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African biomedical scientists and the promises of "big science"

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ABSTRACT

An ongoing genomic revolution in biology has exponentially increased the rate, possibilities, scope and cost of biological research. Infectious disease genomics are often justified by the potential they have to ameliorate Africa's disease burden. The molecular biology revolution that preceded genomic science widened the gap between the skill sets of many African biologists and their contemporaries elsewhere. Gap closure through genomics and the application of genomic data to health problems requires participation of, and leadership from, African scientists. However, few African scientists participate in genomics, and providing biological samples is their predominant contribution. Health-related applications are emerging from genomic activity for some infectious diseases that are endemic in Africa but not for many others. This article argues that the arrival of next-generation diagnostics, surveillance tools, drugs and vaccines could be accelerated by improving the nature and degree of participation of African scientists in genomic and post-genomic inquiry.

KEYWORDS

Genomics; infectious disease; capacity; collaboration; biomedical research

1. Introduction: a crowd-sourced genome project

> What about us as scientists? Nigerian and African scientists have become irrelevant to our people and turned into mere sample collectors. We are burying our heads in the sand of ignorance, complacency and surrender.
>
> Professor Oyewale Tomori (Oyebade 2010)

In the spring of 2011, a massive *Escherichia coli* outbreak began in Germany and within weeks spread across Western Europe. In Germany alone, at least 3816 people were infected and 54 died (Frank et al. 2011). By this time, outbreaks of *E. coli* that produce the deadly Shiga toxin had become common in Europe and North America but there were worrisome differences in this one. To the surprise of many *E. coli* experts, the causative bacterial strain did not belong to the notorious *E. coli* O157 serogroup. Indeed this strain was more virulent than *E. coli* O157, killing young adults and producing deadly hemolytic uremic syndrome in 22% of the infected, compared to under 10% with O157 strains. There was a need to quickly detect the new bacterium, how it was spreading and why it was so virulent. The knowledge would help track it in food and protect people from infection. It would also provide clues as to how to treat the severely ill patients that were crowding hospitals in Germany and elsewhere in Europe.

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We know a good bit about *E. coli* O157 but that knowledge was garnered through work in hundreds of laboratories over about three decades. By 2011, methods for rapid genome sequencing had been perfected and within three days the genome sequence of the new outbreak strain was completed. The rate-determining step for genome analysis at that time was annotation of sequence data – that is, determining what it meant.[1] Annotation in 2011 still required graduate-level scientists to go through the sequence one gene at a time, comparing each probable gene to other sequences in the database and making a determination as to the likely function. To speed up this step and to increase its accuracy, the scientists who sequenced the genome of this unusual *E. coli* isolate elected to release the sequence and depend on crowd-sourcing for the annotation. The sequence would be made freely available on the internet and scientists anywhere could contribute to its analysis. This never before attempted approach to acquire and present valuable scientific knowledge worked! In five days, there was a diagnostic test for the strain and its potential response to all known antibiotics could be predicted. Within three months, a rigorously annotated genome sequence was available to scientists all over the world and was published in the *New England Journal of Medicine*.[2] These were the result of a "burst of crowd-sourced, curiosity-driven analysis carried out by bioinformaticians on *four continents*" (Rohde et al. 2011, 3, emphasis mine).[3]

By the third week of the *E. coli* outbreak, analyses by independent research groups revealed that the new strain was most closely related to an *E. coli* strain belonging to the scientific neglected category known as enteroaggregative *E. coli*. Enteroaggregative *E. coli* are an important cause of diarrhea, malnutrition, growth impairment and death in Africa, South America and South Asia (Okeke and Nataro 2001). The strain in the Germany outbreak was most closely related to an enteroaggregative strain that had previously been isolated in the Central African Republic (Rohde et al. 2011; Rasko et al. 2011; Mellmann et al. 2011). It was curious then that African scientists did not participate in the "crowd-sourced, curiosity-driven analysis." At the time, many of them had internet access and the majority could communicate in English, the principal language employed in this project. A good proportion of the contributors used only online tools and share-ware for their analyses. While some African health professionals are ambivalent, African scientists understand the value of molecular and genomic science and the power it could give them to generate and test important hypotheses (Crane 2013; Okeke 2011; Vogel 2000; Ntoumi et al. 2004). Why then did they not contribute to a high-profile task that threw more light on a pathogen that could be endemic in Africa? And what are the prospects that we will learn more about this threat, its origin and the best means to control it from "global" crowd-sourcing that excludes a continent's worth of biologists?

2. A genomics divide

Most genomic discoveries are "made, and in part are owned, by the developed world" (Pang 2002,1077). In 2001, Peter A. Singer and Abdallah S. Daar suggested that within a decade of their writing, we would know whether the genomics revolution would result in opportunities and resources for poor countries or a "genomics divide" analogous to the "digital divide" (Singer and Daar 2001). 2010 was too early to count actual deliverables from genomics but it turned out to be a good milestone for evaluation because, by then, it was possible to see an uneven but non-dichotomous landscape. Just as the "digital divide" is not a fence between information technology haves and have-nots (Warschauer 2003), but rather a complex

gradient between the over-connected and the under-accessible, the gains from genomics are growing impressively for some infectious diseases and not at all for others. Biology cannot account for these differences and funding does so incompletely. Back in 2001, Singer and Daar underscored an important point: bioinformatics, genomics and systems biology will not inevitably improve the health of the poor. They must be *made* to do so and we need to learn how (Singer and Daar 2001; Wolffers, Adjei, and van der Drift 1998; InterAcademy Council 2004).

Africa could benefit in many ways from genomic science but I have chosen to focus on infectious disease in part because, as a microbiologist, I have the greatest familiarity with this area of human health. However, pathogen genomics is a useful focal point because the genomic revolution occurred earliest there (Fleischmann et al. 1995). Genomic gains will impact infectious diseases more quickly than chronic diseases because we had a better understanding of the etiology of infections before the genomic era began. Furthermore, although there has been recent progress in the field of human genomics (Consortium, The H3Africa 2014), sequencing human genomes from Africa has a more direct effect on health and knowledge outside Africa than does sequencing the genomes of microbes that have been eliminated from the North. Therefore, examining outcomes from pathogen genomics through critical reviews and close reading of the biomedical primary literature makes it easier to parse Africa-specific gains, the focus of this work, than those that have a more general application.

