OPINION

Arthropod-borne diseases: vector control in the genomics era

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Abstract | Diseases that are transmitted by arthropods cause severe morbidity and mortality throughout the world. The burden of many of these diseases is borne largely by developing countries. Advances in vector genomics offer new promise for the control of arthropod vectors of disease. Radical changes in vector-biology research are required if scientists are to exploit genomic data and implement changes in public health

Some of the world's most important communicable diseases have a unique feature: their transmission between humans requires an intermediate host, usually a blood-feeding arthropod vector such as a mosquito or tick. Unfortunately, the available strategies for alleviating the impact of many such vector-borne diseases are insufficient, and the public-health burden of some of the main threats such as malaria, leishmaniasis and dengue is actually increasing[1]. Historically, some of the most effective public-health measures against vector-borne diseases have been those targeted at the vector. The field of vector biology is poised to explore novel strategies for vector-based disease control, which have been made possible by recent advances in the field of vector genomics. However, there is increasing recognition that a paradigm shift in vector-biology research is essential to meet these and other challenges in public health and to convert innovations in genomics into effective disease-control strategies.

Global burden of vector-borne disease

Infectious and parasitic diseases that are transmitted by arthropods cause severe human mortality and morbidity throughout the world and include malaria, trypanosomiasis, encephalitis, leishmaniasis, filariasis, onchocerciasis and dengue. The most important vector-borne diseases in terms of their impact on human health and their corresponding causative disease agents and arthropod vectors are summarized in TABLE 1. In countries that provide statistics to the World Health Organization (WHO), these vector-borne diseases collectively account for more than 1.5 million human deaths per annum[2] (FIG. 1) Malaria, the most significant vector-borne disease in the world, is estimated to cause 1–2 million human deaths per year. After HIV/AIDS and tuberculosis, malaria is the third-highest pathogen-specific cause of death. However, the true impact of

Table 1 | **Major vector-borne diseases of humans, and associated aetiological agents and arthropod vectors**

Disease	Pathogen/parasite	Arthropod disease vector
Protozoan diseases		
Malaria	*Plasmodium falciparum, Plasmodium vivax, Plasmodium ovale, Plasmodium malariae*	*Anopheles* spp. mosquitoes
Leishmaniasis	*Leishmania* spp.	*Lutzomyia* and *Phlebotomus* spp. sandflies
Trypanosomiasis	*Trypanosoma brucei gambiense, Trypanosoma brucei rhodesiense*	*Glossina* spp. (tsetse fly)
Chagas disease	*Trypanosoma cruzi*	*Triatomine* spp.
Viral diseases		
Dengue haemorrhagic fever	DEN-1, DEN-2, DEN-3, DEN-4 flaviviruses	*Aedes aegypti* mosquito
Yellow fever	Yellow fever flavivirus	*Aedes aegypti* mosquito
Encephalitis*	Flavi-, alpha- and bunyaviruses	Various mosquito and ixodid tick species
Filarial nematodes		
Lymphatic filariasis	*Brugia malayi, Brugia timori, Wuchereria bancrofti*	*Anopheles, Culex, Aedes* and *Ochlerotatus* mosquitoes
Onchocerciasis	*Onchocerca volvulus*	*Simulium* spp. blackflies

*Including Japanese encephalitis, West Nile encephalitis, St Louis encephalitis, La Crosse encephalitis and tick-borne encephalitis.

a disease must also be evaluated in terms of the morbidity it causes. Disease burden can be assessed using DALY (disability-adjusted life years) calculations, where one DALY is defined as one lost year of healthy life, and is a measurement of the gap between the current health of a population and an ideal situation where everyone in the population lives into old age in full health. Thus, when judged in terms of an individual's loss of 'health', the burden of malaria, which infects more than 500 million people annually and can cause severe fever, anaemia, fatigue and other serious complications, is markedly greater than that of tuberculosis. The burden of vector-borne disease is generally greatest in developing countries (FIG. 2), and these countries also experience the greatest disparity between the extent of the disease burden and the amount of attention received. Many vector-borne diseases are significantly under-reported, and in many cases the true burden of disease cannot be easily determined. For example, onchocerciasis and lymphatic filariasis (TABLE 1) are rarely fatal, but cause severe disfigurement and reduction in quality of life. Many vector-borne diseases are expected to increase in incidence over the next decade. Furthermore, the emergence of new strains of known pathogens and previously unrecognized disease agents transmitted by arthropods is recognized as an increasing public-health concern.

