IL-7: griffinesque role in GVHD

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The development of graft–versus–host disease (GVHD) and immunoincompetence are the major obstacles to successful utilization of allogeneic hematopoietic stem cell transplantation (allo-HSCT). In this issue, Chung and colleagues report that blockade of IL-7Rα impairs the bad—GVHD, and restores the good—immune reconstitution after allo-HSCT.

IL-7 is critical for the development and maintenance of T cells in humans and for both T and B cells in mice.1 Interleukin–7 receptor (IL-7R) consists of 2 chains, the IL-7Rα and the common cytokine receptor γ-chain. The γ-chain is expressed by most hematopoietic cells, whereas IL-7Rα is expressed exclusively by lymphoid cells.1 Previous studies with infusion of exogenous IL-7 have shown variable effects on GVHD and immune reconstitution.2-5 Now, Chung and colleagues report on the effect of IL-7Rα blockade on GVHD and immune reconstitution after allo-HSCT. They show that inhibition of endogenous IL-7 with anti–IL-7α antibody treatment might eclipse any direct potential inhibitory effect on thymopoiesis. These observations, while in accordance with some earlier observations,1 appear to contradict reports that showed improved immunoreconstitution without worsening GVHD in mice when treated with IL-7.2,3 The different outcomes are likely due to the consequence of potentially distinct effects from the blockade of endogenous IL-7 versus exogenously administered IL-7 in the context of irradiation-induced inflammation and lymphopenia.4 Additionally, the different model systems, T-cell sources, and doses, timing, and duration of cytokine modulation might also explain the divergent results. It is, however, important to note that the extrapolation of IL-7Rα on mature T-cell subsets is variable and influenced by a variety of stimuli, and that it is also expressed on regulatory T cells, NKT cells, and γδ T cells, which modulate GVHD.1

While clinical trials with IL-7 are underway, this study raises important issues. It adds to the growing specter that IL-7 might enhance GVHD and retard immunoreconstitution. It reminds us that insights from animal models, especially when they conflict, must be extrapolated to humans with caution. Along with previous observations, this study further underscores the potent effects of IL-7 on immune modulation and reconstitution after allo-HSCT.2-5 Thus, much like taming the mythical griffin to harness its powerful effects, which could be harmful or beneficial, the potential effects of IL-7 after allo-HSCT need to be understood better before harnessing its clinical utility.

Conflict-of-interest disclosure: The author declares no competing financial interests.

REFERENCES

Comment on Aerbajinai et al, page 2864

THAL for THAL?

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In this issue of Blood, Aerbajinai and colleagues establish that thalidomide can increase fetal γ-globin gene expression in human adult erythroid cells in an ex vivo culture system.

Sickle cell disease and β-thalassemias are the most common monogenic diseases of man. They are found in the “malaria belt” that extends from the Mediterranean and sub-Saharan Africa through southeast Asia and southern China. These hemoglobin mutations...
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