A number of commentators have noted that returns on genomic science investments have been sparse, leading to some skepticism. Development advocates have even begun to suggest that the failure to translate research activity into practical outcomes is deliberate:[4] Notwithstanding the more pessimistic explanations (Molyneux, Ndung'u, and Maudlin 2010; Baker 2011), it has recently been acknowledged that the gains from genomics and related sciences will come more slowly than we had originally anticipated (Weatherall 2003, 2010; Wilkins 2003). Like the other pessimists, my question is not so much when Africa will receive its promised quota of vaccines, diagnostic tests and medicines, but whether that will happen. In identifying cases where it is likely to happen, beyond the more obvious stimulus of funding, an unlikely, coercive stimulus and indeed very effective but largely overlooked driver has emerged – the African scientist. This work is about scientists in Africa and how they have been key lynchpins for health-related gains from some genomes and the missing links for translation of others.

One begins a technical biomedical research grant proposal with an accessible introduction that enumerates the people who die or are disabled by the disease in question. Genomic science papers are similarly framed as is perhaps best illustrated by the earliest pathogen genomics papers that outlined the major findings from a single genome. These were published in the most prestigious scientific journals to which they were typically submitted by 20 or more co-authors. The papers were dense summaries but the genomes themselves linked from them offered a wealth of data that would be used (and cited) by many more scientists in years to come. In spite of the density of these papers, they inevitably included an introductory "justification" paragraph, which explained why it was deemed judicious to devote so many resources to sequencing the said genome and concluded with a "promise" paragraph that explained how the genome would serve humankind. The authors of the genome papers did not claim that they would deliver on the promises themselves (indeed, they are unlikely to have the requisite skill sets). Instead, they expected the scientific

community, to which the data are gifted, to rise to the challenge of the promises made. The publication of the first malaria parasite chromosome is a case in point (Gardner et al. 1998) but virtually all pathogen genome papers published in the late 1990s and early 2000s are similarly structured. For Africa-endemic pathogens, the justification paragraph and the promise paragraph included references to the burden of disease in Africa and the interventions that would influence that burden that could ultimately emanate from the sequence.

Scientists made these promises sincerely, and even carefully. In the words of one optimist-turned-pessimist, the Vietnam-based bacteriologist Stephen Baker:

> 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 … 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 promised concrete benefits – bespoke treatments, next-generation vaccines and low-cost diagnostics – have failed to materialize. (Baker 2011, 287)

Baker goes on to suggest that the problem is that "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." Similarly, Coloma and Harris (2009) blame "technological isolation and [developing country scientists'] limited resources." I agree with all of these authors but, in this paper, I wish to argue that in contrast to Asia and Latin America, where we see significant if modest gains from genomic science,[5] for Africa, potential in these new technologies for addressing some key infectious diseases is lost because there are African scientists working in the parts of the world where endemicity is highest that hardly ever use them. That is to say, the problem that Baker (2011) highlighted for typhoid – the separation of research activity and disease endemicity – is worst for sub-Saharan Africa and therefore, if nothing changes, outcomes here will be least likely. While there is significant progress in a few flagship fields that I will highlight, sadly a significant majority of African biologists are barely literate in the languages of genomics and systems biology or the molecular genetics and chemical biology that preceded them (Chimusa et al. 2015; Tastan Bishop et al. 2015). Current programs are working to address these shortfalls (Tastan Bishop et al. 2015; Adoga, Fatumo, and Agwale 2014; Karikari, Quansah, and Mohamed 2015) but the rate of scientific training is still slower than the rate of change within those rapidly advancing fields. Without the literacy and participation of endemic-area scientists in the genomic and post-genomic revolutions, the expectations from so much on this research will not be fully realized.

3. Pathogen genomics – a "big science" of infectious disease

Science can now sequence whole genomes – that is, all of the DNA – of the pathogens that cause infectious diseases. The genome sequence of each pathogen is its unique signature and contains all the information it needs to survive and produce disease. Elucidating the function of this sequence can unveil how the pathogen overtakes and damages its host and how it can be stopped. Genome-wide approaches provide many more options for intervention than the single gene methods in the early molecular biology era, which studied small stretches of sequence one at a time.

The field of pathogen genomics has made admirable progress in improving our understanding of how harmful organisms cause disease and in tracking these infectious

agents (Koser et al. 2012). The field also repeatedly makes the attractive claim that it will enable rapid development of precise disease control tools – such as drugs, vaccines and diagnostics – or development of tools that are easier to use in resource-limited settings. For vaccines in particular, it is likely that most of the effective and safe shots that can be developed by traditional means already exist and advances for other diseases will require new approaches of which those based on genomics are the most promising (Oyston and Robinson 2012). Genome-level science has reduced the discovery time (but not the development time) for vaccines and expanded the inquiry space so that it is feasible to develop vaccines for some diseases for which there were technological roadblocks in vaccine development only two decades before (Rappuoli 2007; Bambini and Rappuoli 2009). Carol Dahl and Tadataka Yamada of the Bill and Melinda Gates Foundation argue that technology could generate cheaper interventions or ones that can be applied where others have failed to stem or reverse some of the negative impacts of disease in the world's poorest countries (Dahl and Yamada 2008). They highlight genomics and other types of "big science" as means to these ends and observe that in many areas of little progress, genome sequences have not been fully exploited and suggest that scientists have a responsibility for using these new techniques to generate tools for combating disease.

The term "big science" itself was applied to biomedical research by Yamada, in an article co-authored two years prior. Yamada reminded biologists that "big science" was coined by physicist Alvin Weinberg to refer to large-scale scientific approaches that would result in nuclear technologies (Esparza and Yamada 2007). Abstraction of the term by Yamada to biology thus implies that it not only applies to large-scale experiments like genomics (and others including combinatory chemistry and high-throughput screening) but to those experiments that are aimed at a specific and practical outcome. DNA sequencing is, if purely defined, basic science. It should not need to be justified by outcomes. But genomic science is often justified in terms of outcomes for health, agriculture or the environment, more or less embracing the "big science" definition in its original form.

The genomics revolution is actually a follow-on revolution from a molecular biology revolution which began in the 1950s when the structure and function of DNA, ribonucleic acid (RNA), proteins and other biological molecules began to be uncovered. Even though this was a basic science revolution, it ultimately gave us such valuable tools as the *Haemophilus influenzae* (Hib) vaccine, which has improved child survival in Africa and elsewhere (Adegbola et al. 2005). Without the molecular biology revolution that enabled these biotechnologies, it is unlikely that we would know what we do understand about HIV or would have the antiretrovirals that are our stop-gap method of addressing the growing pandemic. However, in spite of this phenomenal progress, and important exceptions like the Hib vaccine notwithstanding, the molecular biology revolution served relatively little to Africa both in terms of impact on health, as well as its impact on science and technology on the continent over the three-quarters of a century since it began (Vaughan 1991; Fullwiley 2011; Feierman 2011).