Historically, vector control has proven successful for disease control. For example, vector-control programmes contributed to the eradication of malaria from most of the temperate-climate countries in the northern hemisphere, and the insecticide phase of the Onchocerciasis Control Programme (OCP) in west Africa has almost eliminated onchocerciasis from 11 west African countries where almost half a million people had been infected (see Onchocerciasis in the Online links box). Despite the evident rationale for vector control, so far there remains a paucity of effective vector-control programmes. The causes are numerous and include past neglect of this area of research, potential environmental effects of existing vector-control agents, reduction of their effectiveness by the emergence of resistance and inherent biological complexities of vector populations. Thus, spraying houses with DDT (dichlorodiphenyltrichloroethane) can reduce disease transmission by mosquitoes, but DDT is too indiscriminate and environmentally unsound to be used on a large scale. Insecticide-treated bednets (ITNs) that are impregnated with synthetic pyrethroids offer a simple and effective approach to reduce vector–human contact and therefore disease transmission; however, limited adoption of this strategy, improper use and the emergence of vector populations with resistance to pyrethroids limit their effectiveness. Moreover, some disease vectors are highly diverse species — their complex ecological and population structures are as-yet poorly understood, which severely limits the development and implementation of successful vector-control programmes.

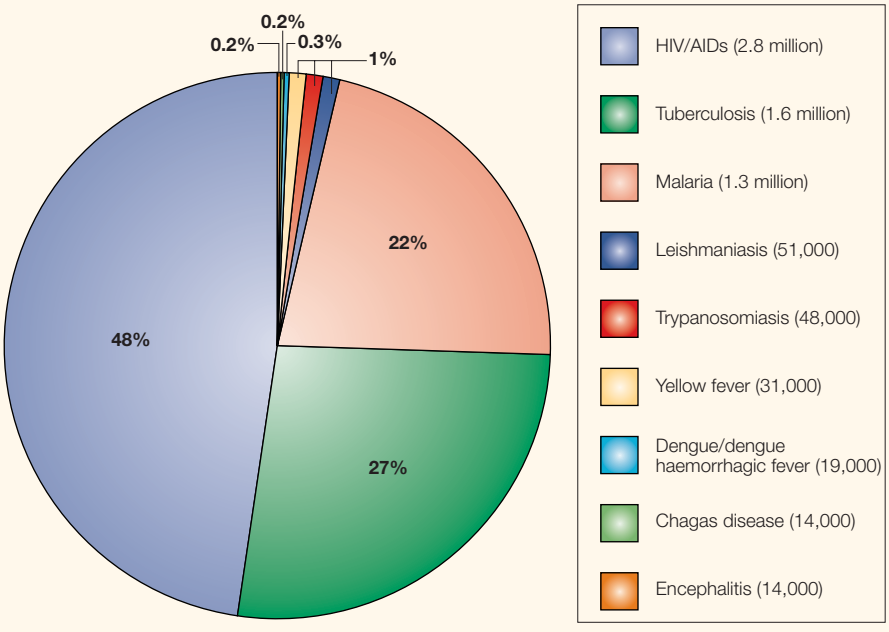

Figure 1 | **Global estimates of human mortality caused by vector-borne diseases.** The total numbers of human deaths that are attributed to specific vector-borne diseases are shown and can be compared with the numbers of human deaths caused by two non-vector-borne diseases — HIV/AIDS and tuberculosis, which are the two leading pathogen-specific causes of human death worldwide. The percentages of human deaths attributed to specific diseases as a percentage of the total number of deaths attributed to all vector-borne diseases are shown in the pie chart. Mortality estimates are based on data collected from 112 countries by the World Health Organization and published in REF. 2. Yellow fever estimate is based on data published by the Centers for Disease Control and Prevention.

