

Viewpoint

Advancing HIV cure research in low- and middle-income countries requires empowerment of the next generation of scientists

Roger Tatoud^{a,*}, R Brad Jones^b, Krista Dong^c, Thumbi Ndung'u^d, Steven Deeks^e, Caroline T. Tiemessen^f

^a Origena Consulting, Ferney Voltaire, France

^b Weill Cornell Medicine Graduate School of Medical Sciences, New York, USA

^c Ragon Institute of MGH, Harvard Medical School, USA

^d Africa Health Research Institute (AHRI), Durban, South Africa

^e University of California, San Francisco, USA

^f National Institute for Communicable Diseases, University of the Witwatersrand, Johannesburg, South Africa



ARTICLE INFO

Keywords:

HIV cure
Research-for-Cure academy
Research capacity
Early-career HIV researchers
Low- and middle-income countries
Africa

ABSTRACT

While low- and middle-income countries (LMICs), especially in Southern and Eastern Africa, bear the largest burden of the HIV globally, investigators working on the front lines in these regions are leading a limited number of research efforts, particularly related to HIV cure. Conducting HIV cure research in high-burden HIV LMICs provides an unparalleled opportunity to formulate innovative research strategies, design trials tailored to the local context, evaluate clinical outcomes within key and vulnerable populations, meaningful involvement of stakeholders, and to shape policies in areas where HIV prevention and cure interventions can yield the most significant impact. Further, the high prevalence of infection, with varied HIV strains affecting large diverse populations, creates a unique environment for studies that would not be feasible in any other part of the world. This underscores the critical importance of addressing obstacles to unlock the full potential of research efforts in these regions. In this viewpoint, we identify significant challenges facing early career investigators in LMICs, particularly in Africa, that hinder their full engagement in HIV cure research. Drawing examples from the International AIDS Society's Research-for-Cure Academy, we provide practical recommendations to overcome barriers that include limited access to funding, effective mentors, educational and career development opportunities, coupled with inadequate investment in infrastructure that contribute towards the limited number of investigators from high-burden HIV LMICs who are spearheading cutting-edge cure research. Addressing these challenges is crucial to empower investigators who possess unique insights and expertise, and who are well positioned to lead HIV cure-related research efforts. We acknowledge and welcome initiatives that promote capacity building and knowledge exchange between early-career investigators in LMICs and their peers and scientific leaders from high-income countries (HICs). Prioritizing investment in global collaboration and partnership will play a pivotal role in empowering the next generation of African scientists and clinicians. To expedite advancements of cure-related strategies that will be effective in high-burden HIV LMICs, we endorse the sustainable expansion of these pivotal initiatives in these regions, to enhance their effectiveness and hasten progress in the pursuit of a global HIV cure.

1. Introduction

While combination antiretroviral treatment (cART) has significantly improved the quality of life of people living with HIV, the need for a safe and affordable HIV cure is paramount, considering the challenges of

adherence to lifelong therapy, side effects and drug resistance associated with long-term cART.¹ Despite global efforts to control the HIV pandemic, Africa bears a disproportionate burden of HIV in comparison to other regions owing to economic, political, social and behavioural factors.^{2,3} Central, Eastern, Western and Southern Africa carry the

* Corresponding author. Ferney Voltaire, France.

E-mail addresses: roger.tatoud@origenaconsulting.fr (R. Tatoud), rbjones@med.cornell.edu (R.B. Jones), kdong@mgh.harvard.edu (K. Dong), thumbi.ndungu@ahri.org (T. Ndung'u), Steven.Deeks@ucsf.edu (S. Deeks), carolinet@nicd.ac.za (C.T. Tiemessen).

<https://doi.org/10.1016/j.jve.2024.100364>

Received 4 January 2024; Accepted 19 February 2024

Available online 6 March 2024

2055-6640/© 2024 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC license (<http://creativecommons.org/licenses/by-nc/4.0/>).

highest burden of HIV, with a reported 25.6 million people living with HIV, of whom only 79% had access to cART in 2021.⁴ Paradoxically, it is in this part of the world that the least HIV cure research is being carried out owing to several constraints.⁵

HIV cure research, especially in LMICs, presents a challenging and complex endeavour that necessitates collaboration between leading scientists and aspiring early- to mid-career researchers⁶ from this region. As early-career researchers immerse themselves in the world of HIV cure research, they confront obstacles that can influence their career development, advancement, and contribution to science. This commentary examines the hurdles to sustained HIV cure research advancement in LMICs, drawing examples from the Research-for-Cure Academy, a fellowship initiative of the IAS – the International AIDS Society.

