cells (5×10^5/recipient) activated by immunization with ovalbumin emulsified in complete Freund's antigen. Amplified numbers and affinities of transgenic T and B cells may induce cell fates that differ from endogenous cells.[6,7] Furthermore, follow-up durations for key experiments were relatively short (<5 days). Indeed, it is possible that with time, transiently, antigen-exposed B cells will be deleted gradually or anergized.

Despite these limitations, these observations may have relevance to transplant recipients. For example, with the ability of B cells to engage with antigens and the capacity to receive T cell help for 24 to 48 hours improve their chances for encountering the rare antigen-specific T cell at the T-B interface. If these B cells do not receive T cell help, they can still undergo repeated rounds of antigen exposure while preserving their ability to become fully functional upon T cell help. Because immunosuppression severely curtails T cell help, the ability of pathogen-specific B cells to return to baseline while becoming fully functional once T cell help becomes available may be critical for immunosuppressed patients in developing protective immunity after immunosuppression is reduced.[8]

These findings also underscore the importance of antigen persistence for B cells to become anergic or deleted. In solid organ transplant recipients, the allograft is a persistent source of antigen yet antibody-mediated rejection is one of the major causes of graft loss, raising the question on why B cell anergy or deletion does not occur. There are several possible explanations, for example, under conventional immunosuppression, the incomplete suppression of T cell help prevents alloreactive B cells from undergoing deletion or anergy. Alternatively, memory B cells have relaxed restimulation requirements as a result of epigenetics, expression of high-affinity BCR and costimulatory molecules,[9] and may therefore be more resistant to anergy and deletion compared with naive B cells. Indeed, the frequency of memory B cells in the peripheral blood of humans has been shown to increase with age.[10] Thus, additional investigations are necessary to define the susceptibility to anergy or deletion of memory compared with naive alloreactive B cell in the presence of solid organ allografts. Solving the conundrum of inducing anergy or deletion of memory B cells, in addition to memory T cells, is likely to be key to achieving successful transplantation tolerance.

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eResources

Tools for Predicting Kidney Transplant Outcomes

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A raft of clinical decisions could be simplified if it were possible to accurately predict individual clinical outcomes after kidney transplantation. There are now many alternative models based on clinical parameters available at the time of transplantation that were developed to predict time-to-graft failure[1-13] or patient survival.[14-18] Several such methods have been made publicly available as online tools [A-C]. Anecdotally, at least, these tools are accessed by kidney transplant recipients. Some attempts have been made to internally validate or compare the performance of these predictive models using registry data, but as yet, few have been externally validated in prospective studies.[11,19-21] Estimated posttransplant survival time

is controversially used to allocate organs for adult, single-kidney transplantation in some countries.[22] Even where Kidney Donor Risk Index[5] is not used for organ allocation, we are aware of nephrologists using this tool to gain an impression whether offered kidneys from "marginal" donors are likely to be suitable as single-organ transplants. We conclude that further studies are clearly needed to determine the accuracy of predictive tools based on common clinical parameters and to relate their performance to more sophisticated biomarker-based predictors of clinical outcome.

Links
[A] www.transplantscore.com/
[B] www.transplantmodels.com
[C] www.renalmed.co.uk/risk-calculator

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People in Transplantation

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