

Editorial

Tissue Stem Cell Transplantation Notice for Mycophenolate Mofetil

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I wish to notify investigators in the rapidly growing field of allogeneic tissue stem cell transplantation that a commonly used immunosuppression agent, mycophenolate mofetil (MMF), may have unrecognized effects on treatment outcomes. Because of its lower toxicity compared to other immunosuppression regimen agents like methotrexate (MTX), previously MMF has been widely used for allogeneic hematopoietic stem cell (HSC) transplantation. The therapeutic target for MMF is inosine monophosphate dehydrogenase (IMPDH), which is potently inhibited by mycophenolic acid (MPA), the active metabolite of MMF. Inhibition of IMPDH activity in lymphocytes is thought to be responsible for MMF's immunosuppressive properties. The type II IMPDH is also responsible for the regulation of the self-renewal pattern of tissue stem cells. Up-regulation of IMPDH II or elevation of the pools of its guanine ribonucleotide products induces tissue stem cells to shift from asymmetric self-renewal to symmetric self-renewal [1]. Given this role for IMPDH II, inhibition by MMF administration could impact the behavior of tissue stem cells in therapeutic transplantation preparations. In HSC transplantation studies, compared to MTX, MMF decreases time to engraftment while providing similar degrees of immunosuppression [2,3]. The mechanism of accelerated engraftment has not been established. One possibility is MMF-induced increases in asymmetric self-renewal by transplanted HSCs, which would promote more rapid production of differentiated neutrophils and other cellular measures of

engraftment efficiency. Given these connections, current and future trials of allogeneic transplantation therapy with other types of tissue stem cells, as well as HSCs, may benefit from new attention to MMF for possible direct stem cell effects.

References

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