The sheer scale of the genomic revolution promised to overcome some of the exclusion of Africa and its scientists from biomedical progress in the decades immediately preceding genome sequencing. In contrast to molecular biology, which in addition to extensive training largely required all participatory laboratories to access costly equipment and labile consumables, genomic science is much more accessible in practical terms. Scientists that do not generate genomic sequence use it. Most important genomic data is available from freely accessible databases and sophisticated analyses can be performed using free software.

Resource-limited scientists all over the world can and do make advances this way, as do undergraduate students in training at research-intensive US Liberal Arts Colleges (Ditty et al. 2010; Goodner et al. 2001; Labar et al. 2012; Sumrall et al. 2014; Fricke, Rasko, and Ravel 2009). Genomic data could be used by resource-poor laboratories in Africa. Also, although genomic and other -omic big sciences are expensive (though prices are dropping rapidly), they can be used to develop very basic and cheap technologies. Therefore one would expect that unlike molecular biology, the fruits of genomics would fall into Africa or that at the very least, some of their juices would trickle in. This is happening in some cases but not in others.

4. Status and equity in bioscience

4.1. Matthew, Dr Fox and Cinderella effects

Nobel laureate Peter Agre advised young scientists to focus their energies towards making original discoveries, earning peer respect and training new scientists (Agre 2010, S11). All of these can be achieved within a "big science" framework but not by all participants. "Big science" approaches integrate less "brainwork" per datum yielded than do smaller projects and are therefore justified by their potential to yield outcomes. None of this implies that "big science" is bad, non-innovative or stifling for scientists. What it simply means is that not all scientists engaged in "big science" will make intellectual input and that a discipline comprised of a mix of "small" and "big" science researchers will most likely maximize gains by being able to draw on the advantages of each one (Weinberg 1967; Esparza and Yamada 2007). Genomic researchers outside large genome institutions can participate in projects through collaborations or use genomic data to ask and answer their own questions independently. The latter mechanism serves scientists based in small institutions elsewhere, notably in the United States.

Status in science determines access to funds and publication, both of which then influence the ability to do science. Intellectual contributions to, and credit from, collaborative "big science" projects vary enormously among participants and therefore if credit is to be distributed fairly, it must be awarded with care. There is also always the danger that important intellectual contributions will not be heard or credited because of the size of the consortium, or perhaps worse, that input from one participant could be attributed to another.

The "Matthew effect in science" was first noted by Robert Merton, who suggested that the biblical verse Matthew 25:29 applied to the rewards and communication of science (Merton 1968). The verse reads: "For unto every one that hath shall be given, and he shall have abundance: but from him that hath not shall be taken away even that which he hath." Merton emphasizes that renowned scientists (Nobel laureates in his analysis) readily admit that discoveries of unknown scientists are often attributed to those who have received awards and other acclaim, with there being little that the losers or beneficiaries of this phenomenon can do to redress the problem. The Dr Fox effect is similar to the Matthew effect in that it advances an individual (a "Dr Fox") whom reviewers believe is highly regarded in the field, even if this is not the case (Naftulin, Ware, and Donnelly 1973). A "Cinderella and the ugly sisters" effect is more ominous in that the beneficiary of the imbalance is, deliberately or not, directly involved in misappropriating credit because of an arbitrary privileging situation. Birgit Jentsch and Catherine Pilley have directly implicated this Cinderella effect to some North–South research partnerships (Jentsch and Pilley 2003).

4.2. The "Little Brother" effect in African bioscience

In the context of partnerships that try but fail to be equitable, it becomes pertinent that I describe another unfavorable relationship, which I prefer to call the "Little Brother" effect. The "Little Brother" effect is perpetuated by a well-meaning "Older Brother" who, unlike the beneficiary of Matthew or Dr Fox effects, is intent on and succeeds in sharing credit and other benefits. But the share is metered as it is meted out to the "Little Brother," who is viewed as being in need of guidance and is required to learn from example. As everyone with an adult "little brother" knows, younger siblings and other mentees start out needing guidance but then they grow. Eventually, most acquire knowledge that can be transmitted to their mentors. The problem with the Little Brother effect is that it persists as a stunted younger brother is consistently cast as the guided beneficiary in this uneven relationship. The Older Brother, who continues to be appreciated for being a caring and committed relative, is constantly in supervisory mode and his only objective is to have the Little Brother perform stated and specific tasks. The relationship remains stuck largely because the senior never looks beyond the performance of these tasks for intellectual contributions.

The Little Brother effect is my adaptation of a more general "Junior Brother" paradigm that has been described before. In its broader context, Africa was baptized "Junior Brother" by a well-meaning European. Chinua Achebe reminded us of Nobel peace laureate Albert Schweitzer's reference to the continent as his "Junior brother," and his intended brotherly instincts that manifested as paternalistic ones (Achebe 1977). Achebe, in his critique of Joseph Conrad's *Heart of Darkness*, highlights from that work the product of such a relationship, as viewed through an even less clouded "Senior Brother's" eyes (Achebe 1977). While Achebe's junior brother framework has not explicitly been used to illustrate African collaborations before, anthropologists have noted that even though modern North–South science partnerships are often cast as balanced relationships, the Northern partners often find themselves playing a paternalistic role that smacks of colonial hegemony (Geissler 2013). Application of the Little Brother paradigm to present-day science is my own attempt to understand some of the dimensions of many of today's "North–South" "partnerships" that have a distinctly rancid colonial appearance even though participants state the best intentions.

In the press for more "equitable" partnerships between Northern and Southern researchers, Little Brother effects are becoming increasingly documented and can be identified in the remarks from Northern and Southern participants. One senior European researcher has been recorded as referring to her younger Beninese "collaborator" as a "boy" (Fullwiley 2011, 181) but less obvious comments are more commonplace. In one more typical example, Okwaro and Geissler (2015) emphasize a statement from an East African scientist who describes his best collaborations as those where he is "allowed" to be principal investigator, suggesting that his collaborative role is one that he cannot negotiate. These ethnographers and Crane (2013) also document multiple clinical collaborations in which the Northern partners contribute financially and intellectually while the African scientists offer only sites, patients and logistic support. These descriptions are from HIV clinical research, from some of the most successful and best-funded scientific initiatives in Africa. HIV, the Human Immunodeficiency Virus, cannot replicate outside human cells. In fields where the pathogen is more readily separated from the patient for study, or the research is preclinical – requiring no patients at all – then the quantifiable "contributions" of scientists that are only providing access to patients or samples to this model shrink considerably or even disappear.

