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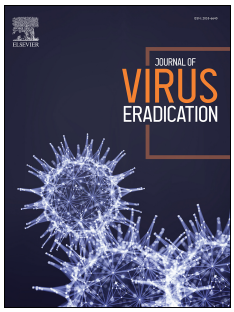

Achieving the Global Agenda toward HIV Cure Calls for Establishing a Research-for-Cure Academy in West and Central Africa

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Achieving the Global Agenda toward HIV Cure Calls for Establishing a Research-for-Cure Academy in West and Central Africa

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≠Equal contribution.

Abstract

Despite global efforts to eliminate HIV as a public health threat, sub-Saharan Africa (SSA) still harbours about the highest burden of the pandemic, home to around 70% of people living with HIV with limited contribution in the field of HIV cure research, especially in West and Central Africa (WCA). This gap is mainly due to challenges that researchers of this region are facing in initiating and advancing HIV cure research locally, with lesser commitment from the French-speaking countries. Furthermore, capacity-building of early career scientists on HIV cure research remains constrained due to limited awareness and language barriers to existing opportunities. Even though HIV non-B subtypes represent 89% of circulating subtypes worldwide, cure research has been extensively focused on subtype B (prevalent in America and Europe). Interestingly, WCA (known as HIV pandemic epicentre with a broad genetic diversity) offers a unique landscape for cure research with a likelihood of generalisability across various HIV subtypes. This viewpoint discusses the importance of establishing an HIV Cure Academy for WCA to support scientists, policymakers and community stakeholders from French-speaking countries in contributing to the global efforts towards HIV cure.

Building on discussions, the establishment of an "HIV Cure Academy" emerges as a hallmark to: (i) raise awareness, (ii) build capacity, (iii) address scientific gaps, (iv) develop networks, and (v) foster advocacy and policy-briefing on integrating HIV cure research into national HIV agenda. The Academy is envisioned as a hub, facilitating relationships between community-based organizations, people living with HIV (PLHIV), research institutions and decision makers. This hub will also champion the "Advocacy for Cure" agenda in the sub-region, enhance multidisciplinary approach to identify local HIV cure research priorities that address the global problem. Of prime importance, research priorities in WCA include: (i) the measurement and characterization of viral reservoirs; (ii) investigation in immune responses including bNAbs, T-cell function, cytokines profiles and hosts genetic factors; (iii) identification of elite and post-treatment controllers; (iv) development of accessible technologies for point-of-care HIV DNA testing, biomarker detection, and latency-modifying agents to support functional cure strategies; (v) innovation in cost-effective and scalable therapeutic interventions suitable for low-resource settings; (vi) the strengthen of community involvement through citizen science, address ethical considerations, and engage PLHIV in the co-design of cure research initiatives; (vii) the establishment of regional training platforms, such as a Research-for-Cure Academy, to enhance scientific capacity and collaboration in West and Central Africa. Following the model of the International AIDS Society (IAS) Research-for-cure academy, the WCA HIV Cure Academy represents a key hub in achieving the goals of HIV cure, through local actions that contribute to addressing a global problem.

Introduction

Antiretroviral therapy (ART) has significantly improved the lifespan of people living with HIV (PLHIV) and reduced by 51% AIDS-related deaths (from 1.3 million in 2010 to 630,000 in 2022) globally, including those living in sub-Saharan Africa (SSA) [1]. However, SSA is still experiencing challenges due to limited therapeutic options, suboptimal treatment monitoring strategies, very high burden of paediatric cases (about 90% worldwide), and frequent events of poor adherence for a lifelong treatment driven by many factors uncommon in other parts of the world (mostly stock rupture and lack of funding to purchase antivirals) [2,3]. These structural and systemic weaknesses significantly hinder progress towards epidemic control and create a persistent health crisis. Moreover, despite increased ART coverage, many countries in SSA face difficulties in achieving the UNAIDS 95-95-95 targets, with gaps particularly notable in early diagnosis and viral suppression among children and adolescents [4]. Importantly, the disproportionate burden of the HIV in SSA compared to other regions is further driven by poverty-related, socio-political and behavioural factors [5–8]. Furthermore, SSA alone is home for more than 25 million PLHIV (representing nearly 70% of the global number of PLHIV) [1], yet research efforts, especially those

