

# Stem Cells and Immune Rejection

*By Suzanne Kadereit*

Immune rejection is a well-studied, but not completely understood complication of organ or cell transplantation. The immune system of the patient recognizes cells and tissues that are not "self" and mounts a rapid response, which consists of attack of the graft. This attack can be rapid and very strong and is called acute rejection, or can be milder but sustained for a longer period of time, and is called chronic rejection. In both cases, however, the loss of the graft ensues.

A complication of the transplantation of hematopoietic stem cells for reconstitution of the blood, is a condition called graft-versus-host disease, in which immune cells contaminating the hematopoietic stem cell graft recognize the new host (the patient) as "foreign" and attack the host's tissues.

Either type of immune rejection can result in loss of the graft or death of the patient. Treatment with immunosuppressive drugs can lessen the severity of the rejection, but usually not suppress an already launched response. In addition it leaves the patient susceptible to infections.

Although in the last few years immunologists have gained major insights into how immune rejection mechanisms are regulated, it has also become more apparent that the complications of cell and organ transplantation will not be easily overcome with prophylaxis or with treatment.

The only way to overcome immune rejection, or rather to avoid it, is to perfectly match the donor and the recipient. A perfect match, however, exists only between identical twins. For all other patients, donor and recipients are matched as

well as possible, and the patients must remain on immunosuppressive drugs for the rest of their lives, to prevent the occurrence of an immune rejection with deadly outcome.

For the vast majority of patients in need of transplants or tissue repair there are no appropriate donors. Therapy with stem cells has the potential to alleviate this very acute donor shortage, and to also treat degenerative diseases. However, the stem cells must either be derived from the patient who will ultimately receive the transplant, or the stem cells must be engineered in a way to circumvent an immune reaction.

Currently, the approach that appears most promising entails using embryonic stem cells whose DNA has been replaced with the patient's DNA, thus becoming "self". This procedure is called therapeutic cloning.

Another approach to avoid immune rejection that is now under clinical investigation, consists of destroying the patient's own immune system and replacing it with immune cells from the organ donor, prior to the organ transplant.

However, current treatments to eliminate the patient's own immune system are extremely hazardous and not always successful. Moreover, it takes several months to establish the new immune system in the patient, during which time the patient is vulnerable to infection.

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