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"Bottom-up" bioremediation

In many respects, the development of environmental treatment is decades behind its counterpart in human medicine. Bioremediation has thus far been a pragmatic science. Problems arise; solutions are sought, sometimes successfully. But then those solutions find no subsequent applications. They contribute little to any knowledge base that might underlie environmental biotechnology. No two environmental problems are the same. Even if the complex mixture of contaminating substances is the same, climatic conditions vary widely from site to site, as do the hydrogeodynamics and the local regulations controlling acceptable levels of pollutants.

It is time, and there is sufficient knowledge, for bioremediation to become more rational. Perhaps by analogy with the reductionist "bottom-up" approach in medicine, we can find a more effective route forward.

To begin, we need to understand the system in which we are working. Many recent blockbuster drugs were identified by screens using well-characterized targets (receptors). The molecular targets of bioremediation are mixtures of recalcitrant, persistent, and toxic chemicals. Of these, common contaminants, such as trichloroethylene and PCBs, are best tackled using natural organisms; more highly chlorinated, recalcitrant, aromatic hydrocarbons that confound natural degradation should be the targets of genetically modified organisms.

In general, the chemistry of pollutants and their degradation is understood. Site-directed mutagenesis has already been used to alter or refine substrate specificities, rates of congener oxidation, etc. And, perhaps in the same way that combinatorial methods are transforming drug discovery, we are starting to use "irrational" iterative approaches to "evolve" complex enzyme pathways rapidly in the laboratory—as Willem Stemmer and colleagues report in this issue (p. 436).

But "in the laboratory" is not where most environmental problems are found. Understanding an environmental s; tem is not merely a matter of throwing technobugs at a polluted site, any more than throwing genes directly at disease has made gene therapy work (despite the fact that a good deal of gene throwing has been performed).

Making bioremediation organisms or consortia work requires more knowledge about how they can be encouraged to persist in the field and retain the catabolic activities with which we have endowed them. In the same way that drug developers are analyzing human populations in greater detail for clinical applications, more information on the physical and biological structure of contaminated sites is required. This will need a wholesale effort in monitoring clean and polluted environments and the response of indigenous and applied microbial flora to changing circumstances. Some of the tools for doing so already exist, including polymerase chain reaction based assays and the use of fluorescent gene markers.

The potential rewards of effective bioremediation approaches are great. And one doesn't need a full understanding of all environments to put bioremediation on a firmer footing: Look what the isolation of a few receptors did for drug development.

IP's shifting sands

Biotechnology is built on that finest of sands, intellectual property (IP). Grains of it recently slipped through the fingers of the two surviving corporate members of biotechnology's "big four" of the 1980s. In two entirely separate hearings in the United States and Europe, judges ruled that early patents granted to Genentech and Biogen, respectively, were invalid. Both patents cover the first product that the companies developed and marketed themselves; Genentech's US patent on human growth hormone was revoked because it was "nondisclosing" (i.e. it did not adequately describe the process for producing the protein); Biogen's claims on the production of beta-interferon were ruled "obvious."

The two rulings are a sharp reminder—if a reminder were really necessary—that in biotechnology especially, IP is an elusive commodity. You, as an individual or a company, may have invented, but until a patent office somewhere grants your patent, you own nothing. Even when a patent is granted, your ownership is still open to challenge. In patent disputes, it not all over until the patent office finally pronounces in your favor.

There is, however, also a positive message in the recent rulings: Even unowned IP can provide a firm foundation for a company. Biogen and Genentech raised large amounts of investment on the presumption that they did own the rights to the protein products. Some of that money was used in R&D to generate additional IP—on the purification of the drugs, for instance. The two companies will, in fact, continue to make money from growth hormone and beta-interferon. IP may be sand, but with enough of it, you can make concrete.

The collective bargain

There are many measurements of the success of an enterprise. As a machine for making vast profits, commercial biotechnology is an abject failure (notwithstanding certain successes in California and Massachusetts, of course). As a developer of new products, biotechnology's performance has been encouraging, but hardly revolutionary. But as a self-propagating, evolving, market-led method for generating new funds for research and development, biotechnology is unsurpassed.

Every single cent of the $5.2 billion (see p. 412) spent by biotechnology companies last year on research was new money. There can be no suspicion that, as often the case with government research allocations, putting more funds into one program necessarily means that others face starvation—robbing Peter to pay Paul.

Some people could argue, of course, that establishing 1500 biotechnology companies is not an efficient mechanism for collecting research funds. They might point out—and they would be correct—that the ratio of recipient researchers to program managers in government grant-giving organizations is significantly lower than the ratio of researchers to nonresearchers in the average biotechnology company. But they would have to recall that those financial, sales, and administrative staff do not just dispense of R&D funding, they also raise it. As our data compilation also shows, public biotechnology companies generated over $12 billion last year selling their products and services. At the same time, private and public biotechnology companies together persuaded investors to part with over $7.5 billion. A company's management, financial, and administrative staff are its tax-collectors or tin shakers as well as its distributors of largesse.