In the last half-century far too many African scientists are engaged in what they themselves view as "collecting" biological specimens, which are then dispatched to laboratories elsewhere on the globe. African scientists have viewed their conduit role in this "postal research" as derogatory (Ntoumi et al. 2004; Oyebade 2010; Crane 2013; Sawyerr 2004; Fullwiley 2011).[6] For them, bioscience has matured, but Little Brother has not. Others spend a few weeks a year hosting "parachute scientists" who visit only to grab specimens and then disappear into the real world of scientific inquiry (Okwaro and Geissler 2015; Fullwiley 2011). "Postal" and "parachute" research inevitably addresses remote or "global" questions, not local ones (Kebede and Polderman 2004; Costello and Zumla 2000; Okeke 2011; Wolffers, Adjei, and van der Drift 1998; Karim and Karim 2010; Fullwiley 2011). We know a lot because of this type of research, but very little of this knowledge has been applied to health care on the continent (Fullwiley 2011).

In collaborative partnerships, scientists can pool limited resources in order to address important questions; therefore all sides should benefit. In intercontinental partnerships, both Northern and African researchers acknowledge that collaborations allow them to access discovery space that would otherwise be inaccessible (Crane 2013). When the voices of African scientists can be disambiguated from those of their Northern colleagues, words such as "dubious" (Binka 2005, 207) or analogies to exploitation and prostitution (Wolffers, Adjei, and van der Drift 1998; Crane 2013; Okwaro and Geissler 2015; Fullwiley 2011) creep into the discourse. This is not to say that Southern collaborators do not value intellectually uneven partnerships. For many, a less than ideal connection is better than none at all because it is a way to get things done.

The lopsidedness of many North–South science partnerships is admittedly driven to a large extent by uneven access to funding and the purpose that the funding is purported to have. The extreme nature of these disparities pushes would-be collaborative partners into positions allied to the giver and receiver of aid. Many African researchers and institutions do not have the administrative and legal expertise needed to protect in-country participants from inequitable research agreements (Sack et al. 2009). Therefore inequities can even be codified.

The reductive nature of genomic science makes it inevitably a benefactor and victim of postal and parachute science. The essential method of genomics filters biological entities through costly sequencing machines, which then generate computational data for analysis. Pathogen genomics has emerged as a sub-discipline precisely because a pathogen can be separated from the infection, and the pathogen's genome and genome attributes can be separated from the microbe itself. It is today possible to be a leader in infectious disease research without ever seeing the disease in a patient or the pathogen in a petri-dish. Expertise can be derived, and new knowledge generated, from a sequence analyzed on a computer. For that type of genomic inquiry, scientists that contribute only to sample acquisition are dispensable.

5. Deconstructing genomic partnerships with African scientists

5.1. Contributions to bacterial comparative genomics

"Partnership is easy to say, but much more difficult to do." (Crane 2011, 1389)

Genomics projects are high-investment endeavors, typically centered outside Africa, and have the potential to offer the individual – based anywhere – more discovery potential than s/he could otherwise access. They also, as "big science" projects do by their very nature, leave some participants faceless or under-acknowledged. Hypothesizing that this was overly the case in projects involving African scientists, I performed a systematic review of bacteriology comparative genomics papers involving African scientists in the Medline-indexed literature. Recent high-impact bacterial genomics papers often use tens or hundreds of genomes to draw broad conclusions about how a pathogen works. In reality, the strain sets used for these comparative genomics studies reflect the geographies and reach of the scientists in the project. Biogeography is an important driver of human genetics and genomics work in Africa (Fullwiley 2011; Rotimi et al. 2014) but more recently has been shown to be critical for understanding pathogen evolution, spread, virulence and mechanisms for control as well (Baker, Hanage, and Holt 2010; Okoro, Kingsley, Connor, et al. 2012). For this reason, and the diversity of species on the African continent, comparative genomics studies that set out to test global hypotheses would be incomplete without significant sampling from Africa.

The systematic review used the Medline database Pubmed (http://www.ncbi.nlm.nih.gov/pubmed), searching for terms listed in Table 1. Abstracts of hit papers published between 2000 and 2015 were reviewed and duplicates were removed. From the abstracts or full text, I identified papers that were multi-country comparative genomics studies comparing six or more genome sequences that included isolates and at least one author with an African affiliation. Of the resulting 16 papers, two papers using microarrays rather than whole genome sequences for comparison were excluded because, although this is a comparative genomics technique, molecular biology wet-lab resources are required for comparisons. One paper was excluded because it included some authors whose research base could not be discerned from the paper.

A total of 13 papers met the inclusion criteria for close reading and further analysis. Collectively, the papers analyzed 3151 bacterial genomes, 383 of which were derived from isolates from Africa. The sum total of authors on the 13 papers was 283 (range 8–73; median of 20 per paper) and the sum total of Africa-based authors was 38 (range 1–8; median two per paper). The 38 Africa-based authors had affiliations in eight different countries: Democratic Republic of Congo, Djibouti, Ghana, Kenya, Madagascar, Malawi, Nigeria and South Africa. Authors with an African affiliation were first, second and last authors on two of the papers, which respectively had four of eight and six of 14 of their authors based in Africa. For the remaining 11 papers, African authors did not occupy any of these three leadership author positions on the papers.

Recognizing the collaborative nature of "big science" inquiry, biomedical journals are increasingly requesting that the contributions of authors to each paper be outlined in the

Table 1. Search terms used for a systematic review of authorship in bacterial comparative genomics papers indexed on Medline.

Search term	Hits	Hits if the word "Africa" is omitted from the search term
bacteria whole genome sequencing phylogeny Africa	47	784
phylogeography bacteria Africa whole genomic sequence	12	51
comparative genomics bacteria Africa	71	4590
comparative genomics bacteria global	345	Not applicable

Table 2. Author contributions to nine bacterial comparative genomics papers.

