

Therapeutic vaccination for lymphoid malignancy

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Abstract

At the present time there is no active immunotherapy approved for treatment of any malignancy.

B-cell malignancy arises from one original B lymphocyte and therefore all the members of a given lymphoma tumor population have the same unique immunoglobulin which can serve as a target for immune therapy. When the idiotype of each immunoglobulin is used as a vaccine, antibodies and T cells can be induced and each can cause rejection of the tumor by the host. This special opportunity for tumor specificity is accompanied by the challenge of constructing a different vaccine for each patient.

The first clinical trial of Id vaccination for lymphoma at Stanford University included patients with low-grade, follicular lymphoma. Over half (14/32) mounted anti-Id immune responses to the vaccine. Development of an immune response is strongly correlated with prolonged freedom from disease progression in comparison to non-responders. Overall survival has also been superior in immune responding patients. The clinical activity of Id-KLH vaccination was confirmed by investigators at the National Cancer Institute. Subsequent phase II trials supported by industry, Genitope and Favril, have led the current phase III trials that hopefully will prove the efficacy of idiotype vaccination.

How can this customized vaccine approach be applied to large numbers of patients? The ability to amplify and clone Id genes from B-cell tumor specimens using PCR has opened up a variety of new strategies that can streamline the production of Id vaccines. It may even be possible to use formalin fixed, paraffin embedded tissues, thus obviating the need for fresh tumor tissue. Once the V region genes are cloned the Id proteins can be produced in mammalian cells, insect cells, plants or bacteria. It may even be possible to produce proteins in a completely cell free transcription/translation system.