Advances in vector genomics

Recent advances in vector genomics offer new hope for vector and vector-borne disease control. Foremost amongst these advances is the sequencing of the genome of the *Anopheles gambiae* mosquito, which is the main mosquito vector of malaria[3] (BOX 1). As the first vector genome to be sequenced, the *A. gambiae* genome heralded the 'genomics era' for vector-biology research. The initiation of similar efforts for *Aedes aegypti* (yellow fever mosquito), *Culex pipiens* (mosquito vector of West Nile virus), *Ixodes scapularis* (Lyme disease tick) and *Glossina morsitans* (tsetse fly vector of African trypanosomiasis)[4] (TABLE 2) highlights the increasing role of genome biology in vector research. These genome projects, together with achievements in insect transgenesis[5–7], arthropod functional genomics[8] and intensified studies of vector populations in the field[9–11], have provided unprecedented opportunities for understanding vectors and devising new methods for their control. The development of new investigative tools such as expressed sequence tags (ESTs), microarrays and RNA interference (RNAi) gene knock-out strategies have facilitated functional studies in many vector species. Furthermore, scientists have succeeded in transforming a variety of mosquito species and have recently produced mosquitoes with a reduced ability to transmit parasites[12]. The identification and validation of novel insecticidal targets for vector control, an understanding of the complex molecular and genetic basis of vector behaviour, ecology and host–parasite–vector interactions, and the genetic manipulation of vectors are now possible.

Over the past decade, there has been a marked increase in the amount of public attention given to tropical diseases, especially to malaria, and this has paralleled advances in the field of vector research. This period has been marked by pivotal scientific meetings aimed at vector-borne diseases and their