aimed at a functional or sterilizing cure, remain alarmingly scarce in the region. Very few HIV cure-related studies are conducted, and consequently cases of cure or post-intervention control are yet to be reported in this part of the globe [9]. While HIV epidemic control is approaching in the western world, low- and middle-income countries (LMICs) especially those in SSA are still reporting considerable numbers of new infections within exposed infants, adolescents, young girls and key populations, as well as cases of HIV-associated advanced diseases and mortality in vulnerable populations [1,2]. The growing disparities between the Global North and SSA regarding HIV outcomes highlight an urgent need for regionally adapted strategies, including targeted research efforts. This ongoing high incidence and mortality are compounded by challenges such as HIV drug resistance, limited access to second and third-line therapies, and fragile health systems, which threaten the sustainability of ART success in the region [4]. The persistence of this life-threatening condition in SSA therefore narrows the focus of African scientists on lifesaving interventions (oriented toward clinical, laboratory and epidemiological surveillance), which in turn provides limited scope for HIV cure research, coupled with hurdles around limited infrastructures (especially laboratory and clinical trial facilities), insufficient capacity-building of early career researchers, scarcity of local mentorship and funding opportunities [9]. These challenges are even more pronounced in Francophone SSA, where researchers face additional barriers such as language exclusion, geopolitical isolation, and limited visibility in global research networks. Additionally, the lack of robust regional networks and platforms for collaboration further restricts the development of a vibrant HIV cure research environment in SSA [10]. In addition, early career researchers especially from West and Central Africa (WCA) are minimally exposed to HIV cure research, most likely due to language barriers for accessing capacity-building and networking opportunities of the International AIDS Society (IAS) for which eligibility is also based on proficiency in English language (figure 1).

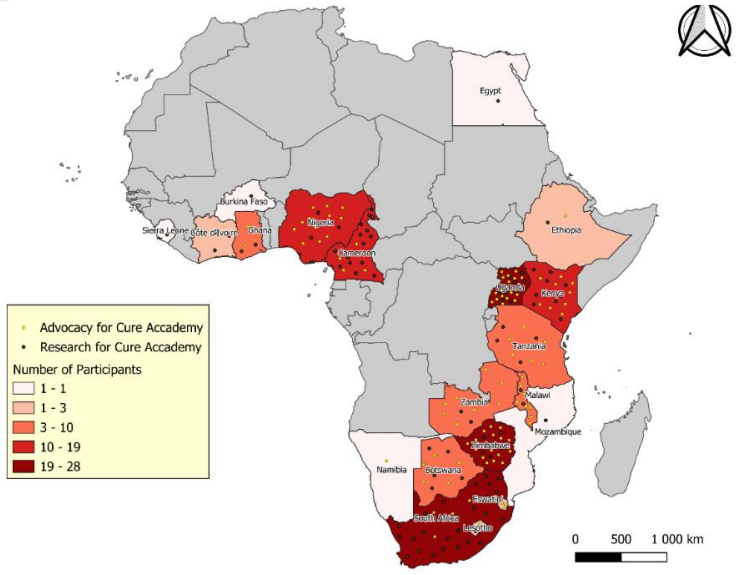

Figure 1: Distribution of Past IAS Research-for-Cure Academy Fellows in Africa.

French-speaking SSA countries are mainly located in WCA and these countries are known to be the epicenter of HIV (origin of the first case in humans) [11].

This viewpoint aims to advocate for an academy that will harness HIV cure research agenda in WCA through the adoption of priority areas of scope, the creation of training for WCA early-career investigators, and the exposure to mentorship opportunities on HIV cure research that contribute substantially in guiding the global efforts.

