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Role of small animal models to advance biological education in developing and underdeveloped countries

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Abstract

Model organisms, such Drosophila, zebrafish, and C. elegans, have been widely used in testing biological hypotheses and investigating the various aspects of human diseases. Compared to vertebrate models such as mouse, these small animal model organisms are relatively easy to handle, easy to culture, and easy to manipulate at molecular and genetic levels. This easy accessibility of model organisms has facilitated biological and medical labs worldwide, including those in developing countries and underdeveloped countries, to leverage these small animal model organisms to replicate human disease models and investigate the mechanisms of action or prevention strategies. Another key benefit of using small animal models is their cost-effectiveness and the associated cost of culturing them compared to other methods involving vertebrates. In developing and underdeveloped nations, cost is a significant driver for researchers and scientists frequently encounter challenges related to insufficient funding and limited resources. To further survive in the competitive landscape, researchers also need to focus on health-related topics that are relevant to the local community so that their research is more easily understood and applicable to the growth of the community. For example, Africa faces a disproportionate burden of significant global diseases caused by parasites and insects and could use more resources and scientific knowledge to tackle its health challenges. It is also suggested to link the research funding in Africa with improved compensation for scientists and creating a sustainable source of research funding. There should be stronger collaboration between scientists from resource-rich countries and African scientists at the institutional level. These suggestions could positively benefit African researchers by increasing local awareness of their activities and providing opportunities for skill development.

Introduction

Laboratory model organisms, such Drosophila, zebrafish, and C. elegans, have been essential in testing hypotheses and advancing our knowledge of human diseases [1-3]. These simple organisms share some important biological processes and genes related to diseases shown in humans, making them suitable candidates for studying complex diseases. Compared to mouse models, these model organisms are relatively easy to handle and to manipulate at a molecular and genetic level [3-6]. This accessibility of

model organisms has allowed biology labs all over the world, including those in developing countries and underdeveloped countries (e.g., Africa), to utilize these model organisms to contribute to medicine. One of the key benefits of using model organisms is their cost-effectiveness and readiness in availability when compared to other methods involving vertebrates [3-10].

For example, *Caenorhabditis elegans* is a type of microscopic worm that provides researchers with an affordable alternative for studying vertebrate and invertebrate animal models such as the fruit fly, *Drosophila melanogaster*. Furthermore, genome manipulation techniques, like RNA interference (RNAi), have become commonplace that allows scientists to replicate human diseases in these model organisms [10-13]. Another model organism is the *Drosophila melanogaster*, commonly known as the fruit fly, which is a popular model organism in biological research. Its short reproductive cycle has made it invaluable to scientists for many decades. *Drosophila melanogaster*, also known as fruit flies, possesses around 13,600 genes. After the completion of the Human Genome Project, it was determined that approximately 60-65% of human disorders can be effectively replicated in this organism [13-20]. As the tools and techniques in biotechnology have progressed, they have been applied on model organisms to recreate disease models to investigate pathways of action. The entire genome of the *D. melanogaster* has been mapped, allowing for even more precise and detailed experimentation [14].

C. elegans as a model organism

C. elegans are soil-dwelling non parasitic microorganisms. They measure about 2 mm in length and have a thickness of 65 μm. In the lab setting , they can easily survive by consuming bacteria, specifically the *Escherichia coli* OP50 strain, which is provided on a solid medium in a small dish. Additionally, C. elegans can be preserved indefinitely by freezing them in liquid nitrogen. C. elegans is ideal for advanced genetic techniques like genome editing and transgenesis through microinjection. The C. elegans genome contains around 20,000 genes and 6 chromosomes, with many similar to those found in humans [20-24]. Its transparent body offers significant benefits for tracking the expression of fluorescent labeled proteins, such as green fluorescent protein, in the live animals. Because of its transparent body and predictable life cycle, it is possible to follow the development of each cell from the fertilized egg to adulthood. These characteristics have been extensively used for studying cell lineages using laser ablation microscopy [24-30]. It possesses various tissues such as muscle cells, the nervous system, epidermis, intestine, gonad, glands, and defecation system, making it applicable for a range of research areas. Due to its short lifespan, C. elegans is commonly utilized in research focused on aging and lifespan. Its transparent structure also makes it suitable for studying gene expression using green fluorescent protein. Many genes have been discovered in C. elegans; some of which are also found in other organisms. Its genome was one of the earliest to be sequenced among multicellular organisms and the second among eukaryotes. This sequencing has facilitated the identification of diseases and the examination of the impacts of different chemicals [27]. Techniques such as RNA interference (RNAi) and the creation of transgenic organisms can be easily employed in *C. elegans*. Despite being a non-mammalian system, C. elegans is widely used as a model