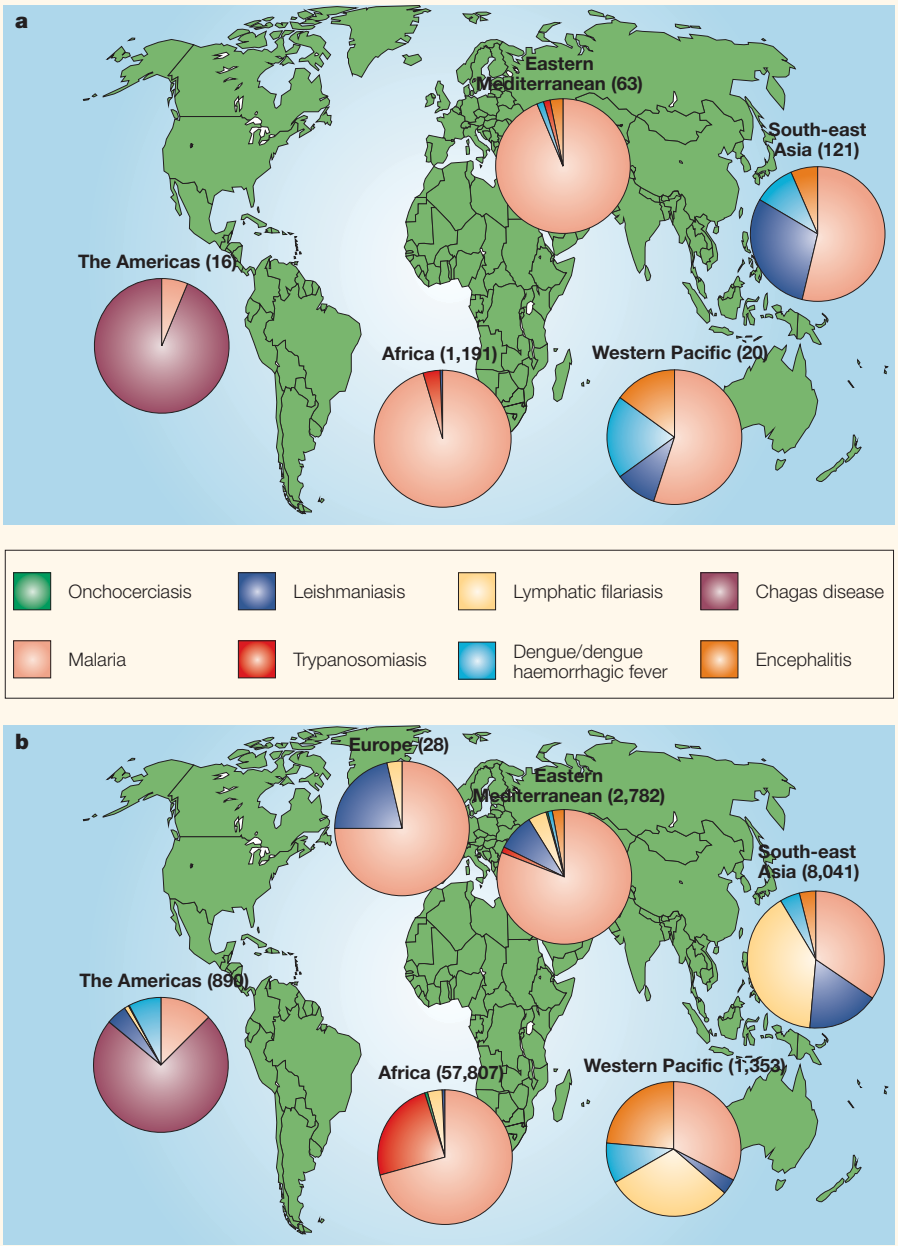

Figure 2 | **The global distribution and burden of major vector-borne diseases. a** | The distribution of mortality due to major vector-borne diseases in different WHO regions. Most vector-borne diseases occur in tropical and subtropical regions of the world and the burden of these diseases is greatest in developing countries. Mortality estimates for all major vector-borne disease (in parentheses) for each region are shown in thousands. **b** | The burden of vector-borne disease in disability-adjusted life years (DALYs) for all major vector-borne diseases in WHO regions (in thousands). Disease burden is calculated based on DALY statistics, one DALY is defined as one lost year of 'healthy' life. The burden of disease is a measurement of the gap between the current health of a population and an ideal situation where everyone in the population lives into old age in full health. Morbidity and mortality estimates are based on data published by the WHO (REF. 2)

control, including the TDR/MacArthur Foundation Vector Biology meeting in Arizona in 1990 and the International Conference on Malaria in Senegal in 1997. In fact, mosquito transformation was first proposed as a method to create mosquitoes unable to host and/or transmit *Plasmodium* parasites at the TDR/MacArthur Foundation Meeting. Stable germline transformation of the malaria vector mosquito *Anopheles stephensi* was achieved 10 years later[7], demonstrating the potential of such community-wide challenges to implement change in a field of research. Most recently, the 'Emerging Technologies for Vector Control' meeting was convened by the Bill and Melinda Gates Foundation in February 2003 to explore new vector-control strategies that have been made possible by the *A. gambiae* genome project and other achievements in mosquito genomics. The outcomes and recommendations developed from this meeting, representing ideas from more than thirty participating scientists, are summarized in BOX 2. This timely and groundbreaking event highlighted the visionary thinking required to identify approaches for vector control in the genomics era, and created a sense of community and interdependence among many researchers.

Vector biology in the genomics era

The growing field of vector biology must now respond to the new opportunities with renewed creativity and commitment. Novel research directions are required, together with a genuine interest in using new breakthroughs, to augment or increase the effectiveness of current vector-control programmes. It is clear that the field of vector biology is poised to explore new strategies for vector-based disease control. Mosquitoes refractory to pathogen infection[12] and novel insecticides[13,14] are increasingly considered as potential new vector-control strategies, and this trend is reflected in the recent outcome of the Bill and Melinda Gates Foundation 'Grand Challenges in Global Health Initiative' (see the Online links box), which identified genetic manipulation of vectors and novel insecticide development as two of the fourteen 'grand challenges' in public health. There is increased recognition that a paradigm shift in vector-biology research will be necessary to meet these and other challenges in public health and to generate real disease-control solutions. It is time for scientists to use genomics to understand the biology of the main vector–pathogen systems involved in disease transmission, to strengthen the laboratory–field interactions and to adjust their approaches towards development of control measures with demonstrated field applicability.

A call for change

The changes mentioned above represent a radical departure from traditional research practices. What does it take to implement such changes? These research strategy changes will need to be driven by both 'top-down' and 'bottom-up' approaches. Funding agencies and other organizations must encourage and reward efforts to implement these changes in their requests for proposals and by the creation of special research programmes. The 'Grand Challenges in Global Health Initiative' provides an example. Forward-thinking