West and Central Africa: a key setting for global HIV cure research

HIV clinical trials including those on cure research remain largely conducted in resource-rich settings, namely USA and Europe, with limited participation of African countries especially the WCA sub-region despite it well known host and HIV diversity [12]. This underrepresentation risks limiting the global applicability and equity of research findings. Based on context gap, HIV cure research carried out in western countries remains tailored predominantly to subtype B (representing only 11% of the estimated 40 million PLHIV), infection from a generally older population, engaging mostly males and key population communities. In contrast, non-B subtypes drive the global epidemics in other parts of the world, characterised by infections circulating in a younger population, mostly heterosexual, significant proportion in female (almost two third) and a very broad genetic diversity. Such disparities underscore the need for tailored research strategies addressing regional virological, immunological and socio-behavioral realities. Even though subtype C represents about 70% of all infections in SSA, CRF02_AG is the most prevalent clade (47%) in WCA followed by CRF/URF (15%), A (~5%), and other pure subtypes [13,14]. Interestingly, little changes in the reservoir size in subtype C (common in Southern African countries) versus B (common in western countries) suggest potential differences in addressing cure strategies based on existing HIV molecular epidemiology [15]. These observations call for in-depth investigations into clade-specific reservoir dynamics. No data is available so far, regarding whether the establishment of reservoir is identical for different subtypes and recombinants, both in terms of quantity and quality.

Preliminary contributions to HIV cure research within Central Africa, notably from Cameroon, highlight the region's potential. These include findings on: (a) high prevalence of archived drug resistance in HIV-1 DNA among adolescents living with perinatal HIV, driven by drug-resistance mutations to non-nucleoside reverse transcriptase inhibitors (NNRTIs) despite virological success[16]; (b) basic characterization of viral reservoirs following perinatal HIV acquisition in SSA[17,18]; (c) evidence of sero-negativization in infants treated early during HIV infection[19]; (d) cohort-analysis of the EDCTP (European and Developing Countries Clinical Trials Partnership)-READY, EDCTP-AVIR and the ongoing CIPHER-ADOLA studies that focus on the genotyping, quantitative evaluation of HIV-1 reservoirs, and

acceptability of long-acting antiretrovirals and the perception of HIV cure research by young populations [17,18,20]. These studies provide valuable building blocks for understanding the virological and immunological underpinnings of potential cure strategies in the region. Investigations on these well-established cohorts will directly impact cure strategies in WCA toward a potential generalisability for upcoming clinical trials and other study designs on (functional) cure. Importantly, Cameroon's established exposure to HIV cure research through IAS initiatives (https://www.iasociety.org/taxonomy/term/343), the VIROFORUM-Africa platform [21], and advocacy meetings further demonstrates a regional momentum. These initiatives can be leveraged to foster a broader, inclusive, and sustainable cure research ecosystem in WCA.

The establishment of an HIV cure academy for WCA as pivotal to support the global cure research agenda: insights from the Advocacy Workshop on "Harnessing our efforts towards HIV Cure Research"

Under the umbrella of the IAS, a research-for-cure-academy has been established [22], aiming to support the scientific pathway of early and mid-career researchers in LMICs through capacity-building in designing HIV cure research. Similar initiatives have been implemented, namely the Sub-Saharan African Network for TB/HIV Research Excellence (SANTHE) and the African Research Excellence Funds (AREF), but their scope and coverage still keep WCA largely uncovered, due to aforementioned barriers. It is therefore pivotal to adapt such initiatives in order to develop and strengthen scientific leadership in WCA in general and specifically within French-speaking countries (owing to the history of colonialization and its sociocultural and political impacts on the respective countries). Language barriers, historical underinvestment in health research infrastructure, and a lack of equitable North-South research partnerships have further compounded these gaps. In this frame, an international scientific meeting called: "***Advocacy workshop harnessing our efforts towards HIV cure research***" was held in Yaoundé-Cameroon on December 10, 2022. Following IAS guidelines, the concepts from the HIV cure Symposium in Belgium and contributions from the Italian cooperation, a local onboarding workshop on Research-for-Cure was organized in Cameroon by Cameroonian IAS fellows and advocates (chaired by J. Fokam and J. Joanes), with experience shared from South-Africa (C. Tiemessen) and participation from HIV scientists and community organizations. This onboarding event served as platform: (a) to raise awareness and interest on HIV cure research in WCA; (b) to delineate the concepts of HIV cure, its scientific understanding and its implications at community-level; (c) to explore barriers and enablers in HIV cure-focused research in WCA; (d) to identify critical needs for a dedicated initiative forward the implementation of cure research; and (e) to set-up priority-areas for contributing to the global agenda of cure research in WCA.