Authorship category	Specific description of the category in journals	Europe	Asia	South America	Other non-African*	Africa	Africa other than South Africa
Study design	Were involved in the study design/designed the study (2)/provided materials and assisted with study design/study design/conceived the study, analyzed the data and co-wrote/conceived and designed the experiments (2)/designed the study/conception and design	26	6	0	7	4	0
Experimental	Analyzed [gene] types/contributed to collecting data and manuscript writing/ sequencing data generation/conducted selection tests/obtained [genus] genotyping data and drug susceptibility test results/performed sequencing, SNP discovery, MassArray and SNP testing/performed the experiments (2)/ acquisition of data	49	6	9	1	6	0
Bioinformatic and computational analyses	Collected the data, analyzed it and performed phylogenetic analyses and comparative genomics –performed Bayesian analysis – did computational coding/analyzed sequence data and performed phylogenetic, BEAST and comparative genomics analyses – wrote the coding scripts for phylogenetic and Bayesian statistical analyses and contributed to manuscript writing/carried out the Bayesian analysis and co-wrote the manuscript/data analysis/analyzed data and wrote the manuscript with comments from all authors/performed population genetics and phylogenetic analyses/performed bioinformatic analyses of the data/performed population genetic analyses/analyzed the data (2)/ analysis and interpretation of data	58	1	0	0	4	0
Supervision and project management	Supervised the work/project oversight	2	1	0	1	0	0
Materials provision	Involved in strain collection and serogroup analysis/contributed to studies from which isolates were drawn and to manuscript writing/provided materials and co-wrote the manuscript/isolate acquisition and processing and clinical data collection/contributed [bacterial] DNA and demographic information/ contributed reagents/materials/analysis tools/contributed reagents/materials/ analysis tools/contributed unpublished essential data or reagents	36	26	4	12	24	20
Writing leadership	Contributed to the manuscript writing/manuscript writing/wrote the manuscript/ wrote the paper/drafting or revising of the manuscript	30	4	0	6	4	0

*North America, Australia and New Zealand.

paper. An "Author Contribution" section was included in nine of the 13 papers that met the criteria for inclusion in this analysis. This subset included 28 of the Africa-based authors and 212 total authors. The author contribution categories used in the papers are quite broad, making it difficult to parse the very specific contributions of authors from these lists. However there are clear categories relating to project design and or management, experimentation and biological material contributions (Table 2). Manuscript writing appeared as a separate category for some journals and was integrated across other categories for others. Where a separate writing category was listed, I included it as a "writing leadership" category because biomedical journals do require co-authors to contribute in some way to writing. As all the papers were in English, non-Anglophone scientists will probably be under-represented in this category. (There were no South American contributors to this category for example.) As it is plausible that some bias could have been included in my categorization, I have included the actual labels for every other category in Table 2. With the exception of writing leadership, most of the nine papers contained at least one type of contribution in each category and none of them was missing more than one of the categories.

The analysis here presented must be carefully placed into a somewhat more dismal context. The vast majority of bacteriology comparative genomics papers actually have no Africa-based co-authors and very few have Africa-derived strains. As shown in Table 1, performing the searches I laid out in the table without "Africa" yields many times more hits. While some of the articles focus on other world regions, the underrepresentation of Africa in these analyses is probably a better reflection of the fact that very few Africans are involved in pathogen genomics research at all than the systematic review presented here. The systematic review was performed to identify African contributions but has other limitations that I must outline. Firstly, research on the comparative genomics of bacterial pathogens of relevance to Africa will suffer from the bias against poverty-related diseases that occurs in the biomedical literature and for funding (Langer et al. 2004; Horton 2003). Thus I am looking to see if there are biases within an area of investigation that is itself marginalized. Secondly, this study categorizes authors by the affiliation that is listed on the papers. African authors that are temporarily or permanently domiciled abroad – as they might be as they train to perform genomic analyses – are therefore categorized by foreign affiliations if they do not list their African institutions. As Africans may bear Western names and vice versa, a more nuanced categorization cannot be performed with only the information available on the paper. Finally, those papers that do include Africa-based authorship and content, those that were selected for my analysis, are predominantly led by groups in Europe (hence the overrepresentation of European authors in the papers included). One each of the papers included in this study was respectively led by an Australian and a South African group. The rest were led by Europeans, with six being UK-led, reflecting that one of the world's foremost genomic research centers, the Wellcome Trust Sanger Institute, is in the UK.

All the papers featured bacterial species that produce a high burden of disease in Africa and/or cause outbreaks. As Table 2 shows, materials provision was the principal contribution made by Africa-based authors. And while materials provision was a category that featured significantly in all world regions, only Africa made very little contribution to the other categories. On a country level, my analysis revealed that the materials provision category was the *only* one to which African authors other than those based in South Africa contributed. For one paper, there were two "Author contribution" subcategories relating to materials provision. One was "Provided materials and assisted with study design" (which I counted

with study design) and the other "provided materials and co-wrote the manuscript," which I have classed with materials provision. For that manuscript, the former category included two Australian authors whilst the latter category was comprised of Belgian, Swiss and the sole Africa-based author. For the one paper that did not have an obvious sample providing the author contribution category, the category that would have provided those specimens was "obtained [genus] genotyping data and drug susceptibility test results." This I classified without difficulty as "experimental." The contributions in that category for the paper in question were made from authors based in Japan, Peru and three South Africa-based scientists. South Africa was the only country where Africa-based scientists co-authored one of the included papers without contributing materials. For all the other world regions profiled, this was the case for some or most of the scientists. The distinction of South Africa is not surprising. That country has made more domestic investments in genomic science and bioinformatics than any other south of the Sahara (Hardy et al. 2008; Mulder et al. 2016). What these findings appear to show is that such investments yield fruit.

In summary, on many of the few bacterial genomics papers that include one or more African co-authors, some interesting points emerge. The papers I analyzed are highly relevant to disease in Africa, hence the effort to include African isolates. However, the Africans contributing to the research are few and their contributions are largely limited to providing biological specimens or isolates. The very nature of the work is such that this will be the contribution of many authors, particularly authors based in parts of the world other than those leading the project. What is peculiar to Africa, relative to other world regions, is that this is the *only* contribution from African countries outside South Africa (Table 2). This is true even in included and non-included papers that represent instances when the focus of the article was to place isolates from Africa in a global context or compare them to one another (Lamelas et al. 2014; Leekitcharoenphon et al. 2013; Blouin et al. 2012; Okoro, Kingsley, Quail, et al. 2012).

Are African biologists no more than postal contributors to bacterial genomics research? An intellectual contribution can appear logistic – for example someone helping to find something in an archeology expedition. However, if the entire object of the project is to find very specific things, then knowing where and how to find them is key. One fast-paced archeological expedition (ironically) along the Congo River was chronicled in a report in the journal *Science*. The expedition was described as being "like a scene from *Heart of Darkness*, but with a happy ending and exciting scientific results" (Bohannon 2010, 1175). Like the pre-colonial and colonial explorers, who pushed through rapidly in their bid to escape the fatal diseases of equatorial Africa centuries before them, the archeologists rushed through the terrain in an admittedly unscientific manner, this time persecuted by the "lawless violence" that accompanies the present-day conflict-ridden Democratic Republic of the Congo. Their aim was to uncover archeological clues of ancient central African civilizations in surveys along the banks of the Congo. (The article itself is titled "Preserving African Cultural Heritage"). Ironically, the "happy ending" had a helper because "the best site was an ancient burial tomb pointed out by a woman [unnamed] from a nearby village" (Bohannon 2010, 1175). She had known it was there and yet the parachute archeologists were able to meet it undisturbed, and only with her guidance.