2. Challenges in conducting HIV cure research in low- and middle-income countries

Although Africa's contribution to global HIV research output has increased over the past 35 years, it remains relatively low compared to the continent's burden of HIV,⁷ further underscoring the magnitude of research disparity between high income countries (HICs) and low and middle income countries (LMICs). Major challenges faced by early-career HIV researchers in LMICs include limited access to finances, infrastructure, and mentorship. Most of these countries face heavier demands on available financial resources, which results in deprioritization of healthcare research.⁸ Indeed, governments often prioritize other pressing public health issues, including infectious diseases control and basic health services, leaving limited resources for research and development. Thus, limited funding remains a significant challenge for early- and mid-career HIV cure researchers who have to compete with all other research areas. HIV cure research is expensive and securing substantial and sustainable financial support for research projects, laboratory equipment, reagents, consumables, analysis tools and personnel is an arduous task. Consequently, researchers struggle to initiate and sustain their projects, which hinders their progress and ability to contribute to solving health challenges in a timely manner. Additionally, these early- and mid-career researchers have limited access to the infrastructure necessary to conduct complex studies, such as well-equipped laboratories and cutting-edge technologies that are crucial for conducting cure research. Resources remain concentrated in well-established research institutions in HICs.

Lengthy procurement processes⁹ and supply chain bottlenecks result in unnecessary delays in acquisition of vital reagents and consumables necessary to conduct comparable research to that done in HICs. Consequently, researchers launch their careers with significant disadvantages of conducting timeous cure research. Furthermore, there is a need to adjust research questions based on assays where reagents and equipment are readily-available in those settings.

Moreover, building collaborations with experienced researchers can be challenging as they rely on existing networks and professional relationships outside LMICs. HIV cure research also requires interdisciplinary knowledge and skills spanning virology, immunology, molecular biology, bioinformatics, and clinical research. Acquiring the diverse skill set needed requires specialised training and collaboration with experts from different fields that are not always easily accessible to early- and mid-career researchers. The need to develop a multidisciplinary approach is time consuming and resource intensive, placing additional strain on early-career researchers and potential mentors. Limited availability of mentorship and career guidance within and beyond the laboratories and institutions in which early- and mid-career researchers are based is another challenge that affects their professional development.

Well-funded and dynamic postgraduate programmes in high-income countries attract and train scientists from LMICs, affording them the opportunity to engage in innovative research using cutting-edge technology. Unfortunately, application of the newfound knowledge and

skills in their home countries is likely to be hampered due to lack of similar technologies and low demand for the level of research they trained in. The consequences of this gap include retrogression of the scientist's skill set or brain drain back to HICs where they can be meaningfully engaged.

3. Africa is full of unique opportunities for advancing HIV cure research

As HIV cure research advances worldwide, it is important to keep in mind that the high burden of HIV in Central, Eastern, Western and Southern Africa¹⁰ provides a substantial pool of individuals for research studies related to HIV cure, allowing for larger sample sizes and greater diversity in the characteristics of study participants. Additionally, the known high genetic diversity of HIV strains, including various subtypes and recombinants in Africa¹¹ and some South American countries,^{12,13} provides research opportunities that cannot be achieved anywhere else in the world.

Understanding the interaction between host factors and HIV dynamics in this diverse population can contribute to developing regionally-adapted HIV cure approaches. For example, the diverse environmental factors faced by individuals of different ancestry in various cohorts may influence clinical outcomes.¹⁴

Various longitudinal cohorts have been established in LMICs with the aim of following up people living with HIV to assess different clinical outcomes. Some existing cohorts are the African Cohort Study (AFRICOS),¹⁵ Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe (DREAMS),¹⁶ Females Rising Through Education Support and Health (FRESH),¹⁷ Ucwangingo Lwabantwana Cohort,¹⁸ the Children with HIV Early Antiretroviral Therapy (CHER),¹⁹ and the Centre for the AIDS Programme of Research in South Africa Acute Infection Cohort.²⁰ In addition to providing well-established cohorts to assess clinical outcomes among key populations, these communities offer researchers the ability to formulate evidence-based recommendations to guide policy making, clinical trial design, product development and future stakeholder engagement. The resultant unique and valuable insights that would have a direct impact on research cure strategies can be obtained only in these regions.