organism for studying various human diseases, including metabolic syndrome, aging, cancer, neurodegenerative diseases, depression, and neural degeneration [29].

Drosophila melanogaster as a model organism

The fruitfly *Drosophila melanogaster* has been extensively utilized in research related to genetics, neuroscience, and developmental biology, providing valuable insights into various human diseases. In Africa, the ancestral continent of many wild Drosophila species, these flies can be easily gathered and domesticated for the purpose of study [30-35]. Another versatile model organism is *Caenorhabditis elegans*, also known as C. elegans. Since its potential as a model organism was first suggested in 1948, C. elegans has gained significant popularity among scientists worldwide, particularly in the fields of genetics and neuroscience [33]. It shares many advantages with Drosophila, but also offers the added benefits of simpler biology, a shorter life cycle, and more cost-effective maintenance. When it comes to vertebrate species, Zebrafish (Danio rerio) has emerged as a preferred choice since its introduction in the 1970s. This fish possesses several advantages for research in developmental biology. For example, its brain and other sense organs develop within a transparent embryo in less than 5 days. Additionally, Zebrafish can be bred in large numbers within a short period of time [34-40].

Even with the abovementioned advantages, the relatively low level of similarity between the human genome and the genomes of C. elegans and D. melanogaster creates obstacles for experiments and restricts our ability to replicate various disease phenotypes in these organisms. The zebrafish (Danio rerio) has emerged as a promising alternative model. As a vertebrate model organism, zebrafish shares greater physiological and anatomical similarities with humans. Furthermore, the close resemblance between the human and zebrafish genomes enables a wider range of developmental disorder modeling compared to C. elegans and D. melanogaster.

Organoids as an alternative to model organisms

Animal models play a vital role in research, but they have limitations in their similarity to humans, which makes it difficult to apply their findings to human biology and pathology. To overcome this challenge, advancements in cell biology, biomaterial design, and imaging technology have opened opportunities to study more complex biological questions. This has led to the development of physiologically in vitro tissue models, such as organoids, which are widely used in developmental studies [4]. When considering the pros and cons of organoids, it can be argued that studying relevant organs or diseases through modeling offers greater advantages than studying a complex system. Organoids created from human stem cells provide more accurate results compared to model organisms, and importantly, no living beings are harmed during or after the study. However, it is worth noting that manufacturing organoids is more challenging and costly than other alternatives [40-46]. The problem of limited communication among different organizations in organoid systems persists. These systems only mimic a specific part of the human body, not the entire body itself. As a result, the intricate interactions that occur within the human body cannot be effectively tested using organoid systems at this stage.

Role of model organisms in Biology Labs in developing and underdeveloped countries

Previous studies have demonstrated that Africa has witnessed significant growth in critical infrastructure and drivers of digital health interventions over the past two decades. This growth includes an increase in internet users, mobile phone subscriptions, broadband subscriptions, high-tech manufacturing, GDP per capita, and adult literacy rates [46-50]. However, the progress of these technological advancements varies across African countries. In

developing and underdeveloped nations, scientists frequently encounter challenges such as insufficient funding and limited research facilities. One way to address these challenges is by utilizing model organisms that are readily available and can be cultured in standard laboratory settings. It is worth mentioning that mouse models are commonly used in neuroscience laboratories for brain imaging and neurodegenerative disease studies. However, the use of vertebrates can be expensive and impractical for large-scale trials. Fortunately, many biological processes are conserved in invertebrates like C. elegans. Despite limited resources, Africa is making progress in advancing science. Research using invertebrate model organisms reveals that countries such as South Africa, Nigeria, Kenya, and Egypt are leading in scientific output. South Africa, in particular, stands out for its significant government funding, which has consistently supported research labs and contributed to scientific advancements in engineering. The success of investments in digital health largely relies on specific demands and supportive environments within each country [48-50]. While governments are responsible for developing infrastructure and digital health technologies, global health initiatives can play a vital role in promoting digital health interventions. This can be achieved through knowledge sharing, facilitating technology transfer for local production, and negotiating prices for the widespread implementation of impactful digital health technologies.

