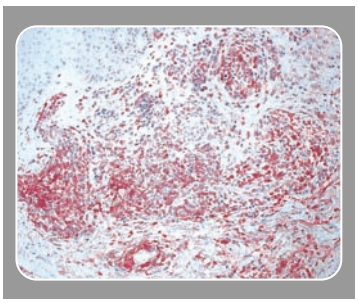
inside blood

Tackling T-cell tumors

Cutaneous T-cell lymphomas represent a tumor with a defined target, the somatically rearranged T-cell receptor (TCR), that should represent a tumor-specific immunologic target analogous to the idiotype (Id)–specific target of B-cell lymphomas. The Id antigen on B-cell lymphomas has been targeted by Levy and others using a variety of vaccine approaches and large prospective clinical trials of this strategy are ongoing. The secreted antibody associated with myeloma has also been demonstrated to be processed and presented on malignant B cells and could be recognized by antigen-specific T cells.[1] Although much less common than B-cell malignancies, the TCR



on T-cell malignancies also represents an attractive immunotherapy target. Unfortunately, the TCR is not secreted and capturing the antigen from an individual's tumor for the creation of a vaccine usually involves creating a whole tumor lysate.

Maier and colleagues (page 2338) performed this experiment, vaccinating 10 cutaneous T-cell lymphoma patients with tumor lysate pulsed onto autologous dendritic cells (DCs) loaded with tumor lysate and given by intranodal injection.[2] Intranodal injection appears to be a important route of delivery since the initial observation that intravenous and subcutaneous delivery in humans lead to little trafficking to lymph nodes, whereas only a fraction of DCs injected into the dermis trafficked to draining lymph nodes.[3]

In this report, Maier and colleagues have shown the induction of antigen-specific T-cell responses and clinical response in patients with cutaneous T-cell lymphoma. The authors noted that delayed-type hypersensitivity to the tumor lysate was increased in treated patients and recognition of autologous tumor cells by peripheral blood mononuclear cells (PBMCs) following vaccination compared with PBMCs obtained prior to vaccination as determined by cell proliferation and cytokine release assays. Significant recognition was notable in 3 patients, all of whom had a clinical response (1 complete and 2 partial responses). One element that was not specifically addressed by this study was whether an immune response to the specific TCR of each tumor was induced.

Nonetheless, the potential to target malignant T-cell tumors is demonstrated in this pilot study. The feasibility and utility of DC vaccination by the intranodal route is again highlighted. Finally, the correlation of autologous tumor-specific immune responses with clinical responses is provocative. The authors did not demonstrate specific immune responses against the TCR of each tumor, a finding that would have important indications for the treatment of this malignancy but also for the therapeutic elimination of T-cell clones in autoimmune disorders. Further investigation of immunotherapy in this promising model system is certainly warranted.

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2. Nestle FO, Alijagic S, Gilliet M, et al. Vaccination of melanoma patients with peptide- or tumor lysate-pulsed dendritic cells. Nat Med. 1998;4:328-332.
3. Morse MA, Coleman RE, Akabani G, Niehaus N, Coleman D, Lyerly HK. Migration of human dendritic cells after injection in patients with metastatic malignancies. Cancer Res. 1999;59:56-58.

To each according to his need

It is the aim of medical science to increase our capacity to treat effectively the most severe manifestations of disease. It is our expectation that society will reward this pursuit of new medical knowledge by providing the enabling resources to translate it to better care for patients. The report in this issue of *Blood* by Gringeri and colleagues (page 2358) entitled "Cost of care and quality of life in hemophilia complicated by inhibitors: the COCIS Study Group" provides compelling data that extensive investment in this particularly problematic subset of the hemophilia population, when applied in the context of a comprehensive hemophilia treatment center care model, can result in an acceptable quality of life for most of these individuals. Certainly the costs for such care, when individualized, are extraordinary: approximately €18 000 per month. This is a cost that is consistent with earlier reports[1] and reflects overwhelmingly the expense associated with the need to use "by-passing" coagulation factor concentrates to achieve hemostasis. As the authors indicate, a significant portion of these exceedingly high costs is attributable to the need for these bypassing agents, and to provide hemostasis for restorative surgery and the resultant rehabilitation—all legacies of the high morbidity of a long-standing factor VIII or IX inhibitor.

Two significant observations distinguish this publication. First, since the cohort is drawn from approximately one third of the individuals meeting accepted definitions of inhibitor classification in a large country (Italy), it permits the authors to extrapolate the cost of care for these rare individuals across the society's entire health care delivery system—an estimated 0.70 per Italian citizen per year. This enables the disinterested observer to place the costs in context. Second, the employment of validated