Box 1 | **The *Anopheles gambiae* genome project**

The *Plasmodium* spp. parasites that cause malaria are transmitted by *Anopheles* spp. mosquitoes. 300–500 million people are infected with malaria and more than 1 million people die from the disease each year, mainly pregnant women and children. More than 90% of malaria cases occur in sub-Saharan Africa. Malaria control is complicated by lack of vaccines, drug-resistant *Plasmodium* parasites and insecticide-resistant mosquitoes. The genome of the main malaria mosquito, *Anopheles gambiae*, was sequenced in 2002 by a partnership between the National Institutes of Health, Genoscope, Celera Genomics and the Institute for Genomic Research (TIGR). This genome completes the 'malaria genome triad' in which the genomes of the *Plasmodium* parasite, the mosquito vector and the human host have been sequenced, and offers new hope for malaria control. The *A. gambiae* genome sequence is being used to identify novel insecticide targets and to understand host location and other mosquito behaviours, mosquito resistance to insecticides and the population genetics of *Anopheles* spp. in Africa.

The *A. gambiae* genome has enabled subsequent vector genome initiatives. The genome of *Aedes aegypti* (yellow fever mosquito) was recently sequenced by the Broad Institute at the Massachusetts Institute of Technology and TIGR, and is currently being assembled and annotated; the completed genome sequence is anticipated to be released in early 2005. The *Culex pipiens* (mosquito vector of West Nile virus) and *Ixodes scapularis* (tick vector of Lyme disease, babesia and anaplasma) genome projects were initiated in 2004 by the National Institutes of Health and will also be sequenced at TIGR and the Broad Institute. The international *Glossina morsitans* (tsetse fly vector of African trypanosomiasis) research community is developing plans to sequence the tsetse fly genome. A *G. morsitans* EST sequencing project has been initiated by the Sanger Centre, UK.

scientists will also need to lead by example; their success will act as a model and an incentive for other researchers. The proposed changes are explored in detail below.

Genomic information provides a range of opportunities to identify novel control strategies that are based on fundamental aspects of vector biology. However, we must focus on the specific vector–pathogen systems that are involved in disease transmission. Model systems are useful, but the information they provide does not necessarily translate directly or easily into a disease-control strategy. When, as in the case of malaria, genomes of the pathogen, vector and human host are all available, the choice of a model system should not be based on convenience alone. In the same way that *A. gambiae* became an important focus of mosquito studies in the past decade, attention must now be directed to its interaction with the main human malaria agent, *Plasmodium falciparum*.

The situation in disease-endemic countries is largely disconnected from the research that is aimed at combating these diseases, which occurs largely in the laboratories of industrialized nations. Training grants and research programmes are needed to empower disease-endemic countries and integrate them within the drug-development continuum. There is an urgent need to strengthen laboratory–field interactions so that control measures that are based on laboratory findings can be assessed rapidly in the field. Novel chemical entities that are effective against an inbred strain of mosquitoes under controlled laboratory conditions for example, may have no effect against mosquito populations in the field. Control of a disease must, by definition, be implemented in a population. Genome biology can facilitate the emergence of novel strategies for disease control, but without the field framework in which these strategies can be explored, the promise of genomics will not progress beyond the laboratory.

The traditional 'single investigator' research model is not designed to generate novel products and processes ready for field deployment, and the development of these products will require new research models. For example, interdisciplinary research programmes need to be linked to infrastructure in disease-endemic countries, and core facilities and shared tools that can be utilized by multiple researchers are needed to avoid duplication of effort. As an example, VectorBase, which is an NIH-supported bioinformatics resource centre for the genomes of all arthropod vectors is now being developed (see the Online links box). Additional, cooperative research initiatives will be needed to convert the vast amount of genomic information into knowledge, and to apply it to knowledge-based vector control. In addition, the field will advance most rapidly if the traditional scientific structure can be circumvented by the creation of networks of investigators from the full range of disciplines who meet frequently and share scientific information and ideas freely in advance of publication. Finally, the field will need not-for-profit networks such as the Medicines for Malaria Venture (see the Online links box) and the Foundation for Innovative New Diagnostics (FIND) (see the Online links box), that have the resources and expertise to direct the results of new research into product development. In the biotechnology and pharmaceutical industries, product

Table 2 | **Current status of genome projects for various arthropod vectors of human disease**

