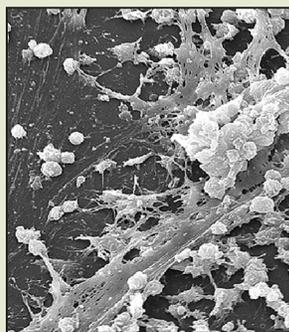


Ironing Out Illness

To help fend off microbial enemies, the human body secretes natural antibiotic substances in body fluids such as tears, nasal mucus, and breast milk. These substances act like molecular armor, killing on contact bacteria that can make us sick. If these defenses fail in preventing an acute (quick onset, short-lived) infection, antibiotic medicines can usually quash the infection. On the other hand, chronic infections, which persist for a long time and resist antibiotics, can be ferociously difficult to treat. One of the hallmarks of many chronic infections is the presence of a bacterial biofilm, a specially constructed “neighborhood” of bacteria encased in a protective matrix that contains a network of channels for the flow



CDC/Rodney M. Donlan, Janice Carr

of nutrients. Biofilms are associated with lung and ear infections as well as with tooth decay. NIGMS grantee **E. Peter Greenberg** of the University of Iowa in Iowa City discovered a biofilm killer, called lactoferrin, hiding in body secretions. Greenberg and his coworkers found that very low levels of this substance could prevent one type of bacteria—the kind that can cause lung infections in people with cystic fibrosis—from forming biofilms. Lactoferrin grips tightly onto iron, an important ingredient for the livelihood of many bacteria. The researchers determined that lactoferrin stimulated the bacteria to “twitch,” or wander around in search of iron and other nutrients. While the small amount of lactoferrin the researchers applied to the bacteria was not enough to kill them, it nevertheless kept the bacteria from settling down into a durable biofilm structure. The findings offer possible strategies to interfere with the formation of biofilms and treat or prevent biofilm-related illnesses.

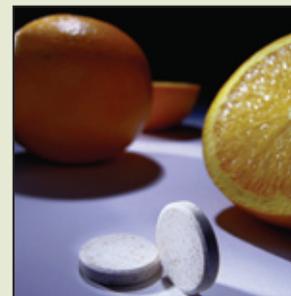
Finding a Cancer Drug’s Mistakes

Years of basic research probing how cells communicate recently led scientists to develop a new kind of cancer drug. Doctors now use this medicine, called Gleevec™, to treat the rare blood cancer chronic myelogenous leukemia (CML). The drug works by blocking a cell-communication stream that is always “on” in this type of cancer. Gleevec’s molecular target is a protein called a kinase, which acts like a molecular relay baton to convey messages inside cells. Although Gleevec’s discovery

was an exciting step forward in the treatment of cancer, in the short time this drug has been in clinical use, cancer cells have scored a gain in the battle against CML. Some patients’ cancer returns because the tumor cells have become resistant to Gleevec. NIGMS student trainee **Mercedes Gorre** and researchers at the University of California, Los Angeles, combed through the human genetic code for Gleevec’s target, a kinase protein named bcr-abl. Working together with UCLA scientist Neil Shah, Gorre obtained blood samples from 32 patients whose disease had returned after Gleevec therapy. Extracting DNA from these samples, the researchers carefully analyzed the “spelling” of the gene that directs the manufacture of the bcr-abl kinase. Of those samples, 29 of 32 had spelling errors that caused the resulting bcr-abl kinase protein to be misshapen, preventing binding to molecules of Gleevec. This work is expected to play a significant role in developing the next generation of drugs to treat CML.

Vitamin C Improves Skin Grafts

Everyone knows the importance of vitamin C as part of a healthy diet. Now, researchers may have found a new medical use for the classic citrus fruit vitamin. According to NIGMS grantee **Steven Boyce** of the Cincinnati Shriners’ Burns Hospital and the University of Cincinnati, vitamin C may improve the treatment of burn patients’ wounds. In a recent study, Boyce and his coworkers found that adding the vitamin to lab-grown cultures of human skin cells improved the grafting properties of cultured skin substitutes, which Boyce created by growing skin cells on top of a polymer sheet. The more closely a cultured skin substitute resembles natural skin, the more effective it is likely to be, and Boyce already knew that cultured skin substitutes tend to grow better when bathed in a special mix of nutrients. In the new study, he and his coworkers discovered that the skin substitutes grown with vitamin C provided a better barrier for covering burn wounds. The team also found that after grafting, wounds covered with the vitamin C-treated cultured skin substitutes closed faster than wounds covered with cultured skin substitutes grown without the vitamin added. Another important benefit of vitamin C, Boyce learned, was that cultured skin substitutes grown with



vitamin C remained viable longer in the lab. In the future, this could mean greater availability of cultured skin substitutes for treating patients with severe burns.

Living Cleansers

As early as preschool, children learn the basics of the food chain—big things eat little things and little things eat littler things. Despite being small and at the bottom of the chain, organisms like microbes and many plants nevertheless play vital roles in maintaining a balanced environment and keeping it healthy for living things of all sizes. Two NIGMS-supported teams of scientists have recently unveiled some of the secrets of how small living cleansers can “eat” toxic chemicals. One case involves chemicals called polychlorinated biphenyls, or PCBs. These chemicals are no longer manufactured in the United States, but they still linger in the environment.

Researchers are seeking environmentally sound ways to rid the planet of such poisons through a process called bioremediation, but they haven't yet found many organisms that are naturally good at doing this. NIGMS grantee **Jeffrey T. Bolin** of Purdue University in West Lafayette, Indiana, along with coworkers at the University of British Columbia in Vancouver, pinpointed a critical chemical reaction in PCB breakdown that most microorganisms simply cannot perform. The researchers have plans to engineer microbes in the lab that are able to perform this reaction, potentially providing a tool for gobbling up harmful PCBs. On another front, scientists have recently discovered how to coax plants into soaking up the chemical pollutant arsenic, a significant threat to worldwide health. By cloning arsenic-tolerance genes from the bacterium *Escherichia coli*, NIGMS grantee



Barry P. Rosen of Wayne State University School of Medicine in Detroit helped his coworkers at the University of Georgia in Athens create genetically engineered plants that could thrive in arsenic. What's more, the two teams designed the plants so that they could accumulate arsenic in their leaves, which can be harvested and disposed of safely. This so-called phytoremediation technique holds promise for improving human health, especially in developing countries where arsenic-contaminated drinking water sickens hundreds of millions of people.

Cocaine Busted

Abusers of cocaine absorb this highly addictive drug into their bodies by chewing, sniffing, injecting, or inhaling it. Any of these methods can lead to the rapid accumulation of poisonous levels of cocaine throughout the body. There is no effective treatment for cocaine overdose, which can result in sudden death. Scientists have reasoned that one way to prevent cocaine's harmful effects on the brain might be to use a natural decoy like a specially made antibody to block cocaine from reaching its molecular targets. Unfortunately, this approach would probably have limited success during an overdose, when overwhelming amounts of cocaine are flowing through the bloodstream. In such a case, rapid breakdown of the drug would be the fastest way to clear this dangerous substance from the body. NIGMS grantee **Ian Wilson** of The Scripps Research Institute in La Jolla, California is making headway in trying to develop this approach. Wilson and his coworkers recently discovered an enzyme that breaks down cocaine into an inactive substance faster than any other such enzyme scientists have examined before. Wilson and his team determined the three-dimensional structure of this enzyme, called a cocaine esterase, which hails from a bacterium that grows in soil adjacent to cocaine-producing plants. The study may point the way to using this protein, or proteins like it, as therapies to rescue people from cocaine overdose.