Cancer Immunotherapy: Will Expanding Knowledge Lead to Success in Pediatric Oncology?

Terry J. Fry, MD[a,*], Arjan C. Lankester, MD, PhD[b]

KEYWORDS

• Cancer vaccines • Adoptive cell transfer • T cells • NK cells
• B cells • Tumor immunity

The initial use of immunotherapy for cancer occurred in the early 1900s when Coley[1] used bacterial products to treat patients who had Ewing sarcoma based on the observation that postoperative infections seemed to diminish the likelihood of tumor recurrence. A number of patients were treated with these bacterial products, resulting in regression in a few.[2] James Ewing was simultaneously testing radiation as a means to treat these sarcomas, and controversy as to which approach was superior ensued. The consistency in response seen with radiation led to this treatment being more widely accepted, and the field of immunotherapy would need to wait approximately 50 years until it was explored further. The past 25 years have seen an increase in our understanding of immunology and further expansion in the clinical use of immunotherapeutic modalities. How immunotherapy will be integrated with chemotherapy, radiation, and surgery remains to be established. Although there have been successes in the field of immunotherapy, they have been inconsistent, and it is hoped that increased understanding of the basic principles of immunology will improve the consistency of beneficial effects. In this article, we briefly provide a general overview of our current understanding of the immune system, with a focus on concepts in tumor immunology, followed by a discussion of how these concepts are being used in the

A version of this article was previously published in the *Pediatric Clinics of North America*, 55:1.
[a] Division, Blood/Marrow Transplantation and Immunology, Center for Cancer and Blood Disorders, Children's National Medical Center, 111 Michigan Avenue, NW, Washington, DC 10010, USA
[b] Department of Pediatrics, BMT-Unit, Leiden University Medical Center, Leiden, the Netherlands
* Corresponding author.
E-mail address: tfry@cnmc.org (T.J. Fry).

Hematol Oncol Clin N Am 24 (2010) 109–127
doi:10.1016/j.hoc.2009.11.010 **hemonc.theclinics.com**
0889-8588/10/$ – see front matter

clinic. Although this overview illustrates the highly integrated nature of the immune system, we divide the clinical section into specific arms of the immune response. It is likely that, as with the natural immune response, immunotherapy is most effective when the components of the immune armamentarium are used in combination.

PRINCIPLES OF THE IMMUNE RESPONSE

The immune system evolved to protect the host from invading pathogens. These processes can effectively clear aberrant self-antigens, including malignant cells.[3] A complete description of the immune response is beyond the scope of this article, but we highlight areas relevant to cancer immunotherapy. In general, the immune system can be divided into the innate response, which allows rapid, nonspecific protection, and the adaptive response, which develops more slowly but provides specific recognition of antigens via expression of carefully rearranged receptors. **Fig. 1** illustrates the various components of the immune response. Although the innate system is an essential part of successful immune clearance, this article focuses on adaptive immunity.

The adaptive immune system contains millions of potential specificities requiring amplification upon initial antigen encounter, which results in delayed onset but allows for a memory effect such that subsequent exposures to antigen result in a more rapid

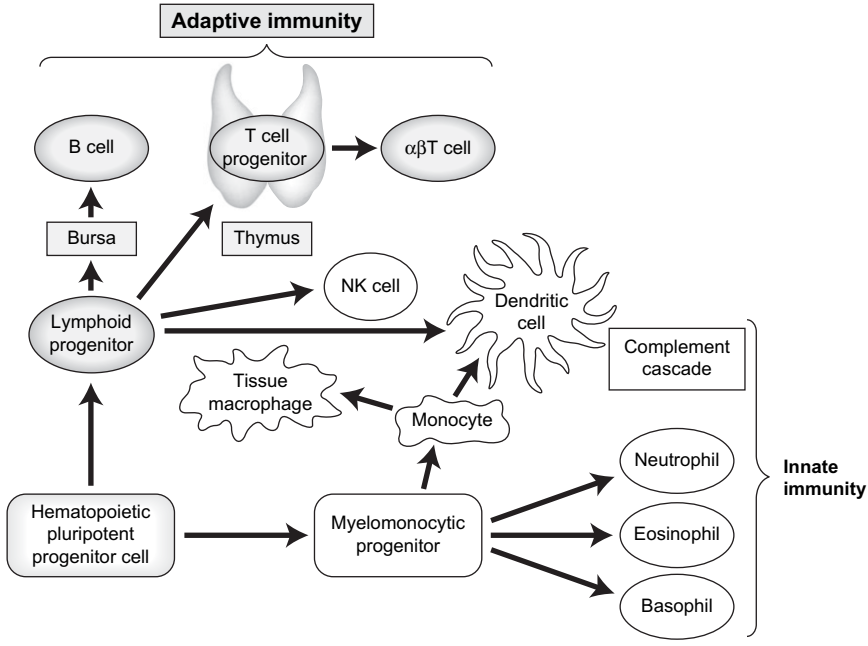

Fig. 1. The immune response can be divided into innate and adaptive components. The innate system provides rapid and relatively nonspecific protection, whereas the adaptive response is delayed but more specific. Innate and adaptive responses are critical for effective immunity, although each plays more or less prominent roles depending on the nature of the immune response (viral, bacterial, etc). Monocytes/macrophages, neutrophils, basophils, and eosinophils serve as the primary players in innate immunity. B cells and αβ T cells represent the central components of adaptive immunity. NK cells are generally considered a member of the innate response, although there is some specificity to NK cell recognition.