4. Building the capacity of young HIV cure researchers: Highlights from the 2023 Research for Cure Academy

In 2017, to address some of the challenges described above and support the scientific development of a new generation of HIV cure researchers in LMICs, the IAS developed a fellowship programme called the "Research-for-Cure Academy". It aims to strengthen research skills by providing training and resources on HIV cure and reinforce tools and methodologies in line with recommendations from the "Research priorities for an HIV cure: International AIDS Society Global Scientific Strategy, 2021".²¹ The 'Research-for-Cure' Academy serves as a platform for promoting collaboration and knowledge and sharing among renowned scientists, medical professionals, and their fellows. It provides a conducive environment for the exchange of ideas, expertise, and resources, as well as for fostering new partnerships with the goal of accelerating HIV cure research. To date, the academy has had five cohorts, cumulatively empowering 115 participants drawn from 30 nations.

The 2023 Research-for-Cure Academy took place from June 16 to June 18, 2023 at the Wits Rural Facility, Bushbuck Ridge, South Africa. The three-day, in-person workshop provided a unique opportunity for early- and mid-career researchers from LMICs with an interest in HIV cure research to come together, learn from leading HIV researchers and clinicians, and present their research as concept notes for advancing the cure research agenda.

The latest research that highlighted important discoveries, novel therapeutic strategies including gene-editing techniques and

immunotherapies, and other innovative approaches under investigation to eradicate or permanently control the viral reservoir were discussed. Notably, participants identified the existing knowledge gaps in the field and highlighted challenges unique to conducting HIV cure-related research in LMICs, underscoring the need for novel research endeavours where they are most needed. Lectures stimulated discussions on the current understanding of the viral reservoir, insights into a paediatric HIV cure, the immune mechanism of viral control, and considerations for implementation of cure trials that prioritize community engagement and equitable enrolment of participants.

Against this background, the IAS has established a faculty to equip the fellows with skills to advance their research ideas. The main goal was for the fellows to leave the Academy having developed a grant-worthy concept note, following a process that included refinement of concise and pertinent research problems, formulation of a strong rationale for proposals, and honing their ability to effectively communicate scientific concepts to different audiences. The structure of the academy included plenary discussions aimed at improving the cohort's scientific writing skills supported by a one-on-one consultation with the faculty. The individualized focus in the 2023 Cure Academy enabled each fellow to improve their scientific reasoning and communication skills (Fig. 1).

5. Recommendations for advancing HIV cure research in LMICs

To advance HIV cure research in LMICs, there is a need to enhance capacity building by providing training opportunities, workshops and educational programs for local researchers interested in cure research. Moreover, transfer of technologies would enable local researchers to conduct cutting-edge cure research. Stabilising research productivity in LMICs as well as strengthening North South and bolstering South South partnerships (while ensuring research equity for those in LMICs) might significantly progress HIV cure research within the most in need contexts. Of note, existing models and networks play a significant role in enhancing capacity and establishing clinical research infrastructure in Africa. However, there is a need for their adaptation to current demands, necessitating further development. These collaborative networks are actively functioning, and it is crucial to reinforce them with sustained funding for long-term viability. Within this framework, acknowledging the pivotal role of LMICs in the global battle against HIV/AIDS is essential, emphasising the importance of working closely and collaboratively.

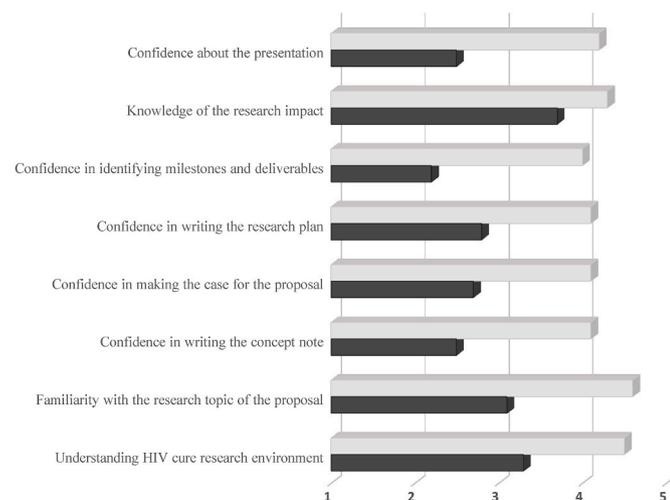


Fig. 1. Self-assessment pre and post training (from 1: low to 5: high). Notes: Black bars – pre training; Grey bars – post training.

