Chemistry

Richard Lipkin reports from Chicago at a meeting of the American Chemical Society.

Drugs target RNA to kill tumors . . .

Most antitumor drugs destroy their targets by attacking cancer cells' DNA, aiming to kill off the malignancy by disrupting the fast-growing cells' reproductive machinery.

That's a perfectly reasonable strategy, says Sidney M. Hecht, a chemist at the University of Virginia in Charlottesville. But it has one serious drawback: It's not very selective.

Antitumor drugs tend to kill off all growing cells in one fell swoop. While doing the most damage to those proliferating most quickly—tumor cells—they also harm many healthy cells.

An alternative approach, Hecht says, involves targeting RNA. A molecule critical to cellular replication, RNA should prove easier to target selectively. But until recently, scientists have lacked the structural information on RNA that they need to cook up such compounds.

Now, Hecht and University of Virginia chemist Angela Snow report that bleomycin, an antitumor agent known to break up DNA, also chops up RNA in at least one type of bacteria.

"This is good news," Hecht says, because the finding indicates the existence of a previously unidentified mechanism for damaging RNA—a mechanism that chemists can perhaps exploit through carefully designed molecules.

A naturally occurring compound produced by bacteria, bleomycin effectively kills several soft-tissue cancers, such as tumors of the skin, lung, and ovaries. Physicians also use the drug to treat Hodgkin's disease, a lymph cancer.

The new finding that bleomycin can split up RNA inside live bacteria means that carefully crafted anticancer agents may someday strike vulnerable spots in tumor cell growth without damaging healthy tissue.

While Hecht admits that such a project will take many years, in the short run he and his colleagues plan to look at bleomycin's effect on RNA in animal and human cells.

. . . and block HIV

The RNA-damage strategy may also curb HIV infections, says Anthony W. Czarnick, a chemist at Parke-Davis in Ann Arbor, Mich. After screening 130,000 molecules, he and his colleagues have found a class of 149 compounds that block RNA activity in HIV-1, the AIDS-causing virus.

His team is looking to cripple the virus with small, easily manufactured molecules that block the ability of the virus' RNA to reproduce. Specifically, Czarnick's group is investigating agents that stick to and disable a chunk of the RNA, known as *trans*-activation response (TAR) RNA. They chose that particular piece of RNA because a critical protein known as TAT binds there.

"We have evidence that preventing the protein TAT from binding to TAR RNA dramatically decreases the replication of cells infected with HIV," Czarnick says. "So the target of our research is the TAT-TAR binding site. We believe that a drug which keeps these two components from interacting will suppress an HIV infection if the drug can reach its target."

Czarnick says that his group's bioassays have shown that the identified agents "clearly inhibit this interaction." The question now, he says, is which ones to target for more study.

Deriving new drugs from thalidomide

Thalidomide, a nausea-fighting sedative synthesized during the 1950s but never approved for use in the United States because of its fetus-harming effects, is spawning a new generation of drugs that can treat inflammation and immune system disorders (SN: 12/24&31/94, p. 424).

George W. Muller and David I. Stirling, chemists at Celgene Corp. in Warren, N.J., reengineered thalidomide to create a new series of therapeutic agents.

The researchers have designed the drugs, they say, to regulate the body's production of tumor necrosis factor alpha. This protein plays a key role in inflammatory and immunological disorders such as rheumatoid arthritis, lupus, inflammatory bowel disease, and leprosy.

Scientists at Johns Hopkins University in Baltimore are currently studying several of these new Celgene agents for treatment of graft-versus-host disease, which often follows bone marrow transplants, Muller adds.

In designing these new molecules, Muller and Stirling said, they improved the potency of the portion of thalidomide exhibiting medicinal properties and removed the segment causing birth defects.

Electron beam cleans dirty water

Zap goes the water. Poof go the impurities.

That's the essence of a new and "very simple" water disinfection system proposed by William J. Cooper, a chemist at Florida International University in Miami. He and his colleagues are treating wastewater, sewage, and sludge with high-energy electron beams that blast apart suspended or dissolved organic matter.

As water flows through the beam of an electron accelerator, its energetic charged particles initiate chemical reactions that destroy organic compounds. The process kills bacteria, viruses, and all other living things present in the water without producing any hazardous by-products, Cooper reports. In small-scale tests at a pilot facility in Dade County, Fla., the technique also cleansed water of toxic organic materials, disinfection by-products, and such common water-borne microbes as *Giardia* and *Cryptosporidium*.

Recently, engineers at High Voltage Environmental Applications in Miami installed a mobile water treatment unit in a 48-foot trailer. Now located in Leipzig, Germany, the mobile unit has completed 27 tests, zapping groundwater and wastewater contaminated with sundry toxins. So far, says Cooper, "the results look good."

Paper pulp and fish kills

In the mid-1980s, Swedish scientists found stunted rates of growth and reproduction among fish breeding near paper-making plants in the Gulf of Bothnia, which separates Sweden and Finland. They correlated these effects with adsorbed organic halogens, a class of compounds present in pulp and paper mill wastes.

Since these compounds are rich in chlorine, the scientists assumed that the chlorinated compounds had adversely affected the fishes' health.

While environmental agencies in Sweden, Finland, and Denmark moved ahead to lessen concentrations of chlorinated pollutants dumped into marine waters, researchers in the United States and Canada continued looking for the specific culprit behind the fishes' ills.

B. Kent Burnison, a microbiologist at Canada's National Water Research Institute in Burlington, Ontario, and his colleagues now report that chemicals other than the chlorinated ones appear to be harming the fish.

Examining various chemicals present in effluents from papermaking, they found that wastewater from "kraft pulping mills" harmed the fish most seriously—even though it contains no chlorinated compounds. High concentrations of certain compounds extracted from the wood itself proved toxic to fish, regardless of chlorine's presence.

Burnison therefore concludes that simply targeting the discharge of chlorinated compounds is "unlikely" to ease fish suffering.