Challenges in developing and underdeveloped countries

The challenges faced by medical research in Africa can be broadly categorized into four segments: (i) problems with infrastructure and resources, (ii) issues within institutions and universities, (iii) financial and economic obstacles, and (iv) educational and academic limitations [51-65]. Limited funding is a significant barrier to democratizing medical research in Africa, where insufficient resources and communication tools hinder the progress in research and development. The career paths within medical schools and research institutions are not well-defined which forces scientists and researchers into administrative duties that do not fully utilize their potential. This dearth of productive research opportunities contributes to the brain drain phenomenon in Africa. The curriculum in biomedical science and medicine needs to be revamped in many African universities which currently fail to integrate recent medical advancements and is unable to motivate students to pursue career paths in medical research. In Africa, medical professionals often receive inadequate compensation, resulting in diminished motivation among those who have dedicated several years to their training. This contributes to the migration of skilled healthcare workers from Africa to other countries. Despite significant investments in medical education and training in certain African nations, the situation on the ground remains largely unchanged.

Potential solutions to boost medical research in developing and underdeveloped countries

In order to tackle these challenges, there are potential solutions suggested by the academic community. It is imperative for African governments to recognize the vital role of medical research in the economic and social advancement of their countries [58-63]. Consequently, they should prioritize and augment funding for essential research programs. This can be accomplished through a combination of government funding and support from bilateral donors, specifically designated for medical research. These funds should be distributed through a competitive process that aligns with research priorities. While there are already some existing funding structures in place, it is crucial to further fortify and broaden funding opportunities across various categories. This will enable scientists at different points in their careers to access the

necessary resources and support for their work. Funding should be made available for research proposals at all academic levels, including Masters, PhD, post-doctoral, and for seasoned scientists. It is crucial to determine if ongoing funding is justified. Colleges and universities must prioritize emphasizing the significance of medical research to students who are contemplating a career in this field. Regrettably, numerous graduates are oblivious to the potential job prospects in research. To tackle this issue, it would be advantageous to extend invitations to accomplished research scientists to discuss the various career possibilities in medical research during open days at universities. The issue is compounded by the fact that there are few African role models, which may discourage potential candidates from pursuing a career in research. Furthermore, the limited funding available to researchers creates the perception that this field is not worth pursuing.

It is important to note that Africa, despite making up 15% of the global population, bears 25% of the world's disease burden and produces only 2% of the global research output. Researchers in Africa face numerous challenges, including a lack of access to scholarly resources and inadequate support services. This can lead to a loss of talented individuals and perpetuate inadequate training environments. Additionally, the remnants of colonialism, such as foreign researchers and biased funding structures, further impede progress. How can we break this cycle? Our suggestion is to prioritize capacity building efforts led by Africans and focus on knowledge production in the global South. By drawing on the lessons learned from a research consortium, we believe this approach will have a lasting impact.

Over the last decade, there has been a noticeable increase in research and capacity building investments in Africa, which is a positive sign [60-66]. While these investments have primarily come from countries in the global North, African governments have also taken steps to boost local and regional funding for scientific research and capacity building. This support is expected to continue growing as its importance becomes more recognized. In the past, capacity-building programs have utilized different approaches, such as strengthening partnerships between countries in the global North and South or within national borders. As a result, multiple funding initiatives and consortia have emerged, each with varying levels of success and potential for sustainability. These efforts have significantly contributed to enhancing scientific research capacity on the continent, particularly in fields like epidemiology and research ethics, which yield relatively quick results. They have also laid a strong foundation for further development, although research capacity remains uneven across the continent [63]. However, it is important to note that most efforts in Africa thus far have not only been financially supported but also propelled by external sources, both at the official program level and among individual scientists.

