troponin T. They suggest thrombocytopenia and a fall in plasma fibrinogen precede conventional signs of graft failure and if present; further investigation of graft status is warranted [5].

The techniques used in Iwase et al. provide a valuable tool to know even earlier than current indicators, when to start rescue therapies for a transplanted whole organ xenograft. Early indications of graft failure are extremely important in xenotransplantation because of the many redundant pathways in the body by which foreign tissue can be rejected. For clinical xenotransplantation to be successful, these pathways must be controlled.

Conflicts of interest

None.

Provenance and peer review

Invited Commentary, internally reviewed.

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References

[1] K. Kindy, L. Bernstein, D. Keating, Lives lost, organs wasted. The Washington post (2018, Dec. 20) retrieved from, http://www.washingtonpost.com/graphics/2018/national/organ-transplant-shortages/.
[2] M. Hryhorowicz, J. Zeyland, R. Stomski, D. Lipinski, Genetically modified pigs as organ donors for xenotransplantation, Mol. Biotechnol. 59 (2017) 435–444.
[3] I.A. Rosales, R.B. Colvin, The pathology of solid organ xenotransplantation, Curr. Opin. Organ Transplant. 24 (5) (2019 Oct.) 535–542.
[4] R. Bottino, M. Wijkstrom, D.J. van der Windt, H. Hara, M. Ezzelarab, N. Murase, S. Bertera, J. He, C. Phelps, D. Ayares, D.K.C. Cooper, M. Trucco, Pig-to monkey islet xenotransplantation using multi-transgenic pigs, Am. J. Transplant. 14 (2014) 2275–2287.

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1743-9191/

[5] H. Iwase, A. Jagdale, T. Yamamoto, G. Zhang, Q. Li, J. Foote, D. Ayares, B. Ekser, H. Hara, D.K. Cooper, Indicators of impending pig kidney and heart xenograft failure: relevance to clinical organ xenotransplantation, pii: S1743-9191, IJ Surg (19) (2019 Aug 21) 30215–30218, https://doi.org/10.1016/j.ijsu.2019.08.024 ([Epub ahead of print]).

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