Anti-ASGM1, NK Cell, Activated T Cell, and Graft-vs-Host Disease

To the Editor:
In 1978, Korngold et al demonstrated that removal of "all mature" T lymphocytes by anti-Thy-1.2 and complement was very effective in preventing the development of significant graft-vs-host disease (GVHD) in mice [1]. However, implementation of this strategy in patients using OKT3 failed to achieve similar impressive results [2]. Having learned of the work of Lopez who demonstrated that the severity of GVHD in man was closely related to initial NK activity of the recipients [3], Charley and his colleagues began investigating the effect of anti-asialo GM1 (aASGM1), an antiserum believed to be NK-specific, on the incidence and severity of GVHD in mice recipients and found this antiserum to be highly effective in preventing lethal (but not all) GVHD [4].

However, they later found aASGM1 to be nonspecific for NK cells [5], and the mechanism by which aASGM1 prevented lethal GVHD was, in fact, related to its ability to bind and extinguish T cells which became activated after transplantation [6]. This latter finding confirms that T cells are vital to the development of significant GVHD in human, as well as in murine model.

To explain these seemingly contradictory findings, it is necessary to explore the technics employed to remove T cells and to understand the various surface antigens involved.

Korngold et al used anti-Thy-1.2 and complement to remove "all mature" T cells [1]. Since Thy-1 is the first surface antigen, expressed on the surface of murine T lymphocytes, immature T cells and possibly some other noncommitted hematopoietic precursors are also removed by this technic. On the contrary, T3 (recognized by OKT3) appears on the surface relatively late in the ontogeny of T lymphocytes [7]. OKT3 therefore removes only more-mature forms of T cells. As demonstrated by Korngold, that contamination of the graft by as few as 0.3% T cells was enough to cause a high incidence of lethal GVHD [1]. It is thus not surprising why Filipovich et al failed to achieve a result comparable to that reported in the murine experiment.

Depletion of T lymphocytes by sequential use of soybean agglutinin and differential sedimentation of sheep E-rosette forming cells [8] is a different approach because the sheep RBC receptor, T11 antigen, is the first to be expressed on T cell surface [7]. More importantly, this receptor had been shown to facilitate T lymphocyte-target cell interactions and to activate resting T cells independently of a specific antigen and the MHC [9]. This method can therefore achieve a better result as experienced by Reisner et al, since more of the immature forms are also removed.

Both OKT11 and aASGM1 can be very useful in the prevention of significant GVHD in patients undergoing bone-marrow transplantation and deserve further attention. Monoclonal antibodies have been increasingly useful both as a probe and as a therapeutic agent. New antibodies are continuously introduced at a very rapid pace. It is therefore imperative to understand their power and limitation. Inference from finding of study using monoclonal antibodies should be made with great caution.

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REFERENCES

REPLY
Dr. Sriprachya-anunt's letter cautions against extrapolating murine experimental results too readily to the human situation. We certainly concur that only additional investigations will determine whether the use of antibodies against asialo-GM1 may be applicable in human bone marrow transplantation to prevent GVHD. However, we cannot resist a further speculation, with the same caveat noted.

Recent findings of Murphy, Kumar and Bennett have conclusively implicated both mouse NK cells and T lymphocytes in the rejection of donor marrow [1,2]. Because asialo GM1 is constitutively expressed on NK cells and becomes expressed on activated T cells, it is possible that administration of anti-asialo GM1 will simultaneously prevent GVHD and marrow rejection.

REFERENCES

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