6. Conclusion

Initiatives such as the Research-for-Cure Academy play an essential role in building research capacity and empowering the next generation of scientists and clinicians. The curated workshops, mentorship programmes and knowledge-sharing sessions provide forums where early-career researchers are able to benchmark, network and hone the skills needed to address critical research questions and significantly contribute to advancing HIV cure research in LMICs. To keep the capacity utilization momentum going, fellows suggest that the Research-for-Cure Academy could serve as a link to other programmes, such as the Sub-Saharan African Network for TB/HIV Research Excellence (SANTHE) and African Research Excellence Funds (AREF). Additionally, the fellows encourage the Academy to incorporate sessions devoted to updates of the latest methodology and technical skills relevant to upcoming scientists in HIV. Initiatives similar to the IAS Research-for-Cure Academy have the potential to result in establishment of collaborations between LMICs that will provide exciting capacity utilization opportunities, reduction in the brain drain to HICs, and concerted efforts towards HIV cure in regions that need it the most.

Funding

The Research-for-Cure Academy is organized by the International AIDS Society, through funding from MSD, ANRS and the IAS Corporate Partnership Programme, in partnership with the South African Department of Science and Innovation and the Faculty of Health Sciences at the University of Witwatersrand, which also provided funding for the event.

The 2023 Research-for-Cure Academy Fellows

Alejandro Czernikier (a.czernikier@gmail.com), Instituto de Investigaciones Biomédicas en Retrovirus y Sida, Universidad de Buenos Aires y Consejo Nacional de Investigaciones Científicas y Técnicas, Buenos Aires, Argentina; Aude Christelle Ka'e (kae.audechristelle@gmail.com), Chantal Biya International Reference Centre for Research on HIV/AIDS Prevention and Management (CIRCB), Yaounde, Cameroon; Christopher Zaab-Yen Abana (cabana@noguchi.ug.edu.gh), Virology Department, Noguchi Memorial Institute for Medical Research, University of Ghana, Legon; Gabriela ZL Cromhout (gabrielacromhout@gmail.com) Department of Paediatrics and Child Health, University of KwaZulu-Natal, Durban, South Africa; Hillary Tene (hillary.tene@yahoo.fr); Centre de Recherche sur les Maladies Émergentes et Réémergentes CREMER/IMP/MINRESI; Jeanne Omony (jeanneomony@aol.com), BioNTech SE, and University of the Western Cape, Cape Town, South Africa; Leonore Greybe (greybe@sun.ac.za) Department of Paediatrics and Child Health, Stellenbosch University, Cape Town, South Africa; Mark Appeaning (mark.appeaning@ktu.edu.gh), Medical Laboratory Science Department, Koforidua Technical University, Koforidua, Ghana; Masauso Moses Phir (missiphiri@gmail.com), School of Medicine, University of Zambia; Mqondisi Tshabalala (MqondisiT@nicd.ac.za), National Institutes for Communicable Diseases (NICD) and Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; Rachel Kyeyune Bakyayita (rbkyeyune@gmail.com), Joint Clinical Research Centre, Uganda; Romeo Djourda (djourdaromeo@gmail.com), Centre de Recherche sur les Maladies Émergentes et Réémergentes CREMER/IMP/MINRESI; Sherazaan D Ismail (Sherazaan.Ismail@uct.ac.za), Institute of Infectious Disease and Molecular Medicine, University of Cape Town, Cape Town, South Africa; Teresia Muhomah (terrymuhomah@uonbi.ac.ke), KAVI- Institute of Clinical Research, University of Nairobi, Nairobi, Kenya; Winnie Rotich (rotichwinnie890@gmail.com), Kapkatet Hospital, Kericho, Kenya.

CRedit authorship contribution statement

Roger Tatoud: The 2023 Research-for-Cure Academy Fellows,

Conceptualization, Validation, Writing – original draft, Writing – review & editing. **R Brad Jones:** Conceptualization, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Krista Dong:** Conceptualization, Visualization, Writing – original draft, Writing – review & editing. **Thumbi Ndung'u:** Supervision, Validation, Writing – original draft, Writing – review & editing. **Steven Deeks:** Validation, Writing – original draft, Writing – review & editing. **Caroline T. Tiemessen:** Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

Acknowledgement

Publication costs were supported by the National Institutes of Allergy and Infectious Diseases of the National Institutes of Health under award UM1AI164565 (R B J), with co-funding from the National Institute of Mental Health, the National Institute of Diabetes and Digestive and Kidney Diseases, the National Institute of Neurological Disorders and Stroke, the National Institute on Drug Abuse, and the National Heart, Lung, and Blood Institute. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. All the fellows would like to thank the International AIDS Society, as well as the faculty of the 2023 Research-for-Cure Academy, for all the knowledge shared. All our gratitude to Sharon Lewin and Rosanne Lamplough who were critical in putting this all together. We would also like to thank Riccardo Maddalozzo and Asli Heitzer for all the support provided before and during the training.

