look for the signal first, then try to find the material in the rocks that Raman [scans] indicate contain something.”

Indeed, the researchers from Prague are evaluating portable Raman instruments for their usefulness in field studies looking for evidence of microbial life at remote sites. “We have tested some of these especially for mineralogy and identification of pure organics in field conditions,” Vitek says. However, he points out, “It is hard to detect organics without sample pretreatment and without microscopic localization of particular microbial colonies.” Separately, a miniaturized Raman spectrometer is now being designed for use on the Mars mission that is scheduled for launch in 2018.

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Triclosan Derivatives Prove Effective against T. gondii Parasites

Compounds that are based on triclosan, a widely used antiseptic compound, make it “more druggable,” and improve its effectiveness against parasites, says Rima McLeod, an infectious disease specialist at the University of Chicago in Chicago, Ill. Several of these derivatives of triclosan, which is added to consumer products such as soap, toothpaste, shaving cream, and fabrics, block a key enzyme in the protozoan parasite Toxoplasma gondii. At least 2 in a set of 53 triclosan-based compounds will undergo further development, according to McLeod and her collaborators, whose findings appear in the September 2010 Journal of Medicinal Chemistry (53:6287–6300).

Toxoplasma infects as many as one-third the population, making T. gondii “the most successful parasite of humans in the world,” McLeod says. It can cause chronic eye and brain infections, and expectant mothers can transmit the parasite to their fetuses. Although infected infants may look normal, about half are at high risk for meningoencephalitis and many develop eye disease. The life cycle of T. gondii involves active tachyzoites, and latent bradyzoites, or cysts, which can persist in the host central nervous system. Available drugs target only the tachyzoites, and some of those drugs induce hypersensitivity reactions in patients.

The T. gondii enzyme enoyl reductase (ENR), which is not found in mammals, is required for producing fatty acids during both life stages of this parasite, according to McLeod and her collaborators at Johns Hopkins University in Baltimore, Md., Sheffield University in England, and the University of Strathclyde in Scotland. Although triclosan inhibits ENR and blocks parasite replication, it is not soluble in the bloodstream and cannot cross parasite membranes and cyst walls unless it is linked to carrier molecules.

Turbidity-Based Model Tracks Bacteriolytic Enzymes

Turbidity assays can be used to probe the dynamics of bacterial lysis and to infer microscopic details through use of a model that integrates the chemistry of bond cleavage with physical mechanisms leading to cell wall failure, according to Joshua Weitz of Georgia Institute of Technology in Atlanta, Ga., Daniel Nelson of the University of Maryland, Rockville, Md., and their collaborators. The model also helps to solve “an inverse problem,” namely estimating reaction rate constants and susceptibilities to lysis among target cells. This approach is expected to facilitate the engineering of lytic enzymes with specific killing properties for use in treating and preventing bacterial infections, Weitz says. Details appear in the December 2010 Physical Biology.
Two new triclosan derivatives excel in blocking parasite growth and inhibiting ENR activity, according to McLeod and her collaborators. Moreover, they are not toxic to host fibroblasts at the highest concentrations tested. They also prove effective when used to treat mice that were infected with a virulent laboratory strain of *T. gondii*. Both lead compounds effectively reduce the burden of tachyzoites in mice.

The two triclosan derivatives in the new study “certainly are superior to triclosan in in-vitro assays,” says Louis Weiss, a professor of medicine and pathology at Albert Einstein College of Medicine, Bronx, New York. The very promising work is built on developing inhibitors based on plant metabolic pathways found in parasites like *T. gondii* and the malaria parasite *Plasmodium falciparum*. “I have no doubt that other parasites will be inhibited by the same class of drugs,” he says.

McLeod and her collaborators are further modifying the promising triclosan derivatives, seeking compounds that will cross multiple membranes of the parasite and kill both tachyzoites and bradyzoites. By tinkering with this chemical family, they hope to make compounds that remain highly soluble and gain the capacity to cross the mammalian blood-brain barrier. “We want to treat active disease and eliminate cysts at the same time to reduce recurrences,” McLeod says. A key goal is to treat infected pregnant women to prevent their transmitting the parasite to fetuses.

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