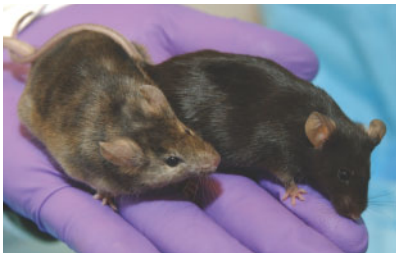
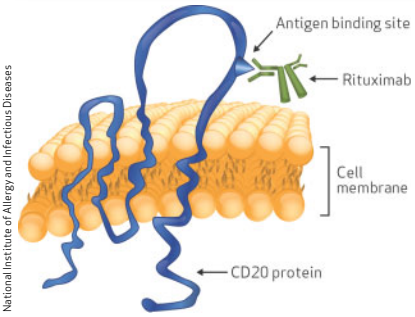


Maggie Bartlett, National Human Genome Research Institute

The Knockout Mouse Project will generate about 5,000 strains of adult mice and document their appearance, behavior, and other characteristics. Here, a mouse in which a gene affecting hair growth has been knocked out (left) is shown next to a normal lab mouse.

KOMP will enable researchers to establish the traits associated with the function of every protein-coding gene. Such information will aid in the discovery of the genetic causes of human cancers and other diseases, as well as efforts to identify new drug targets. The data will be placed in a public database, allowing researchers to explore gene function without having to generate their own lines of knockout mice, an often expensive and inefficient approach. For more information, go to www.komp.org. ■

BATTLES IN THE WAR ON CANCER: MAKING ANTIBODIES



National Institute of Allergy and Infectious Diseases

The monoclonal antibody rituximab binds to the CD20 protein on the surface of malignant B cells, induces apoptosis, and targets the cells for destruction by the immune system.

Since antibodies were first described in the late 1800s, scientists have wondered whether these proteins might be manufactured or manipulated to attack cancer cells. However, propagating cells that could churn out a specific antibody remained a stumbling block until 1975, when immunologists Georges J.F. Köhler and César Milstein fused a mouse myeloma cell and a B cell, forming a hybridoma. This cell pumped out antibodies that were identical clones.

But researchers met with little success in using monoclonal antibodies (mAb) to treat human cancer because tumor-specific antigens hadn't been identified in humans. "In the mid-1980s, the field was dead in the water," recalls Lee M. Nadler, MD, who joined Dana-Farber Cancer Institute (DFCI) in 1977.

Nadler and his team immunized mice with cells from a patient with Burkitt's lymphoma, and in 1979 created a hybridoma that produced a mAb that only reacted with the patient's normal and cancerous B cells. Because it was the first B-cell–specific antigen ever discovered, they named the antigen B1. (Nadler, now senior vice president of Experimental Medicine at DFCI and dean for Clinical and Translational Research at Harvard, renamed it CD20 in 1985.)

In 1979, Nadler also treated a patient with a mAb for the first time in the world.

After the advent of recombinant DNA tools, in 1991 IDEC Pharmaceuticals began to develop a mAb that latched on to the CD20 antigen, which sticks out of the surface of B cells, to treat non-Hodgkin lymphoma. Known as rituximab (Rituxan; Biogen Idec), the mAb drug induced apoptosis, activated complement, and recruited macrophages and other effector cells to slay tumor cells.

In clinical trials conducted at Stanford, M.D. Anderson Cancer Center, and other institutions, more than 40% of patients responded to rituximab alone. When it was combined with a standard chemotherapy, patients lived significantly longer. "It did just what we engineered it to do," says Antonio Grillo-López, MD, who was chief medical officer at IDEC Pharmaceuticals from 1992 to 2001.

Approved in 1997, rituximab was the first mAb approved to treat cancer. Today, more than a dozen such agents, including the breast cancer drug trastuzumab (Herceptin; Genentech), have been approved.

This article is the fourth in a 5-part series commemorating the passage of the National Cancer Act in 1971.

NOTED

- Fred Hutchinson Cancer Research Center and the Uganda Cancer Institute have broken ground on **the first comprehensive cancer center jointly constructed by U.S. and African institutions in sub-Saharan Africa**. The collaboration aims to increase survival rates for common infection-caused cancers from 10% to 90% over the next 3 years while researching new ways to prevent those cancers.
- Exelixis Inc.'s **cabozantinib more than doubled survival time for patients with advanced medullary thyroid cancer** in a trial with 315 patients whose cancer had progressed, was inoperable, or had metastasized. The company says that patients who received the drug had median survival of 11 months before death or disease progression, compared to 4 months for patients given a placebo.
- Analysis of more than 10,000 breast cancer patients in 17 trials worldwide shows that **following breast-conserving surgery, radiotherapy almost halves 10-year risk of recurrence** and reduces 15-year risk of mortality by a sixth. The report from the Early Breast Cancer Trialists' Collaborative Group was published in *The Lancet*.
- Over the next decade, **the population of U.S. cancer survivors over 65 years of age will increase by approximately 42%**, to about 11 million, according to a study in *Cancer Epidemiology, Biomarkers & Prevention*. "We're seeing yet another effect of the baby boom generation and we need to prepare for this increase," noted senior author Julia Rowland, PhD, director of the Office of Cancer Survivorship in NCI's Division of Cancer Control and Population Sciences.
- Interviewing 28 cancer researchers about the process of cancer metastasis, researchers at the University of Chicago found **ubiquitous disagreement around assumptions in any model of metastasis**, according to their report in *PLoS Computational Biology*.
- Complete Genomics, working with the Scripps Health system in San Diego, is funding and **gathering whole-genome sequences for 1,000 elderly people** in the "Wellderly Study," which examines people from ages 80 through 108 years without any major diseases or long-term health complications.

For more news on cancer research, visit *Cancer Discovery* online at www.AACR.org/CDnews.

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Cancer Discovery 2011;1:459.