



Invited Commentary

Search for the best site in islet xenotransplantation



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Islet transplantation might replace human solid organ pancreas transplantation for the treatment of type 1 diabetes (T1D) with improving results over the years and its nature of less invasiveness. Although the technology, immunological advances, and our understanding of how to transplant islets will help us to achieve better results, the shortage of human pancreata will impact our ability to offer this treatment to millions of people with T1D. Therefore, clinical islet xenotransplantation using pig pancreas cells will overcome the shortage of transplantable islets [1].

Although initial trials in clinical islet xenotransplantation showed encouraging results, the cure of T1D was not achieved [1]. The clinical trial was done with encapsulated wild-type pig islets, transplanting them freely into the peritoneal space [1]. Many pre-clinical studies in pig-to-primate islet xenotransplantation showed prolonged survival with the correction of T1D using islets from genetically-engineered pigs, transplanting them mainly into the liver via portal vein [2]. However, other sites for islet xenotransplantation were explored, such as, renal subcapsule, spleen, skin, omentum, gastric submucosa, pancreas, and muscle [2].

In the current issue of International Journal of Surgery, Smood et al. have reviewed a viable option, renal subcapsule, as the site for islet xenotransplantation [3]. This extensive and timely review showed that renal subcapsular space could be a good site for islet xenotransplantation, especially when it is done simultaneously with pig kidney xenotransplantation. Simultaneous pig kidney and islet xenotransplant could mimic simultaneous pancreas and kidney transplant for the cure of patients with end-stage renal disease with and/or due to T1D [3]. Although a desirable site for islet transplantation should have all characteristics, as shown in Table 1, ongoing research showed that there is no perfect site. In the review by Smood et al. advantages and disadvantages of renal subcapsular space were compared with the most common islet transplantation site, liver via intraportal injection [3]. While the renal subcapsular space would

Table 1

Desired characteristics for the efficient site of islet xenotransplantation.

Efficacy of clinical trial
Patient safety
High oxygen tension
Rich vasculature/re-vascularization
Site of insulin released by the graft – portal system
Surgery – less invasiveness
No instant blood-mediated inflammatory response
Possibility of biopsy to follow up rejection

have the advantage of (i) less exposure of transplanted islets to drugs and toxins, (ii) better immune protection, (iii) no instant blood-mediated inflammatory response (IBMIR), the main disadvantage is poor blood supply and therefore delayed revascularization [3]. Another important factor is that blood return of the renal subcapsular space is to the caval system bypassing the portal system. Some researchers explored the use of gastric submucosal space as a site of islet transplantation. Although the experience was limited, gastric submucosal space could have several advantages, such as (i) reachability and transplantability via endoscopy, (ii) blood return to the portal system, (iii) avoidance of IBMIR, and (iv) the feasibility of biopsy via endoscopy [4].

We are now in an exciting era for clinical xenotransplantation. With better and newer co-stimulation-based immunosuppression regimen for solid organ and islet xenotransplantation [5], availability of genetically-engineered multi-gene pigs, and prolonged survivals in pre-clinical (pig-to-nonhuman primate) trials, kidney, heart, liver (as a bridge), and islet xenotransplantation will soon be a clinical reality.

Conflicts of interest

All authors have no conflicts of interest to disclose.

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