There are clear parallels with this example and those of researchers who need samples for genomic sequencing and downstream analysis. True "postal research" involves collecting specimens according to prescription, packaging them and shipping them away to the

analyst. Knowledge and information around the specimen is either not documented or is lost. This is detrimental to the sender when s/he is a specialist, as well as to the project. There are aspects of specimen collection and presentation that are intellectually demanding, require highly specialized techniques and a good understanding of the disease landscape. Feeding these features down a "big science" pipeline will enrich a project for content that is relevant to the disease under study. As organizations like the US Centers for Disease Control, the Public Health Agency of Canada or their UK equivalent, Public Health England, demonstrate, it is possible for investigators that bring this type of expertise to *lead* genomic projects (Reimer et al. 2011; Chattaway et al. 2016). While collection is purely logistic, sample curation should feature in project conception, design and in data analysis. The troubling find in the bacterial comparative genomics systematic review therefore is not that Africa-based scientists were providing material, but that they were not listed as contributors to other aspects of the papers.

Comparative genomics projects are large enough to provide fascinating and valuable data even if some directions or findings from the research are lost. Lost information from endemic areas matters for "big science" because of its stated intention to provide outcomes. Diane Fullwiley's (2011) sickle cell anemia ethnography illustrates that improving the understanding of a disease's biogeography does not itself yield interventions that address the disease. In her work, Senegalese scientists and physicians are cognizant, even proud, of the findings of global genome-wide association studies of the disease and the revelation that their patients may in fact carry a potentially tractable form of the disease. This knowledge did little to provide access to even existing therapies for the disease that are available elsewhere let alone specific therapies for the supposedly variant form of the disease. An important point evident from Fullwiley's work is that Senegalese experts have no ownership of the data that characterized their patients' disease even though they or their country's colleagues contributed to generating it.

If you don't have particular expertise, you cannot contribute it to a project. Can the dearth of contributions from Africa-based scientists be put down to the lack of genomics and bioinformatics expertise on the continent? In part, perhaps (Tastan Bishop et al. 2015; Adoga, Fatumo, and Agwale 2014; Karikari, Quansah, and Mohamed 2015), but not entirely. Genomics is such a new field that almost all leaders that have been working in the field for over 20 years are self-trained. New entrants in the field can now enter purpose-designed post-graduate programs but the model for entry for many years, an alternative that some scientists still use today, was to begin a collaborative endeavor with an insider and, through apprenticeship, learn the nuts and bolts of DNA sequence analysis. Thus many genomic scientists began as those who brought strains or other logistical components to a partnership until they acquired the skills to ask and address their own questions.

Okeke and Wain (2008) have likened today's scientific communities, and particularly genomic science, to fast-moving merry-go-rounds. If you are not stationed on it before it begins to spin, you cannot board a fast-moving merry-go-round. You can only ride if it slows down, you break into a run and then leap, or if someone swings you in. Science slows down for no one. And while some exceptionally talented biologists have leapt onto the genomics merry-go-round, many more are swung in by mentors and colleagues. If skill base is the integration problem and external collaborators are colleagues rather than "Older Brothers," the repertoire of contributions from Africa should broaden over time. As comparative genomics is rather new, this is something that only time will tell.

Cinderella-Ugly Sisters and Little Brother effects are almost inevitable when scientists with uneven access to research support collaborate. Almost every Northern participant in a Northern-supported "North–South Partnership" with an African scientist has found themselves in an Ugly Sister or Older Brother position at some point during the collaboration. Some of the awkward positioning is difficult to circumvent in today's framework for international collaborative research. However, as Geissler and Okwaro (2014) point out, altering the terrain is difficult because fundamental inequalities are not even acknowledged. As those ethnographers document, where inequalities may impede research, they are often managed by African scientists in ways that are not revealed to their Northern partners. A most important component to collaborative relationships, and one that is often overlooked in long-term North–South links, is that the roles of collaborators within a partnership will grow and change. African scientists and their Northern colleagues may well want to consider explicitly reviewing their roles and contributions on a regular basis, and in the course of acknowledging any unanticipated inequalities.

5.2. Partnerships that yield health-related outcomes

Buruli ulcer is a disease first described in the mid-twentieth century with the earliest reports coming from Bairnsdale, Australia and parts of Africa including Buruli, Uganda. Today, it is most common around certain lakes and slow-moving rivers in West and Central Africa, and infection foci also occur in Australia. In endemic communities in Africa, its prevalence exceeds those of common mycobacterial diseases such as tuberculosis and leprosy. The disease is rarely lethal but is disfiguring, disabling and impoverishing. Buruli ulcer is caused by the species *Mycobacterium ulcerans* and has been studied by only a very small number of researchers working on it worldwide. Most of them are part of a research network that calls itself "Stop-Buruli." As at October 2010, the network was comprised of only nine research groups, focused on all aspects of *M. ulcerans* transmission, diagnostics and pathogenesis as well as treatment, control and socio-economic aspects of the disease. The groups are located in Australia, Belgium, Benin, Cameroon, Ghana, Switzerland and the USA. Five of the nine groups (there were two in Benin – one discontinued by 2014 – and two in the USA) are located at, or close to, endemic hotspots, most of these in Africa. The Buruli ulcer research network is like few others for tropical diseases in that investigators are commonly in endemic countries *and* the research includes a significant "big science" component. Although they themselves do not work at the world's major genomic institutes, Buruli researchers have been able to mobilize funding and resources for a modest genomic initiative and one that, although uncovering important knowledge on mycobacterial evolution, is predominantly concerned with controlling the disease.

Perhaps one of the most important facets of this short history of *M. ulcerans* genomics is that although both African and Western scientists have co-authored papers that present and use genomic data in this field, papers that include an African author as lead (first) or senior (last) author almost always have direct application to disease control. For example: "A quick and cost effective method for the diagnosis of *Mycobacterium ulcerans* infection" (de Souza et al. 2012), "Source tracking *Mycobacterium ulcerans* infections in the Ashanti region, Ghana" (Narh et al. 2015) or "Response to treatment in a prospective cohort of patients with large ulcerated lesions suspected to be Buruli ulcer (*Mycobacterium ulcerans* disease)" (Kibadi et al. 2010).