References

1. Castro-Gonzalez S, Colomer-Lluch M, Serra-Moreno R. Barriers for HIV cure: the latent reservoir. *AIDS Res Hum Retrovir*. 2018;34(9):739–759.
2. Mbirimengerenji ND. Is HIV/AIDS epidemic outcome of poverty in sub-Saharan Africa? *Croat Med J*. 2007;48(5):605–617.
3. Nyindo M. Complementary factors contributing to the rapid spread of HIV-1 in sub-Saharan Africa: a review. *East Afr Med J*. 2005;82(1):40–46.
4. The Joint United Nations Programme on HIV/AIDS (UNAIDS). Global HIV statistics. *Fact Sheet 2023; 2023* [Internet] https://www.unaids.org/en/resources/documents/2023/UNAIDS_FactSheet.
5. Ismail SD, Pankrac J, Ndashimye E, et al. Addressing an HIV cure in LMIC. *Retrovirology*. 2021;18(1):1–19. <https://doi.org/10.1186/s12977-021-00565-1> [Internet].
6. Dybul M, Attoye T, Baptiste S, et al. The case for an HIV cure and how to get there. *Lancet HIV*. 2021;8(1):e51–e58.
7. Ijaiya MA, Olowu A, Oguntade HA, Anjorin S, Uthman OA. HIV research output in African Countries between 1986–2020. *PLoS Glob Public Health*. 2023;3(6), e0000544. <https://doi.org/10.1371/journal.pgph.0000544> [Internet].
8. Franzen SRP, Chandler C, Lang T. Health research capacity development in low and middle income countries: reality or rhetoric? A systematic meta-narrative review of the qualitative literature. *BMJ Open*. 2017;7(1).
9. El Hajj T, Gregorius S, Pulford J, Bates I. Strengthening capacity for natural sciences research: a qualitative assessment to identify good practices, capacity gaps and investment priorities in African research institutions. *PLoS One*. 2020;15(1):1–21. <https://doi.org/10.1371/journal.pone.0228261> [Internet].
10. UNAIDS. Global HIV statistics [Internet] *Fact Sheet 2021; 2022* (June):1–3. Available from: https://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_n.pdf.
11. Giovanetti M, Ciccozzi M, Parolin C, Borsetti A. Molecular epidemiology of HIV-1 in African countries: a comprehensive overview. *Pathogens*. 2020;9(12):1–10.
12. Russell KL, Carcamo C, Watts DM, et al. Emerging genetic diversity of HIV-1 in South America. *AIDS*. 2000;14(12):1785–1791.
13. Alves BM, Siqueira JD, Prellwitz IM, et al. Estimating HIV-1 genetic diversity in Brazil through next-generation sequencing. *Front Microbiol*. 2019;10(APR):1–11.
14. Meditz AL, MaWhinney S, Allshouse A, et al. Sex, race, and geographic region influence clinical outcomes following primary HIV-1 infection. *J Infect Dis*. 2011;203(4):442–451.
15. Dear N, Esber A, Iroezindu M, et al. Routine HIV clinic visit adherence in the African Cohort Study. *AIDS Res Ther*. 2022;19(1):1–12.
16. Risher KA, Cori A, Reniers G, et al. Age patterns of HIV incidence in eastern and southern Africa: a modelling analysis of observational population-based cohort studies. *Lancet HIV*. 2021;8(7):e429–e439. [https://doi.org/10.1016/S2352-3018\(21\)00069-2](https://doi.org/10.1016/S2352-3018(21)00069-2) [Internet].
17. Ndung'u T, Dong KL, Kwon DS, Walker BD. A FRESH approach: combining basic science and social good. *Sci Immunol*. 2018;3(27):1–4.
18. Millar JR, Bengu N, Fillis R, et al. High-frequency failure of combination antiretroviral therapy in paediatric HIV infection is associated with unmet maternal needs causing maternal non-adherence. *EClinicalMedicine*. 2020;8:100344. <https://doi.org/10.1016/j.eclinm.2020.100344>.
19. Violari A, Cotton MF, Gibb DM, et al. Early antiretroviral therapy and mortality among HIV-infected infants. *N Engl J Med*. 2008;359(21):2233–2244.
20. Van Loggerenberg F, Mlisana K, Williamson C, et al. Establishing a cohort at high risk of HIV infection in South Africa: challenges and experiences of the CAPRISA 002 acute infection study. *PLoS One*. 2008 Apr 16;3(4), e1954. <https://doi.org/10.1371/journal.pone.0001954>.
21. Deeks SG, Archin N, Cannon P, et al. Research priorities for an HIV cure: International AIDS Society Global Scientific Strategy 2021. *Nat Med*. 2021;27(12):2085–2098.