Genomic medicine has failed the poor

A decade on from a landmark genetic-sequencing study, promised progress on typhoid fever has not materialized, says **Stephen Baker**.

Genome sequences come thick and fast in modern science. *Nature* has just published an analysis of the genome of the naked mole rat, and a historic sequence of the plague bacterium *Yersinia pestis*, reconstructed from medieval victims of the Black Death.

What is the value of such research? In my field, infectious disease, the genomics revolution has been substantially less beneficial than was anticipated. To those of us who work in poor countries in which infectious diseases that have been all but eliminated in the West are still common, it is clear that the wide-eyed optimism and persuasive advocacy for genomics that were expressed at the turn of the century were at best naive, and at worst potentially damaging, diverting resources from more worthy causes. Certainly, the outcomes have not matched those promised as justification for funding the research.

I have personal experience of the hype and the reality. Ten years ago, I was an author on the paper that announced the genome sequence of *Salmonella enterica* Typhi, the microorganism that causes typhoid fever (J. Parkhill *et al.* *Nature* **413**, 848–852; 2001). The research was promoted with great fanfare, which declared that scientists were at a turning point in the fight against the disease. A decade on, we are no closer to a global solution.

The *S. enterica* Typhi sequence did help us to understand the biology of the organism and to address enigmas such as why it causes disease only in humans, how it develops resistance to antimicrobial agents and how it modulates the human immune response. And although not even the most optimistic genomics or public-health expert would have predicted eradication of the disease within a decade, the sequencing did at least make elimination a realistic target.

But the promised concrete benefits — bespoke treatments, next-generation vaccines and low-cost diagnostics — have failed to materialize.

The technological expertise and funding for genomics work and subsequent studies are concentrated in countries that, owing to geography and economics, are not affected by typhoid. Researchers and funders are detached from the disease's realities. As a consequence, follow-up funding, expertise and advocacy are weakened. There is no motivation like seeing a patient every day, seeing a disease rife in your community or knowing someone with a serious illness.

By contrast, HIV does affect the scientific superpowers. In wealthy countries, there has been remarkable progress in public health and clinical practice since the virus was discovered and subsequently sequenced. This is a testament to the power of scientific investment allied with political and community support, and powerful activism.

In this light, the reasons for a lack of success with typhoid — and other infectious diseases

endemic to low- and middle-income countries — are depressingly obvious. Affected people simply do not have the clout to force the scientific community to build on laboratory research.

There are no advocacy groups for typhoid and other diseases of poverty similar to those that exist for HIV. Affected people and communities are not powerful constituencies. Decision-makers in endemic countries are typically drawn from the wealthier classes, and few have had typhoid fever, or have known someone who has died from the disease.

The position of major international donors — including the Bill & Melinda Gates Foundation in Seattle, Washington, and the US National Institutes of Health in Bethesda, Maryland — does not help. They focus on a narrowing range of diseases such as malaria and tuberculosis: priorities typically determined by metrics and disease league tables. Anything else is left mostly untouched.

It can be a vicious circle. Take diagnosis: there is still no good way to detect typhoid, so global estimates of the extent of the problem are based on guesswork and are almost certainly underestimates. The disease thus has low priority in international assessments. Genome-based diagnostic methods are being explored, yet they rarely reach the field — partly because they are designed for use in well funded, technologically advanced laboratories. Academic funding focuses on research, with little left to support development and testing in endemic locations. Many methods simply die before testing, or as a consequence of trials poorly executed on shoestring budgets.

We need a new approach. Scientists who fight diseases such as typhoid through laboratory research must work more closely with those of us who do the same in the field.

Funding agencies that support investigators who use genomics research must give them more opportunities to see the nature of the infection in endemic countries. One way is to increase support for consortia and collaborations that already aim to bridge the geographical and technological gap.

Such initiatives also require more support and advocacy from ministries of health in developing countries, to welcome international collaboration and make possible academic and public-health partnerships.

If these crucial issues are not addressed, I fear that the sequence of the *S. enterica* Typhi genome, and others like it, will persist as a fascinating academic advance, mostly useless in a public-health context. ■

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