Efficient production pipelines can lead to the sustainability of certain activities in the local socioeconomic context. Recently, major international funders have recognized the importance of shifting research and capacity building efforts to be more African. This shift is significant because Africans are often best positioned to identify and understand local issues, which should shape national and international research partnerships. While external support and collaboration are still important, addressing certain challenges may not always require enhanced research. In some cases, resolving issues like insufficient childhood vaccinations, inclusive community engagement, and affordable quality education simply requires political will. However, it is widely believed that scientific health research and capacity in Africa cannot improve or be sustainable without Africans taking on a more prominent role. This shift would immediately benefit African researchers by increasing local ownership of activities and providing continuous opportunities for skill development.

Focusing on topics that are relevant to the local community can increase the likelihood of African researchers effectively communicating their findings, making them more easily understood and applicable to the culture and policies of the region. Africa faces a disproportionate burden of significant global diseases, but lacks the necessary knowledge production to tackle its health challenges. It is crucial to link research funding in Africa with improved compensation for scientists, matching that of their counterparts in developed countries. This equality is essential for African scientists to develop and compete for international funding, allowing them more dedicated research time and resulting in better outcomes and increased global opportunities. Donors supporting research in Africa should provide resources like research materials and internet access to African universities and research institutions. This will prevent scientists from falling behind in scientific research and funding opportunities. Furthermore, organizers of major scientific conferences should allocate funds to support and offer scholarships for African scientists to attend and present their research findings.

To attract more research funding to the continent, there should be stronger collaboration between scientists from resource-rich countries and African scientists at the institutional level. Africa's research efforts need to gain attention and funding. To achieve this, all parties involved must actively participate. Collaboration among African nations has the potential to improve on a global scale. This is because interdisciplinary research is necessary to address real-world issues in medicine and biology. For instance, a scientist specializing in agricultural science, specifically pest and vector control, could broaden their expertise to include neuroscience. By doing so, they would be able to develop more environmentally friendly methods for pest and vector control. In Africa, mood disorders like depression, bipolar disorder, and seasonal affective disorder are prevalent and have a significant impact on individuals' quality of life. These disorders may be influenced by Africa's unique physical and social environment. Unfortunately, underdeveloped countries have limited research policies and capacity to understand the molecular mechanisms behind these disorders. However, there is a positive aspect - cost-effective models that simulate neurological disorders such as depression, dementia, and epilepsy have proven successful for research purposes. Furthermore, scientists see a promising opportunity to advance molecular psychiatry by combining human genetics and neurobiology using these model organisms.

Conclusion

When looking at different methods of research, model organisms prove to be a simpler and more cost-effective option compared to organoids and in-silico models. This method allows for realistic results since it involves working with living organisms. However, there is a limitation in the genomic similarity of the animals used, which is currently capped at 70%. On the other hand, organoids derived from human stem cells do not face this issue and offer a higher degree of similarity. However, they are more challenging to produce and come with a higher price tag. In contrast, in silico modeling is user-friendly and easily applicable in future research, especially when the right algorithm is chosen and integrated. It is also more convenient to use than organoids. However, the standard deviation rate may vary depending on the algorithm used, so the standardization process is crucial. Moving forward, we should prioritize empowering researchers in Africa directly as a key area for capacity building. Supporting young African scientists and their colleagues is crucial, as is promoting effective information sharing and collaboration. However, it is essential to secure ongoing funding for this capacity building to ensure its success. This requires addressing various obstacles and evaluating existing programs with a focus on long-term sustainability. Additionally, diversifying funding sources, such as local taxpayers and philanthropic organizations, is important. Although African governments are increasing their investment in science, there is still a need for greater domestic research funding to accelerate progress in health and development. By 2030, aligning with the Sustainable Development Goals, Africa must take ownership of funding its own research. Progress is already being made in building scientific capabilities on the continent, but these efforts must continue

until Africa achieves a science-driven transformation that leads to prosperity in both health and economy.

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