from $7 per pound in 2003 to $130 per pound in 2010. A low-cost process for recovering dysprosium from mining sites and contaminated water at industrial sites could increase its supply and reduce costs. With current concerns over sustaining the supply of dysprosium and other valuable rare-earth elements required for clean energy technology, “fungal systems have a clear potential for the immobilization and biorecovery of these important substances,” Gadd says.

There are precedents for using microorganisms on an industrial scale to recover metals and radioactive elements, according to Gadd. Sulfate-reducing bacteria are used to precipitate and recover metals such as zinc in a commercial system available through Paques BV, headquartered in the Netherlands. Other industrial-scale systems rely on acidophilic bacteria to make sulfuric acid for leaching copper, gold, and uranium, he says. Amid interest in finding microbes to recycle rare-earth elements, he adds, “so far there are no industrial processes.”

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RESEARCH ADVANCES

Outbreak Spurred Several Approaches to Developing Ebola Therapeutic Products

Jeffrey L. Fox

Several distinct types of Ebola therapeutic products are under development—some more or less conventional antiviral agents, while others depend on more recently developed techniques to disrupt viral gene activity or use antibodies to bind the virus and trigger host immune responses.

Some of these candidate drugs block replication of the virus genome. For example, BCX4430, under development by BioCryst of Research Triangle Park, N.C., targets the RNA polymerase of the Ebola and Marburg viruses. It proves effective in treating nonhuman primates infected with either of those viruses. Favipiravir, also called T-705, initially was developed by Toyama Chemical, part of FujiFilm Corp. of Tokyo, Japan, because of its activity against influenza virus strains. Although the drug failed to help patients with advanced Ebola infections during the recent outbreak in West Africa, it appeared to help in preventing deaths among those with more moderate infections.

Sequence-specific inhibitors of the Ebola virus include phosphorodiamidate morpholino oligomers (PMOs), being developed by Sarepta Therapeutics of Cambridge, Mass., and lipid-encapsulated siRNA oligomers, being developed by Tekmira Pharmaceuticals of Vancouver, British Columbia, Canada. The Sarepta PMOs target Ebola or Marburg virus matrix proteins. “These compounds have protected up to 80–100% of nonhuman primates to Ebola and Marburg virus challenge infections, respectively,” says Michael Wong of Sarepta. Despite such promising findings, however, the Department of Defense (DoD) Joint Product Management Office of BioDefense Therapeutics recently dropped its sponsorship of PMOs.

DoD continues to support the RNA silencing candidate products that Tekmira is developing, including its lead candidate, TKM-Ebola-Guinea, which was adjusted to accommodate minor sequence changes in the genome of the viral strain that circulated in West Africa during the outbreak. The lipid-encapsulated siRNA “triggers” target the genes VP35 and L polymerase of the Ebola virus, which function in viral replication and, in the case of VP35, also in blocking the host immune response to the virus, according to Tekmira.

Meanwhile, several mixtures containing specific monoclonal antibodies (mAbs)—typically, two or more mAbs aimed at more than one target on the Ebola virus—are now being evaluated as therapeutic products. Treatment results are anecdotal, but similar mixtures of these mAbs seem to be having an effect in patients infected with the Ebola virus, according to Gary Kobinger of the National Microbiology Laboratory in Winnipeg, Canada, part of the Public Health Agency of Canada (PHAC).

Prominent among these candidates
is ZMapp, a triple monoclonal cocktail of humanized antibodies that are directed against the Zaire species of Ebola virus. Originally developed several years ago in collaboration with the U.S. Army Medical Research Institute of Infectious Disease (USAMRIID) in Frederick, Md., commercial development of ZMapp was handed over to Mapp Biopharmaceuticals in partnership with LeafBio, both in San Diego, Calif. ZMapp is produced in tobacco plants at Kentucky BioProcessing in Owensboro. A similar mAbs cocktail was formulated by PHAC researchers in Winnipeg. Efforts are under way to produce enough of these and similar mAbs to evaluate them in clinical trials.

Jeffrey L. Fox is the Microbe Current Topics and Features Editor.

NEW IN ASM JOURNALS

Fungus Gardening Ant Gut Flora Are Few but Intriguing

Fungus gardening termites have diverse gut microbiotas. Now, for the first time, researchers form the University of Copenhagen have investigated that of fungus-gardening ants, whose gardening techniques are fundamentally different. Termites predigest their plant substrate whereas ants deposit it directly on the fungus garden. Panagiotis Sapountzis et al. show that there are but four major species of gut bacteria in Acromyrmex leaf-cutting ants, but that these are intriguing. A Rhizobiales symbiont inhabits the hindgut as a biofilm, and fixes atmospheric nitrogen—just like congeners that abide in root nodules of legumes on human farms. Obtaining sufficient nitrogen “is an obvious challenge when the farmers no longer hunt the meat of insect prey,” says Sapountzis. He notes that “leaf cutting ants are serious pests for human agriculture as they defoliate many crops, to nourish their underground fungus farms.” The research might lead to environmentally friendly biopesticides to replace the contaminating organochlorines now used, he says.