Diane Fullwiley (2011) proposes that a Senegal-specific hemoglobin allele (gene variant) reputed to encode a relatively mild version of sickle cell anemia derives some of its perceived non-severity from enculturation. While Fullwiley refers largely to patients and their communities ameliorating interactions with the gene, she also highlights enculturation that comes from interfaces with local experts. I would argue that in contrast to many other bacterial genomes, which though free, remain foreign intellectual items, enculturation of *M. ulcerans* genomes accounts for practical outcomes for Buruli ulcer in Ghana, Benin and other African endemic foci. Additionally, endemic area clinical research on *M. ulcerans* disease that cannot be described as "genomic" has blossomed since genomic research began because other researchers are employing tools and methods that were developed using genomic data. Finally, what has been learned about *Mycobacterium ulcerans* is applicable to the biology of other organisms with "reduced" genomes[7] – that is, organisms that become pathogens by losing, rather than gaining genetic material (Rondini et al. 2007). Thus the knowledge generated by the Buruli consortium has value to others working in unrelated fields in non-endemic parts of the world.

Buruli ulcer is a neglected disease that makes a compelling case study for outcomes from genomic research. Similar, equally compelling outcomes have been seen in the malaria research community, which also integrates endemic-area researchers better than many other fields of genomics. October 2002 was a genomic milestone for malaria research because the first issues of *Nature* and *Science* respectively contained the publications of the genomes of *P. falciparum* and its mosquito vector *Anopheles gambiae* (Holt et al. 2002; Gardner et al. 2002). The three genomes that interact to produce malaria – the vector, the parasite and its host, *Homo sapiens* – were complete. The concluding section of the parasite paper began with the statement that the genomes "represent new starting points in the centuries-long search for solutions to the malaria problem" (Gardner et al. 2002, 508). Unlike many other pathogen genomics papers, this was no empty promise. Insight from malaria genomics has allowed repurposing of existing antibacterial drugs, which have now entered the antimalarial pipeline. It has also identified other antimalarial drug leads and spurred preclinical vaccine research (for example, Goodman, Su, and McFadden 2007; Waller et al. 1998; Kohler et al. 1997; Jomaa et al. 1999; Borrmann, Issifou, et al. 2004; Borrmann, Adegnika, et al. 2004; Wiesner and Jomaa 2007; Editors 2006; Francis et al. 2007).

Scientists in all corners of the world deserve credit for the leads in malaria. However, the link between endemic area scientists and technologies for malaria control is an important but often overlooked one. According to Ebrahim Samba (2004), African malariologists have been vital in the quest to generate and test new intervention tools and understand the ecology of this vector-borne disease. In stark contrast to many bacterial diseases, there are a number of well-known malariologists based in Africa who are engaged in parasite as well as vector and human genomics research.

How exactly did a vibrant, energetic and productive African malaria research community come to be? Prior to the 1990s, there were malaria researchers in Africa, but they were few and far between (Vogel 2000). At the publication of the malaria genome sequence, old school malariologist Fred Binka from Ghana, as pessimistic as scientists in other biomedical fields at this time, was quoted as saying "I'm sure [the sequencing] will lead to more drugs and maybe a vaccine. That's our hope … But on the sad side, we think we're just going to be spectators" (Jaffe 2002). A new generation of malariologists was rescued from the fate of spectatorism that persists in other areas of infectious disease (Oyebade 2010), in large parts

by their own determination and by the Multilateral Initiative on Malaria (MIM) (Marshall 2000). Early in the malaria post-genomic era, four of them, Francine Ntoumi from Gabon, Abdoulaye Djimdé from Mali, Wilfred Mbacham from Cameroon and Thomas Egwang from Uganda wrote: "The goals of malaria control may never be achieved without strong involvement of those scientists who are directly affected by this terrible disease in their daily life" (Ntoumi et al. 2004, iv). An initial MIM meeting was held in Dakar and attended by 22 African malariologists and 75 participants from elsewhere. While the participants from malaria laboratories in Europe and America were well known to one another, many of the African scientists had never met them, or each other. When private-sector funding for MIM was not forthcoming, the program was bankrolled by the World Health Organization, the US National Institutes of Health (NIH) and philanthropic foundations.

Prior to the MIM, "Translating the outcomes of research into practical knowledge for control and effective delivery of interventions to at-risk populations [had] proven to be a great challenge to public health systems of malarious areas within and outside Africa" (Samba 2004, ii). MIM was founded by agencies based in the US and Europe but its stated objectives included fostering scientific collaboration with and within the African continent. One of its nine priority action areas was sequencing *Plasmodium* genomes and three more related to building and maintaining scientific research capacity in Africa (Rugemalila et al. 2007; Marshall 2000). African malariologists received access to e-mails ahead of other African scientists through the MIM communication network and once the genome projects were underway, they had access to data, partners and training workshops. In addition to building and connecting human resources on the continent, the long-standing initiative has kept them there (Samba 2004) through opportunities to interact regularly with collaborators elsewhere, funding and easy access to research reagents. When PlasmoDB, a genome-navigating database, was launched in the early 2000s, most African researchers had no, or slow internet access. The database was therefore also released in CD format, allowing unconnected scientists to query it for their research (Kissinger et al. 2002; Bahl et al. 2002).

The malaria community in Africa is still too small to meet the endemic research needs of the continent. Nonetheless, the community is more robust than most in Africa and even though there were recently only a handful of research leaders, a new generation has been trained and is growing in strength. The African malaria research community includes a mix of scientists working at large research institutions on the continent – such as the Malaria Research and Training Center in Mali – and independent researchers working in smaller laboratories. These talented African researchers have made direct contributions to genomic and other "big science" initiatives but, as with the Buruli ulcer field, their most common publications relate to the epidemiology, ecology, treatment and prevention of the disease. They publish in well-known international journals, and speak at international conferences. They not only compete internationally for prestigious awards open to scientists of different fields, they also win.[8]

The malaria and Buruli ulcer disease research communities illustrate that endemic area scientists that use genomic information generate knowledge that connects "big science" to health-related applications. Their inclusion is mediated through their own efforts and objectives (Kariuki et al. 2011) as well as some "swinging in" (Okeke and Wain 2008) by Western science. Is endemic research principally enabled by Western researchers who foster it so that they can get access to samples or is it maintained by African researchers who are motivated to work on locally relevant problems? I suspect a little of both, but cannot be sure.[9] The

important thing is that African scientists want to connect today's advances to the needs of their people (Kariuki et al. 2011). Common to malaria and Buruli research programs – and absent in many others – is the strong links *among* African scientists. So-called "South–South" collaborations are often touted but less commonly actualized (Gonzalez Block 2006; Nchinda 2002). African scientists and health professionals are more likely to share research goals with one another than with investigators based elsewhere (Feierman 2011). "Multi-site" programs, that is programs that work with multiple sites rather than draw from them, could foster such links. In time, as is certainly evident among malariologists, they grow on their own.