Arthropod	Disease(s)	Type	Status	Additional information
Mosquito				
Anopheles gambiae	Malaria	WGS	Complete	http://www.anobase.org/ http://www.ensembl.org/Anopheles_gambiae/
*Aedes aegypti**	Yellow fever, dengue	WGS	Complete, assembly and annotation ongoing	http://www.tigr.org/tdb/e2k1/aabe/ http://www.nd.edu/~dseverso/genome.html
*Culex pipiens**	West Nile virus	WGS	Ongoing	
Tick				
*Ixodes scapularis**	Lyme disease babesiosis, anaplasmosis	WGS	Ongoing	http://www.entm.purdue.edu/igp/default.html
Fly				
Glossina morsitans	African trypanosomiasis		Planned	

Complete, ongoing and planned arthropod vector genome projects are shown. *Genome projects approved by the NIH Microbial Sequencing Centers Program. WGS, whole-genome random shotgun sequencing, including automated assembly and annotation.

development and commercialization follow a set of well-defined steps that drive novel molecules through the drug pipeline, from the initial research and development phases to clinical trials and eventual product registration. Although not currently available, partnership networks that are based on and link to the industry model will be required for the development of vector-control products. Many pharmaceutical companies are taking the lead in initiatives to combat HIV/AIDS and tuberculosis but an equivalent is yet to be developed for vector-borne diseases. As an example, a partnership has recently been formed between Eli Lilly and Company, academic institutions in the United States, the WHO, the US Department of Health and Human Services, and the Centers for Disease Control and Prevention to produce antibiotics to treat multidrug-resistant tuberculosis. In countries where tuberculosis is prevalent, the consortium will provide scientists with appropriate training to manufacture tuberculosis drugs profitably to fill a shortage in the drug market and to encourage appropriate drug use within the population.

The implementation of new genome-based control strategies in disease-endemic countries will encounter the same challenges as existing measures. Ultimately, new strategies will be used in countries that might lack the economic, human and technological resources, and the stable social and political environment necessary to support basic control measures. The development of stronger laboratory–field networks, infrastructure and training and recruitment in disease-endemic countries, which are common themes from the 'Emerging Technologies for Vector Control' meeting (BOX 2), will be essential to overcome these barriers. Philanthropic support and programmes such as the pharmaceutical–academic consortia discussed above are needed. Ultimately, the responsibility rests with scientists to drive the development of the most appropriate genome-based solutions. Transgenic mosquitoes with impaired ability to transmit parasites may have their origins in the laboratories of industrialized nations, but the approach is attractive because the mass rearing of 'disarmed' vectors in disease-endemic countries is likely to be economically viable and relatively 'low technology'. Elucidating the molecular basis of many mosquito behaviours may be an expensive research investment, but the simple traps and repellant devices anticipated from this research could be easily adopted in malaria-endemic countries.

Box 2 | **Specific opportunities and recommendations**

The participants of the 'Emerging Technologies for Vector Control' meeting that was hosted by the Bill and Melinda Gates Foundation in February 2003 identified four main research themes with the potential to generate innovative vector-control strategies. The specific opportunities and recommendations associated with these topics are outlined below.

Genetic manipulation of vectors

The ability to exploit natural driver systems or develop artificial driver systems of vectors would enable the regional or global transformation of one or more disease vectors to reduce the human disease burden. This would require increased research into the use of the relevant techniques, contained laboratory facilities and isolated field-test sites in non-endemic and endemic countries.

Vector immunity and vector–parasite interactions

The study of vector immunity and vector–parasite interactions will enable the characterization of important parasite surface molecules and improve our understanding of vector immune responses, their effects on parasite transmission and the role of polymorphisms in both parasite and vector species biology. This knowledge could be used to develop vaccines that block parasite transmission and antimalarial agents that target vector immunity and parasite development, and to genetically manipulate vector competence and capacity.

In addition to increased research capacity in disease-endemic countries, these aims require improved interactions among the vector research community; the development of facilities for high-throughout screens and transgenesis; improved systems for data capture, management and dissemination; and the development of new research centres for the storage of important mosquito species and vector strains.

Vector behaviour and other approaches to vector control

This topic can be considered in terms of research initiatives, infrastructure initiatives and network development.

