Like many colleagues, I sometimes thought I’d never see the day when three small parasites would be so celebrated. After all, why should people outside of the small cohort of dedicated scientists and sponsors pay any attention to these “Tritryps”—Trypanosoma brucei, Trypanosoma cruzi, and Leishmania major—whose genomes appear in this issue of Science?

These three motile, unicellular, nucleated (eukaryotic) protozoa belong to a family of ubiquitous parasites of insects, plants, fish, amphibians, reptiles, birds, and mammals. Notably, the family contains species—represented by these genomes—that are responsible for major region-specific human diseases. All three organisms and their diseases have been studied for more than 100 years. Surprisingly, some of the highly toxic and inadequate drugs that are used to combat them today—based on arsenic or antimony—have their origins almost as long ago. Why is this? The answer is simple: These are primarily geographically restricted diseases of the ultra-poor in underdeveloped countries.

Trypanosoma brucei and its relatives are responsible for devastating diseases of humans (“sleeping sickness”) and livestock in equatorial Africa, and have also spread to South America and Asia. Although its relative importance has paled in comparison with the impact of HIV, the parasite presents a continual threat of sleeping sickness epidemics because of the ubiquity of its animal reservoirs (and of the tsetse fly that transmits it), combined with the breakdown of social and economic infrastructure.

Trypanosoma cruzi is responsible for Chagas’ disease. It primarily affects rural South America but also constitutes a potential hazard in the United States, primarily through blood and organ donations. How many Americans have pondered the question “Have you EVER had Chagas’ disease?” on a blood donor questionnaire?

Leishmania major is responsible for one variety of leishmaniasis. Other species contribute to a broad spectrum of invasive diseases throughout South and Central America, across the Mediterranean, and throughout Asia. In Europe and the United States, outbreaks of leishmaniasis and Chagas’ disease have occurred in dogs, but there have been few cases in humans, save for those contracted by expeditionary military personnel.

The human devastation dealt by these parasites continues, but is this what has kept them alive in the minds of scientists? Not entirely. The Tritryps happen to be amenable to laboratory investigation, making them the best-studied examples of ancient eukaryotes. These organisms have followed an evolutionary track distinct from those that are extolled for their conservation of key features, from yeast to human. Some universal cellular pathways operate in Tritryps in interestingly different ways, and some of the things Tritryps do are striking because they represent unique mechanisms of pathogenicity, yet reflect genetic mechanisms that occur elsewhere. RNA editing and the anchoring of proteins to membranes with a lipid moiety were famously discovered in trypanosomes.

The Tritryp genomes are thus intrinsically interesting—but what will they contribute to the amelioration of disease? Because of their distinct evolution, trypanosomes present a plethora of potential drug targets, and potential drugs are almost certainly languishing in the chemical libraries of pharmaceutical companies. There have been several initiatives to tackle diseases of neglected people: The Drugs for Neglected Diseases Initiative exists entirely for the purpose of Tritryps drug development; the World Health Organization fosters drug research on neglected diseases; the Bill and Melinda Gates Foundation provides major funds; Medicines for Malaria Venture is a key organization. But we need resources and commitment on a far larger scale to transform drug targets into clinical successes. It is clear that the traditional pharmaceutical industry will not become effectively involved in this area, and the current promotion-and-reward system in academia does not attract or sustain the necessary human and financial resources. Consortia move slowly and are frequently restrained by similar problems, compounded by the egos of scientists and sponsors.

What are the solutions, then? Perhaps we need research institutes that are solely dedicated to drug development for “diseases of the poor.” Governments of the wealthier nations need to place such diseases higher on their priority lists, but we shouldn’t hold our breath on that, even as these diseases continue to expand their geographical reach. What about other donors? There is an ominous call at the gates—can anyone hear it?

George A. M. Cross

George A. M. Cross heads the Laboratory of Molecular Parasitology, Rockefeller University, New York, NY 10021, USA.

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Trypanosomes at the Gates
George A. M. Cross (July 14, 2005)
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Editor's Summary

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