6. Conclusion: Africa collaborations and the global genomics enterprise

> 'Holes' in science … not necessarily as voids but as spaces where possibilities could happen. (Fullwiley 2011, 29)

Genomic and other "big" sciences are necessarily collaborative, but Little Brother, Cinderella, Matthew and Dr Fox effects deduct from the reputations, credibility and potential of African researchers who choose to engage. However, as Merton himself observed, the dangers of Matthew effects extend beyond apportioning of credit and career development (Merton 1968). In the area of African infectious disease research, they create a knowledge environment in which the voices of researchers in the North are more likely to be heard than the ideas and discoveries of their endemic-area-based colleagues, even though the latter could be more directly applicable to disease control. The Matthew effect biases resources towards scientists that are better known in Northern networks and, in this specific instance of interest, away from researchers working in endemic areas. In cases where more credit may not be due because the research is essentially, or almost entirely, postal, Little Brother effects may prevent such lopsided partnerships from evening up over time. Because Matthew and Little Brother effects have such untoward consequences for global scientific knowledge, active interventions must be taken to counteract them.

In this paper, I have focused on the African scientist as a necessary component to arriving at health interventions from genomic science. Domestic investments in science in general and genomics in particular are an essential component to activating genomic expertise. Testimony to that effect can be seen from the recent progress in South Africa as one example, as well as from China and Brazil (Hardy et al. 2008; Mulder et al. 2016; Folarin, Happi, and Happi 2014). Participation of African scientists in today's post-genomic science is of interest to more than the continent alone. The earlier finding that Northern researchers who collaborated in Africa sacrificed research output to do so (Jentsch and Pilley 2003) is no longer true. Recent analysis found that Africans engaged in international collaborations published more and higher impact papers than their African colleagues that were not. The same research also found that Northern scientists who collaborated with African scientists also published more and better research than their peers who did not: the collaborations don't just "help" African scientists, they lift all boats (Blom, Lan, and Adil 2016).

In addition to furthering their careers, proper integration of Africans into genomic research will advance knowledge. Currently, genomic data is produced at a much more rapid rate than is possible for analyses. There is an insidious downside to the glut in genome-scale data and our limited capability to rigorously parse it in what is the fastest-moving field biology has ever known. Valuable knowledge could be obscured, buried in unsifted terabytes, and analyses that are insufficiently thorough are prone to error, or worse misinterpretation. These

are real worries for today's big biology (Error prone 2012; Hanage 2014). Those who can meticulously refine study design or turn genome-level data into applicable knowledge are scientists with years of training in general and computational biology. It is much easier to add the necessary genomics skills onto the skill base of a knowledgeable biologist – a feat that can be achieved in two years or less – than to train a new genomic biologist from scratch in at least eight years of higher education. Underemployed biologists who would like to interrogate genomic data represent an available and untapped resource that deserves to be appropriately exploited in Africa as elsewhere.

Notes

1. Many presume that sequencing is the important part in a genomics project. It is, in that nothing else can be accomplished without generating the sequence, but sequencing is automated and largely accomplished by robots and computers. Scientists do need to oversee the process and "close gaps" but their involvement is relatively small and diminishing as automated sequencing improves. It is sequence analysis that requires high-end human resources. Indeed, many recent "donations" of manual and less automated sequencing equipment to developing countries are in fact allied to e-dumping. In most parts of the world, scientists that do not run fully automated sequencers can more cheaply contract the sequencing portion of the work to companies that do.
2. As at February 2015, the *New England Journal of Medicine* genome paper describing the *E. coli* strain that caused the European outbreak outlined in the opening of this paper (Rasko et al. 2011) had been cited 425 times since its 2011 publication (Google scholar, 20 February 2015). This illustrates the exponential potential of knowledge generation from genomic science and the value that particular crowd-sourced initiative has provided.
3. One of the authors of the paper, Mark Pallen, confirmed in a personal communication that the four continents that did contribute were Europe, North America, Asia and Australasia.
4. For example,"Could it be that we have here a silent conspiracy of professional interests whose scientific work is justified on the basis of poverty reduction but who would be devastated if they were actually successful in these terms?" (Clarke, quoted in Molyneux, Ndung'u, and Maudlin 2010).
5. For example, Indian scientists are prominent in genomics-based searches for new drugs and vaccines for tuberculosis (Mukhopadhyay, Nair, and Ghosh 2012; Tyagi and Dhar 2003; Tyagi, Nangpal, and Satchidanandam 2011) and Brazilian scientists are making important contributions to Toxoplasmosis (Pinzan et al. 2015), the animal pathogen *Cornyebacterium pseudotuberculosis* (Dorella et al. 2013; Santana-Jorge et al. 2016) and *Trypanosoma cruzi* (Sadok Menna-Barreto et al. 2014). There has also been some "South–South" genomics collaborations among and between countries in South America and Asia (Ali et al. 2015). China is a world leader in pathogen genomics research (Liu et al. 2012).
6. There are Northern laboratories that design research studies, collect samples and then subcontract the analyses to biotechnological companies. While this can resemble postal research from a distance, it is not because the source laboratory designs the study, "owns" the question and samples, and then performs or directs the analysis. Therefore there is a truly collaborative mode in which samples could be shipped but the research itself is not "postal." African scientists engaged in "postal" research do not participate (or participate insufficiently) in these intellectual pursuits.
7. For example, the causes of leprosy and dysentery, and the endosymbionts of insects and nematodes.
8. For example, Malian malariologist Abdoulaye Djimde, who in 2009–2011 was also the only Africa-based Howard Hughes Medical Institute (HHMI) international research scholar, won the 2009 award for the best francophone pharmacist worldwide (http://www.edctp.org/Announcement.403+M514493a2c0d.0.html, http://www.hhmi.org/research/international/djimde_bio.html).

9. The causative organisms of malaria and Buruli ulcer are difficult to culture away from infected patients so that, in effect, many of the features that draw HIV researchers to high-burden African countries apply in the case of these two diseases.

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