Research initiatives

These initiatives involve an increased research focus on the complex behaviour of vectors, and include: modification of vector behaviour for disease control and basic research to understand the genetic and environmental components of vector behaviour and reproductive biology; mosquito genomics, including functional genomics studies of *Anopheles gambiae* and *Aedes aegypti*, comparative genomics to provide information about lineage-specific adaptations and the development of gene chips and microarrays; population biology, ecology and genetics, including understanding the dynamics, regulation and variation (both temporal and spatial) of vector populations, and to understand vector survival strategies; and entomology and epidemiology studies, including the correlation of entomological measures of risk to infection and disease, evaluation of the impact of interventions on epidemiology and disease, and quantitiative analyses of mosquito biology, disease and control.

Infrastructure initiatives

These include the development of field-study centres for long-term research programmes, research centres of excellence in disease-endemic countries, multi-disciplinary research strategies, databases to monitor long-term, and an infrastructure network to facilitate studies and training, and the provision of opportunities for technology transfer and recruitment.

Network development

These include creating an international consortium to integrate the results of laboratory and field-based approaches to develop and compare new and existing strategies; promoting the rapid communication of scientific advances, making particular use of internet-based resources; promoting recruitment and training; and improving existing control strategies.

Field-based control programmes: existing and new insecticides

Current approaches provide opportunities to mitigate pesticide resistance in the field and improve access to insecticides, improve environmental and economic management, improve risk assessment systems and develop effective repellants and attractants.

The development of novel control strategies should focus on: the identification of novel targets for insecticides; the development of interventions based on vector behaviour and genetic control systems; the development of microbial agents for control (for example, bacteria, densoviruses and baculoviruses); and interventions based on vector–parasite–host interactions (for example, smart sprays, bait and immunization strategies).

For the successful implementation of these strategies, a long-term network support system that is focused on disease control in the endemic environment should be developed to facilitate the exchange of information between operational control, laboratory and field-based personnel. Web-based communication systems should also be developed.

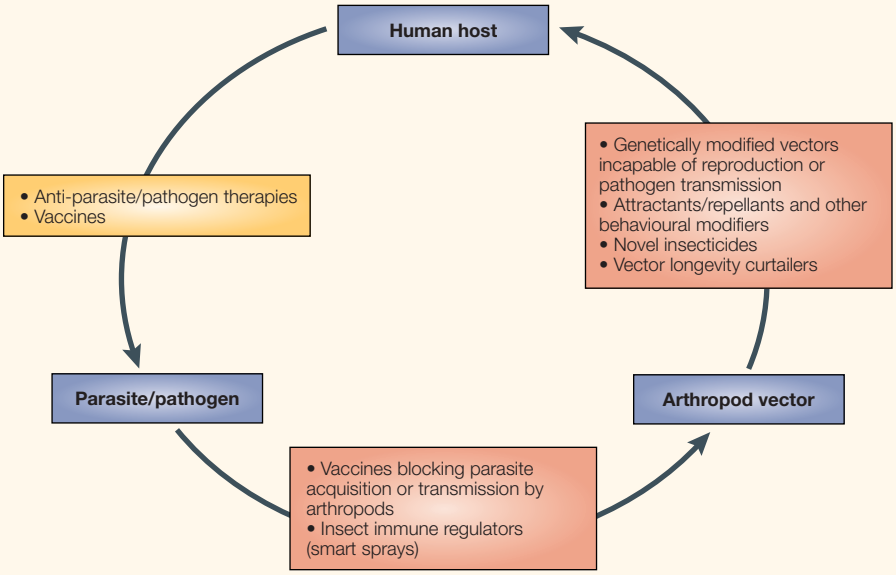

Figure 3 | **Potential new targets for development of novel vector- and disease-control strategies using vector genomics resources.** Schematic showing the typical transmission cycle of a vector-borne parasite or pathogen between a human host and an arthropod vector, and potential steps for intervention. Examples of novel control strategies developed based on arthropod genome resources (red shaded text boxes) and the parasite or human host genome resources (yellow text box) are shown.

