EDITORIAL

New ideas for old problems: how scientific advances can change the future of organ transplantation

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Organ transplantation is facing major changes. After a long time of small step improvements, recent scientific advances may provide innovative solutions to fundamental unresolved barriers. Organ scarcity is among the most important ones: despite sustained efforts through remarkable medical and political initiatives, in most countries the number of available organs is not sufficient and the number of patients waiting for a transplant continues to grow. This *Focus Issue* of *Transplant International* presents a selection of approaches based on scientific innovation, which might contribute to overcome this problem. The topics covered by the review articles range from clinical applications of organ reperfusion to the most recent advances in stem cell biology and regenerative medicine. Biomedical research is moving forward at a very fast pace with new technologies being developed every month: the purpose of this review article was not to provide a comprehensive review of all recent discoveries, but to show how different strategies are being pursued to achieve this important aim.

Naganuma *et al.* [1] highlight the importance of understanding developmental biology to generate organoids and tissues starting from pluripotent stem cells. In the last years it was possible to generate organoids with complex structures, but major technical issues need to be solved to obtain transplantable organs. The authors systematically summarized the major hurdles to be overcome in the particularly challenging field of renal biology, such as the integration of vascular structures and the need to generate large structures, such as a ureter. The fascinating idea of generating human organs in large animals by taking advantage of genome editing techniques might provide an optimal solution for several of those problems but raises additional challenges and important ethical issues. Though not ready for the clinic, the transplant community must follow the fast development of these technologies towards first applications with human tissues, start considering regenerative medicine as an integral component of its future and take in hand the ethical discussion related to it.

A potential solution to facilitate the correct microscopical organization of tissue and to obtain organs with a sufficient size and macroscopic structure to be transplanted might be offered by bioengineering technologies. As an example, Hillebrandt *et al.* [2] summarize the concept behind organ decellularization and recellularization and the most recent achievements and drawbacks reported by the scientific community trying to move forward this technology for the generation of a transplantable heart, lung, liver, kidney, pancreas and intestine. In some cases, this approach resulted in short-term organ function in animal models, but long-term functionality remains illusory. Starting from induced pluripotent stem cells, it would be theoretically possible to re-cellularize an organ scaffold (obtained from humans or animals) with patient-derived cells and therefore to proceed to transplantation without immunosuppression. This new source of tissues would presumably lead to an unrestricted availability of transplantable organs and therefore dramatically change the therapeutic approach in patients with organ failure, but – also in this case – several hurdles (such as the immunogenicity of the scaffolds and the combination of different cell types required to obtain functional complex tissues) need to be overcome prior to a clinical application.

As opposed to the first two review articles focused on basic science and biotechnology, Weissenbacher *et al.* [3] reviewed the most recent advances in the clinical application of organ perfusion and preconditioning. Organ preservation is a fundamental topic in transplantation, but novel technologies promise to redefine the benchmarks for organ quality and ultimately expand the donor pool by obtaining sufficient organ quality from marginal donors. In addition, the renewed interest for organ perfusion is paving the way to *ex vivo* organ therapies aiming at tissue repair, high-precision tumour

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targeting, immunomodulation and genetic engineering. This might expand the therapeutic options in transplantation surgery and change patient care after organ transplantation.

Transplantation medicine is evolving: recent scientific discoveries give us hope for successful solutions to fundamental limitations and for unexplored options in transplantation medicine. By presenting different strategies that might revolutionize the future of organ transplantation, this *Focus Issue* of *Transplant International* aims at stimulating discussion in the transplant community and at accelerating the translational process towards the clinic. It is time to start thinking about the technical, clinical, political and – most importantly – ethical issues related to scientific innovation in transplantation and particularly to novel sources of transplantable organs.

REFERENCES

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