Mesenchymal stromal cells to induce tolerance to solid organ transplantation

PROPOSITIONS

Mesenchymal stromal cells to induce tolerance to solid organ transplantation

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The current state of the art of solid organ transplantation evokes the aphorism that actually successful transplantation is not a cure, but rather substitutes the manageable disease of immunosuppression for the incurable and fatal disease of organ failure. Thus, successful transplantation would be a realistic therapeutic option only whether donor-specific immunologic tolerance could be reliably and safely induced.

We now recognize that transplantation of MHC incompatible graft triggers the activation of graft destructive effector T cells and graft protective regulatory T cells (Tregs); it is the balance of such opposing subsets that ultimately determines the fate of an allotransplant.
The emerging data suggest that MSCs dampen effector T cell response, including memory cells, while promoting the emergence of Tregs. By skewing this balance MSC hold great promise as immunomodulatory cell therapy for tolerance induction in organ transplantation.

(This thesis)

Small studies with a few patients intensively studied will hopefully allow us to determine when and where MSCs should be administered and how they function to regulate host immunity. These considerations may be particularly imperative for new biological agents such as MSCs for which, despite encouraging initial results, uncertainty about safety and efficacy still exists

(This thesis)

The phenotype of B cells repopulating the peripheral blood in kidney transplant recipients after alemtuzumab, but not Bas/rATG, induction underwent significant variations that can be summarized in three phases: in the early post-transplant period, the few remaining B cells were composed primarily by Ag-experienced Bm3+4 and switched memory B cells. The second phase (midterm post-transplant, 2–6 mo) was characterized by a transient increase in transitional B cells, followed by the emergence of Bm2' B cells, processes that are mediated by the increase in serum levels of BAFF. The third phase in the long-term (>24 mo post-transplant) was characterized by a progressive increase in circulating B cell numbers, primarily due to the expansion of B cells with a naive phenotype. Both early and late changes in the B cell compartment were associated with an

increased incidence of de novo DSA at 1 y post-transplantation, coupled with worse long-term graft function.

(Todeschini M et al, 2013)

There are different kind of stem cells in different tissues, and even when the appropriate stem cell is selected for an indication it take years of research to learn how to administered the cell safely and effectively, as demonstrated by the decades of research that was required to transplant bone marrow safely and effectively. Thus, grasping the unique nature of specific stem cells is necessary to identify how to harness science for therapy, which may involve a broad range of intermediate steps. MSC are the newcomers to the club or are perhaps the founders of a new one.
Give them time and serious effort.

(Paolo Bianco et al, 2013)

Joy in looking and comprehending is nature's most beautiful gift

(Albert Einstein, 1879-1955)

Behind every problem there is an opportunity

(Galileo Galilei, 1564-1642)