Vector biology: future opportunities

Genome projects illuminate unique or previously unrecognized aspects of vector biology and generate many new avenues for scientific exploration. Scientists are pursuing new prospects for mosquito control in the wake of the *A. gambiae* genome project; some of the most promising opportunities are represented in FIG. 3 and can be considered examples for other branches of vector-biology research. For example, novel targets in the mosquito gut and salivary glands that are involved in digestion of the blood meal and host–parasite–vector interactions could be used to develop vaccines that block the transmission of parasites and mosquito immune regulators or 'smart sprays' that disrupt the development of the parasite in the mosquito. The *A. gambiae* genome sequence is shedding new light on mosquito behavioural processes and could give rise to novel repellant or attractant products and other behavioural intervention devices for effective vector control. Biochemical pathways that are unique to the mosquito could be exploited for the development of new insecticides. Other products might decrease mosquito longevity and therefore the vectorial capacity of the mosquito. Genetic control strategies that render a vector non-viable or incapable of pathogen transmission in the field may be developed. Of the many opportunities on the horizon, genetic control of vectors, new insecticides and behavioural intervention strategies are increasingly considered as potential vector-control tactics. We explore the approaches discussed above within the framework of these three popular research topics.

Genetic control of vectors is a controversial, but attractive and potentially self-propagating approach to disease management that we cannot afford to dismiss. The development of genetically modified vectors refractory to pathogen infection that can be released into natural populations as a mechanism to reduce or eliminate disease transmission has gained considerable interest and attention in recent years. Although this strategy has much promise, many questions remain unanswered about the feasibility and consequences of this approach. Scientists must address serious issues such as the reduced fitness of modified vectors, the ecological impact of transgenic arthropods and the evolutionary consequences of their release[15]. Tools for genetically engineering vectors have been developed and used in the laboratory to produce vector strains that are refractory to their pathogens[12,16]. Clear goals can be set for the near future: identification of efficient effector genes that cause a desired phenotype in the transformed insect (for example, genes that block parasite development); design of suitable gene drive mechanisms for driving effector genes into a wild population; and modelling of the effects of the release of these genetically modified organisms into the environment. Background vector population, ecological and parasite epidemiological data will be required from field sites that must be studied intensively over a period of time sufficient to reveal both annual variation and long-range patterns. Fully contained field trials in geographical or ecological islands will be required before any broader releases can be contemplated, but the ultimate targets for genetic control must be the vast and complex metapopulations that are typical of the most important vector species such as *A. gambiae* and *A. aegypti*.

Currently, we know little about vector behaviour, although such information could lead to novel control methods. Analysis of the *A. gambiae* genome has revealed candidate odorant, gustatory and photoreceptors that are predicted to be involved in the mosquito sensory processes of smell, taste and sight[13,17,18]. These receptors might function in the mosquito to locate hosts, mates and oviposition sites, and their identification might enable targeted intervention aimed at exploiting aspects of mosquito behaviour through the development of novel attractants, repellants and traps. However, proof-of-concept studies are essential to validate candidates for behaviour disruption in both the laboratory and the field and to demonstrate subsequent control of natural mosquito populations. Methods that have been used for drug and pesticide development are applicable for these molecular targets, including target validation and high-throughput compound library screening, structure–activity studies, toxicity evaluation and compound formulation. Such studies require access to industry-based infrastructure and well-developed laboratory–field networks.

Additional features of vector biology are suitable for the development of designer chemicals for specific control. Recent advances in vector genomic and post-genomic technologies such as microarrays, transgenesis and RNAi[19] allow us not only to identify numerous genes as potential intervention targets but also to validate experimentally their *in vivo* relevance. Pharmacogenomic approaches using high-throughput validation and screening strategies that are currently available in the pharmaceutical and agricultural pesticide industries could help develop vector-specific control agents, such as novel insecticides and agents that reduce the vector lifespan, and therefore the resulting parasite transmission rate to less than the threshold necessary to sustain the parasite population. Immune regulators that prevent parasite development while preserving the competitiveness of the vector in the field would be particularly interesting. Recent post-genomic discoveries in *A. gambiae*[14] are making it possible to contemplate such ecologically friendly 'smart sprays'.

New strategies can be criticized as lacking demonstrated feasibility and safety. Although outstanding progress has been made in vector genomics, we do face major challenges in converting novel ideas to practice. However, the human cost of vector-borne diseases makes it irresponsible not to try. Meetings such as that organized by the Bill and Melinda Gates Foundation and the more recent Disease Vector Control meeting at the International Centre of Insect Physiology and Ecology (ICIPE) in Nairobi, are helping to create a tightly networked, interdisciplinary research community committed to addressing these challenges cooperatively and creatively.

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Competing interests statement
The authors declare no competing financial interests.

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