CANCER RESEARCH

POLYSACCHARIDES TO INHIBIT TUMOR GROWTH

HANNOVER, F.R.G.—Pharmaceutical applications of polysaccharides are expected to grow over the next decade, said Gerhard Franz, speaking during the BioTechnica International Trade Fair and Congress held here in October. Researchers have shown an increasing interest in polysaccharides as anti-inflammatories and hypoglycemic agents. Their most dramatic applications, however, may come as biological response modifiers (BRMs) in the treatment of cancer. "We have the Japanese largely to thank for our present understanding of the action of these substances on the immune system," said Franz. "They kept the research going, after the U.S. pulled out of this field during the 1970s."

Franz described his group's work at the University of Regensburg (F.R.G.) in which doses of just one milligram of polysaccharide per kilogram animal weight have consistently achieved 99-percent tumor inhibitions. Franz screens potential BRMs by using the allogeneic tumor Sarcoma 180. When transplanted into female CD1 mice, it grows rapidly over

a period of 30 days and can be measured without sacrificing the animals. Test substances are injected intraperitoneally at 24-hour intervals for 10 consecutive days. One particularly promising polysaccharide is glucan A₁, a branched glucan extracted from the cell walls of *Phytophthora parasitica*. It has proved to be an extremely potent immune modulator, with an antitumor activity in animal tests greater than that of Schizophyllan (Kaken Pharmaceutical, Tokyo), a BRM already used clinically to treat various cancers.

Despite its efficacy, which approaches 100 percent *in vivo*, glucan A₁ had no antineoplastic activity when tested in an *in vitro* Sarcoma 180 assay. This finding, and the fact that the polysaccharide begins to work *in vivo* only after 10 days of injection, confirms that it has no direct cytotoxic effect on cancer tissue, but operates instead by stimulating the host's immune system. Investigating one possible mechanism for the immunological action, Franz treated mice with trypan blue, a dye that specifically inhibits macrophages but itself has no ef-

fect on tumor growth. In the presence of the dye the activity of glucan A₁ declined slightly, indicating that the polysaccharide works only partly by activating macrophages.

Side-effects of the polysaccharides in clinical use (principally Schizophyllan and Lentinan [Ajinomoto, Tokyo]) have been limited almost entirely to occasional soreness at the injection site. Reflecting this experience, the glucans being developed in Regensburg have proved entirely nontoxic in the mouse tests.

Work with the existing substances has shown that beta-1,3-linkages in the main chain of the glucan are prerequisites for activity against tumor cells. In an attempt to learn more about the relationship between structure and antineoplastic action, the Regensburg researchers have selected barley glucan—a polysaccharide that has relatively poor activity in the *in vitro* Sarcoma 180 assay. By chemically adding side chains to this molecule, they have found that the longer and the more polar the side chains, the greater the anti-tumor activity.

—Bernard Dixon

FELLOWSHIP PROGRAM

1990 FUNDING UNCERTAIN FOR NIH EFFORT

WASHINGTON, D.C.—The National Institute of General Medical Sciences (NIGMS) of the National Institutes of Health (NIH, Bethesda, MD) recently awarded the first postdoctoral fellowships and predoctoral training grants in the new Chiles biotechnology training program. The program's future growth seems uncertain, however, following the retirement of Senator Lawton Chiles (D-FL), who introduced and then championed legislation to establish the program. Moreover, general federal constraints as well as specific points of disagreement between the Senate and the House of Representatives over this part of the NIH budget make unclear just how much new money will be made available to the program for the upcoming fiscal year.

Congress budgeted \$2.8 million for the program's initial phase in fiscal year (FY) 1989. According to NIGMS special assistant Irene Glowinski, this money is being used to support three dozen postdoctoral and senior fellows as well as about 83 predoctoral trainees in nine programs. Training grants were awarded to the California

Institute of Technology (Pasadena), University of California at Berkeley, University of Kansas (Lawrence), University of Wisconsin (Madison), University of Colorado (Boulder), Washington State University (Pullman), Lehigh University (Bethlehem, PA), Massachusetts Institute of Technology (Cambridge) and Rutgers University (New Brunswick, NJ).

Just what Congress intends for FY 1990 remains unclear. Senate members earlier sought an additional \$2.8-million allotment, but the House version of the 1990 budget did not include any new money for the program. The House-Senate conference committee, which is supposed to resolve such discrepancies, left matters vague; its very brief report did not address the question of 1990 funding. Conference committees often average the amounts proposed by the House and Senate; \$1.4 million of new money would be enough to fund six new training programs.

The NIH biotechnology training initiative is being launched with enthusiasm despite the budgetary uncertainties. It differs from other NIH training efforts in two important

ways, according to Marvin Cassman, acting deputy director of NIGMS, who is in charge of the program. "It explicitly encourages incorporation of chemical engineering and other physical science approaches, bringing them more into the mainstream of working with biological systems," he says.

Moreover, Cassman continues, "There is a requirement for industry involvement at several levels of these [academic] training programs." Industry representatives will advise and teach graduate students—at least on an informal basis—and will encourage students to seek internships in industrial laboratories, as well as explore other interactions between companies and academic institutions.

Although the program will emphasize interdisciplinary training, predoctoral students will still receive Ph.D.s from specific academic departments. The program does not mandate a new academic discipline labeled "biotechnology." Instead, each academic institution is free to develop its own design for a biotechnology training program.

—Jeffrey L. Fox