

CANCER THERAPY

RIBI'S BIOLOGICAL RESPONSE MODIFIERS

NEW YORK—The \$9.5 million Ribi ImmunoChem Research raised in August will help the innovative Hamilton, MT, R&D company increase its research and capital expenditure 12 to 15 fold over the next three years. To date, the company has spent almost nothing on R&D—only \$1 million cumulative since 1981. Compare this with Cetus and Genentech: in 1984 alone, R&D expenditures were \$31 million and \$55 million, respectively.

Ribi ImmunoChem has developed three anti-tumor drugs, one of which has been on the market for over two years. Ribigen™, used to treat sarcoid tumors in horses and cancer eye in cattle, gained USDA approval in April 1983. Detox™, used to treat melanomas and head and neck cancers in humans, is in phase II clinical trials. And Ovamid™, designed to treat ovarian and cervical cancers, has proven effective enough in mouse systems that Ribi ImmunoChem is now writing an Investigational New Drug application to commence phase I clinicals. The company's funds will

now go primarily to the clinical testing of Detox and Ovamid. Both drugs are intended to complement existing cancer treatments.

Ribi ImmunoChem's anti-tumor compounds are actually biological response modifiers: they are immunopotentiating agents that initially stimulate the macrophages. This sets off the delicately balanced and complex cascade of interactions involved in an immune response. The biological response modifiers—which consist of detoxified bacterial endotoxin and bacterial cell wall skeletons in an oil-in-water emulsion—are injected directly into a tumor. It is probable that the immune system is fooled into thinking there is a massive bacterial infection. As macrophages and lymphocytes gather at the site, they effectively destroy the tumor.

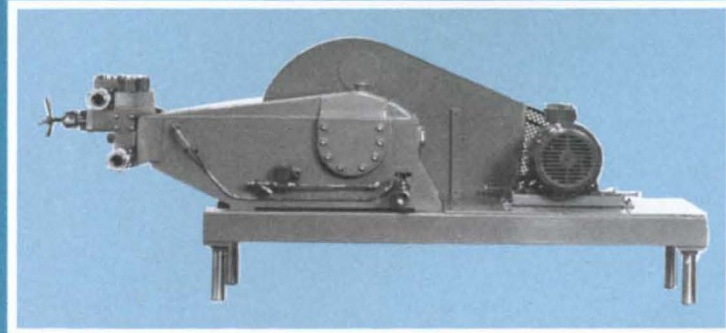
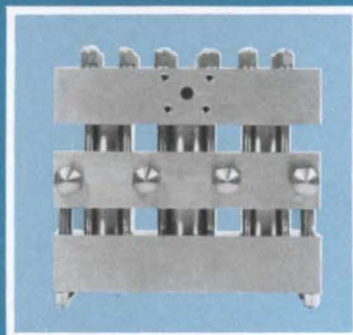
Bacterial endotoxin, found in the cell walls of gram-negative bacteria, is one of the most potent immune stimulators known. Endotoxin is also responsible for the fever, shock, and even death that can be associated with bacterial infections. William B. Coley,

a surgeon at New York's Memorial Hospital, observed in the late 1800s that an infection by these bacteria can also cause tumor regression. However, early attempts at separating the beneficial effects of endotoxin from the toxic ones were unsuccessful. Edgar Ribi, chief executive officer of Ribi ImmunoChem and an internationally recognized authority on bacterial cell fractionation and bacterial endotoxins, has defined the chemical structure of the endotoxin molecule and detoxified it without losing its beneficial biological properties. Detoxified endotoxin not only activates macrophages; it also acts as an adjuvant and as a mitogen, and stimulates the production of interleukin-1. Ribi and his colleagues have also isolated the biologically active immunostimulating components of the walls of *Mycobacterium bovis* (BCG strain) and *Corynebacterium parvum*. To be effective the microbial products must be incorporated into oil droplets to form an oil-in-water emulsion, containing one percent oil.

—Jennifer Van Brunt

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