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Editor's note:


Abstract:

Prior to the first successful allogeneic organ transplantation in 1954, virtually every attempt at transplanting organs in humans [5] had resulted in death, and understanding the role of the immune mechanisms that induced graft rejection served as one of the biggest obstacles impeding its success. While the eventual achievement of organ transplantation is touted as one of the most important success stories in modern medicine, there still remains a physiological need for immunosuppression in order to make organ transplantation work. One such solution in the field of experimental regenerative medicine [6] is interspecies blastocyst [7] complementation, a means of growing patient-specific human organs within animals. To address the progression of immune-related constraints on organ transplantation, the first part of this thesis contains a historical analysis tracing early transplant motivations and the events that led to the discoveries broadly related to tolerance, rejection, and compatibility. Despite the advancement of those concepts over time, this early history shows that immunosuppression was one of the earliest limiting barriers to successful organ transplantation, and remains one of the most significant technical challenges. Then, the second part of this thesis determines the extent at which interspecies blastocyst [7] complementation could satisfy modern technical limitations of organ transplantation. Demonstrated in 2010, this process involves using human progenitor cells derived from induced pluripotent stem cells [8] (iPSCs) to manipulate an animal blastocyst genetically modified to lack one or more functional genes [9] responsible for the development of the intended organ. Instead of directly modulating the immune response, the use of iPSCs with interspecies blastocyst [7] complementation could theoretically eliminate the need for immunosuppression entirely based on the establishment of tolerance and elimination of rejection, while also satisfying the logistical demands imposed by the national organ shortage. Although the technology will require some further refinement, it remains a promising solution to eliminate the requirement of immunosuppression after an organ transplant.

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