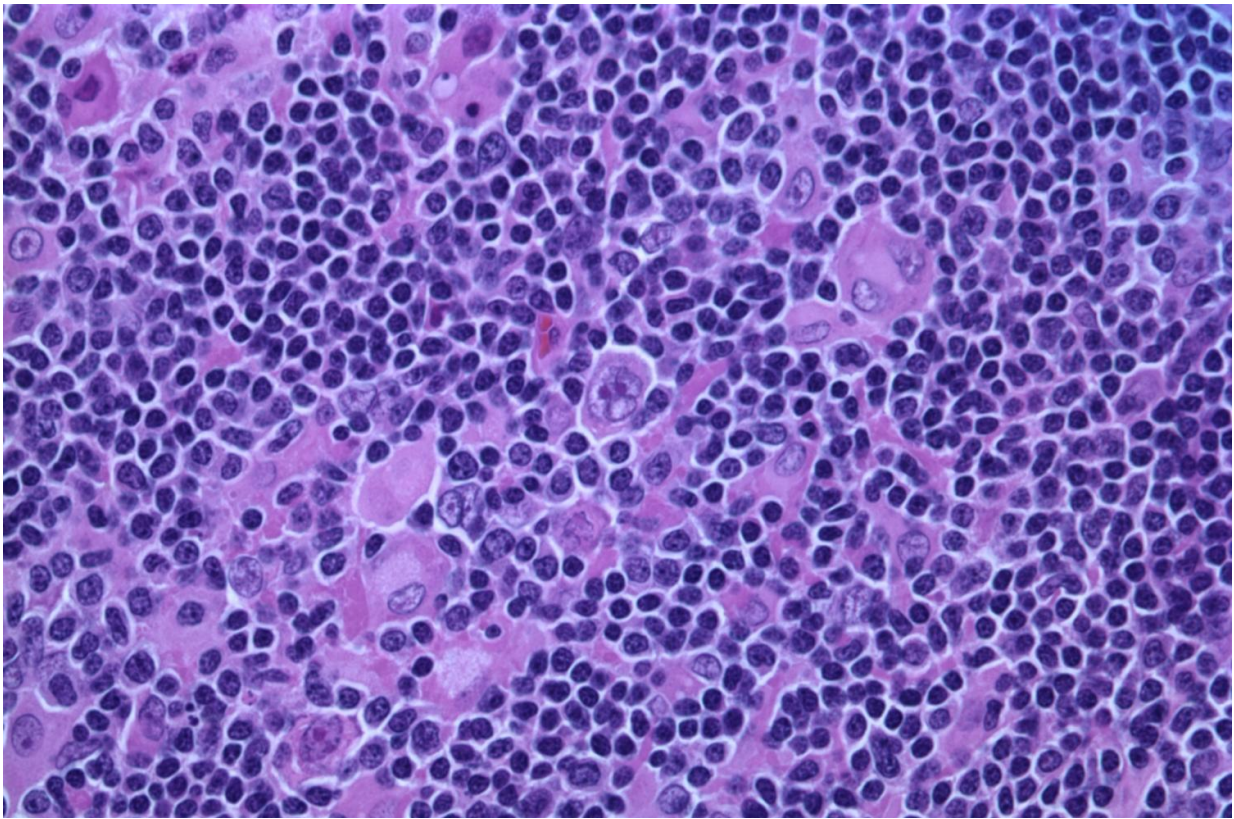


# New look at an old therapy may resurrect individualized lymphoma therapy

April 27 2016, by Bob Yirka

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Hodgkin lymphoma, nodular lymphocyte predominant (high-power view) Credit: Gabriel Caponetti, MD./Wikipedia/CC BY-SA 3.0

(Medical Xpress)—A trio of researches at Stanford University has published the results of a study done to take a second look at an

approach developed in the 1980's to provide individualized lymphoma therapy to patients. In their paper published in *Proceedings of the National Academy of Sciences*, graduate student James Torchia, Kipp Weiskopf and physician-researcher Ronald Levy, describe the original technique and a new way of lowering the cost of manufacture of the original drug that could make it inexpensive enough for use in patients.

The therapy was first developed over thirty years ago by Levy and colleagues—it was a monoclonal antibody, a semisynthetic and personalized antibody-like molecule that was meant to seek out a receptor that was involved in the development of [lymphoma](#) (cancer of the lymph nodes). Testing showed back then that it was capable of finding its target and successfully destroying tumor cells and in some cases "cured" human lymphoma in some mice. The drug made it to [clinical trials](#) and was given to 50 patients, many of whom lived cancer free for several decades. Unfortunately, the company that paid for the development of the drug, Idec Pharmaceuticals, shelved the idea because it was deemed too expensive to produce. Instead, they turned to the development of Rituxan, which after release for general use in 1997 went on to become the first monoclonal antibody approved for use in treating cancer and a cash cow for its developers.

In this new effort, the team reports that it was Torchia who first looked into possibly resurrecting the old technique but with a new twist, changing a part of the process that would make the [drug](#) much cheaper to produce. In its new incarnation, the team calls the hybrid molecules "peptibodies" which are made of bits from peptides, which can be inexpensively synthesized and bound to an antibody base. They kill the tumors, the team reports, by causing macrophages to take action against them, all without killing healthy B cells, which, the team notes, cannot be said for Rituxan. The researchers believe they have a winner and expect their therapy product to go to clinical trials within a year.

**More information:** James Torchia et al. Targeting lymphoma with precision using semisynthetic anti-idiotypic peptibodies, *Proceedings of the National Academy of Sciences* (2016). [DOI: 10.1073/pnas.1603335113](https://doi.org/10.1073/pnas.1603335113)

## Abstract

B-cell lymphomas express a functionally active and truly tumor-specific cell-surface product, the variable region of the B-cell receptor (BCR), otherwise known as idiotype. The tumor idiotype differs, however, from patient to patient, making it a technical challenge to exploit for therapy. We have developed a method of targeting idiotype by using a semisynthetic personalized therapeutic that is more practical to produce on a patient-by-patient basis than monoclonal antibodies. In this method, a small peptide with affinity for a tumor idiotype is identified by screening a library, chemically synthesized, and then affixed to the amino terminus of a premade IgG Fc protein. We demonstrate that the resultant semisynthetic anti-idiotypic peptibodies kill tumor cells in vitro with specificity, trigger tumor cell phagocytosis by macrophages, and efficiently clear human lymphoma in a murine xenograft model. This method could be used to target tumor with true precision on a personalized basis.

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