Emerging Immunology of Stem Cell Transplantation

Elaine S. DeMeyer

Objectives: *To review critical areas of recent advances in immunology related to hematopoietic stem cell transplantation (SCT) and developing science that hopefully will be translated into improvements in patient care.*

Data Sources: *Review of literature and electronic data.*

Conclusion: *An overwhelming amount of diverse information related to the science of immunology and hematopoietic SCT is available. Hot topics of clinical focus appear to be in the area of donor selection and human leukocyte antigen testing, cellular functioning as it relates to immune modulation, immune reconstitution, and the source of stem cells.*

Implications for Nursing Practice: *The concept of immunity introduced over 200 years ago has evolved into everyday language in hematopoietic SCT. Nurses are challenged to keep their knowledge current with recent advances and the integration of immunotherapy into traditional care.*

Key Words: *Transplant immunology, human leukocyte antigen, HLA typing, dendritic cells, immune reconstitution.*

TRANSPLANT immunology is a general term for the complex phenomena of the pathobiology of the immune system in transplantation. Internet search results mostly lead to solid organ transplant with narrowing to stem cell transplant (SCT) pointing to a wide array of subjects from hematopoietic stem cell transplantation (HSCT), to embryonic stem cells, to heart or brain regeneration. Entire journals are dedicated to the science of transplant.

Elaine S. DeMeyer RN, MSN, AOCN®: *President and CEO, Creative Cancer Concepts, Inc., Rockwall, TX.*

Address correspondence to Elaine S. DeMeyer RN, MSN, AOCN®, Creative Cancer Concepts, Inc., 705 N. Goliad, Suite A, Rockwall, TX 75087; e-mail: elaine@creativecancerconcepts.com

0749-2081/09/2502-$32.00/0.
doi:10.1016/j.soncn.2009.03.001

This article will cover four current and emerging issues in SCT immunology. These include 1) tissue typing advances in human leukocyte antigen (HLA) and the role of HLA-DP, 2) cellular functioning, specifically activated T cells and dendritic cells (DCs), 3) sources of stem cells, and 4) immune reconstitution. Particular emphasis is placed on attempting to balance science and real-world application to clinical practice.

Human Leukocyte Antigen (HLA) Typing

With the completion of the human genome project and more clinical experience with HSCT, it is clear that there are more genetic differences between individuals than originally hypothesized (Fig 1), which has encouraged discovery of more HLA alleles than the 500 already identified. With DNA sequencing technology, a genome-wide analysis is able to help with optimal donor selection and better prediction of patient outcome. For

example, testing for certain genetic polymorphisms in innate immunity can help identify patients at increased risk for infection post HSCT.[1]

Selection of donors becomes especially critical among adult unrelated donors. According to the National Marrow Donor Program, over half of patients in the United States will have 10 or greater matched donors based on tissue typing of the HLA, also called the major histocompatibility complex (MHC). Two main classes of MHC or HLA are Class I and Class II. Class I major antigen present from inside cells and are found on almost all nucleated cells and include A, B, and C. Class II are found on antigen-presenting cells such as macrophages, B cells, and DCs and include DR, DQ, DP.[2,3] Each parent contributes one haplotype to make an HLA phenotype consisting of two sets of six major antigens. HLA typing is performed, typically searching for 10 alleles—HLA A, B, C, DR, DQ (Fig 2),[4] but can vary between labs. High-resolution tissue typing with matching for these alleles has resulted in improved outcomes. The contribution of minor Class I antigens HLA E, F, G remains unclear.

One area of controversy is whether HLA typing should be done for HLA DP and what is the clinical significance. Studies with unrelated donor transplant suggest that DP mismatch worsens survival regardless of other HLA typing and causes an increased risk of acute graft-versus-host disease (GVHD).[5-8] Another area of debate is what other factors need to be considered after HLA typing. Donor characteristics for consideration typically include gender, weight, number of pregnancies, overall health, and age. What is not known is if a donor with favorable characteristics (eg, male, younger, good size, healthy) but one HLA mismatch will provide better outcomes than a donor with unfavorable characteristics (eg, female, smaller, with > 2 pregnancies) but is a full match.[9]

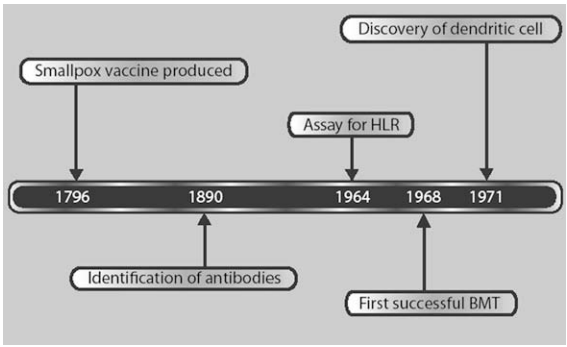

FIGURE 1. Landmarks in SCT immunology history.

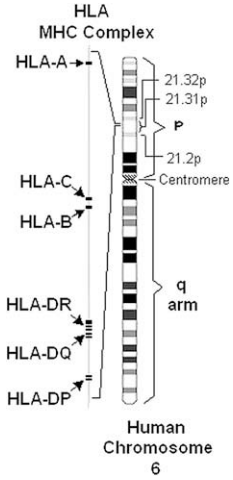

FIGURE 2. HLA/MHC complex. (Reprinted with permission from Deitiker.[4])

Cellular Functioning

Allogeneic HSCT is more than stem cell rescue after conditioning. It is a form of adoptive cellular immunotherapy that involves the potential immune recognition and attack between both donor and host. Immunobiologic reactions include host-versus-graft (HVG) reactions, GVHD, graft-versus-tumor (GVT) activity, and immune reconstitution to prevent opportunistic infections.[10] Each cell of the immune system can be thought of as a player in the immune system orchestra. Without one type of instrument, the resulting sound is not complete. Critical to the orchestra is the conductor, which in the immune system is the DC. DCs play an important role in activating T cells for tumor kill GVT and GVHD. Besides DCs and T lymphocytes, the other key cell in transplant immunology is the natural killer (NK) cell.

The immune system of the donor has the ability to kill cancer cells of the host. Donor graft-killing cancer cells (GVT) can occur in two main ways: 1) through T-cell receptor (TCR) interaction through antigen presentation, and 2) by the donor NK cells.[11] Most of the antitumor activity of the allogeneic donor cells is contained within the DCs through interaction with the TCR. The targets are then lysed with peptides perforin, granzyme, and Fas L. In order for the TCR to recognize the target, the antigen must be presented by antigen-