Based on the presentations and discussions during the sessions of the onboarding workshop, the establishment of an HIV cure academy" (figure 2) in WCA emerged as a strategic and imperative hallmark in advancing and scaling-up such efforts in this setting, taking into consideration the aforementioned challenges. The workshop further shed light on the limited understanding of HIV cure research approaches and strategies in WCA. The proposed WCA HIV Cure Academy would therefore serve as an educational hub, addressing knowledge gaps and fostering a comprehensive and complementary understanding of the complexities involved in HIV cure-focused research. This initiative would help bridge the knowledge gap, promote local leadership, and accelerate regional ownership of HIV cure research. The importance of building long-term, formal and informal relationships between community organizations, PLHIV, HIV program managers, policymakers and research institutions was emphasized as a key strategy. This subregional HIV Cure Academy can play a pivotal role in facilitating such collaborations, by acting as a central platform for stakeholders to connect, share insights, and collectively contribute to achieving an HIV cure research agenda within the WCA subregion. Proceedings during this onboarding event also made it evident that HIV cure research is relatively unknown and underexplored across the WCA sub-region. Henceforth, establishing an Academy can pave the way for an advocacy body established locally with locally-known scientists/experts involved, championing the "Advocacy for Cure" agenda in order to inspire and generate discussions at various levels including the academia, the health sector, community-based organizations, civil societies, PLHIV, policymakers, the industries and other related stakeholders, as per the citizen science approach. This will create a culture of inclusive scientific citizenship and empower affected communities to take part in shaping research priorities and implementation. By endorsing the HIV cure research agenda, this WCA academy can catalyze interest, initiate dialogues, and enhance capabilities and access to HIV cure research within these French-speaking settings considering also the state-of-the-art, infrastructural and financial realities to initiate and advance HIV cure research in LMICs. In this frame, challenges associated with limited local funding for HIV cure research were acknowledged together with the limited local opportunities for capacity-building of early-career researchers within WCA. Additionally, limited affordability to international opportunities (language barriers to attend capacity-building events) and the “difficulty-to-govern” collaborations between African and other LMICs remain gaps to be addressed within the frame of the proposed academia. By facilitating capacity-building of early/mid-term career investigators and inter-country collaborations, the WCA academy will prompt the development of grant proposals, coordinate multidisciplinary efforts, and contribute to the implementation of high-quality studies on HIV cure research within the WCA subregion. This could foster a new generation of researchers embedded in the local reality yet connected to global scientific ecosystems.

In order to drive meaningful progress in HIV cure research in WCA, there is a need to foster stewardship, trust, community engagement, multidisciplinary/complementary and international collaborations, political endorsement as well as government financial commitment for sustainability in the HIV/AIDS programmatic response, surveillance and research. The successful implementation of this concept around HIV cure research could only be effective through a solid WCA academia under the leadership of local stakeholders. The onboarding workshop concluded with the identification of opportunities for strengthening collaboration and the commitment to establishing a research-for-cure academy. Once implemented, this initiative will shape the agenda of WCA for HIV research, which includes implementation science, operational research, clinical studies, clinical trials as well as basic research towards HIV cure, as identified by the workshop's participants. The academy will therefore serve as an incubator, a think tank or a hub that catalyzes the transformation of identified research concepts into effective field operations within the subregion, by integrating the local clinical, programmatic and epidemiological features into the HIV cure research design and implementation. Such integration is essential to ensure the relevance, scalability, and sustainability of research outcomes.

As the geographical setting with the highest gap in the global HIV/AIDS response at the time of this concept paper development, WCA had: (a) seven trained IAS Research-for-cure academy fellows who have the profile to initiate and advance cure-related research; (b) local collaborators such as the Partners for Relief and Development Organization (PARDO) that have real-life community experience in HIV Cure research Advocacy (with support from IAS); (c) HIV program managers sensitized or involved in the cure research agenda. Taking into consideration these local realities, WCA Africa countries and Cameroon in particular (host of the onboarding workshop and with a considerable number of trained IAS fellows) contributed in designing the research priorities for WCA, in line with the IAS research priorities for toward HIV cure[23]. These priorities consist firstly to raise awareness and engagement of healthcare workers and PLHIV on all the aspects of HIV cure research following the citizen science approach in WCA where French-speaking countries are more represented, secondly to implement research that evaluates the profile of intact reservoirs among PLHIV experiencing viral control, and finally to identify post-treatment controllers in these settings considering the broad diversity of HIV clades. These priorities set a roadmap for impactful, inclusive, and regionally grounded HIV cure research in West and Central Africa.

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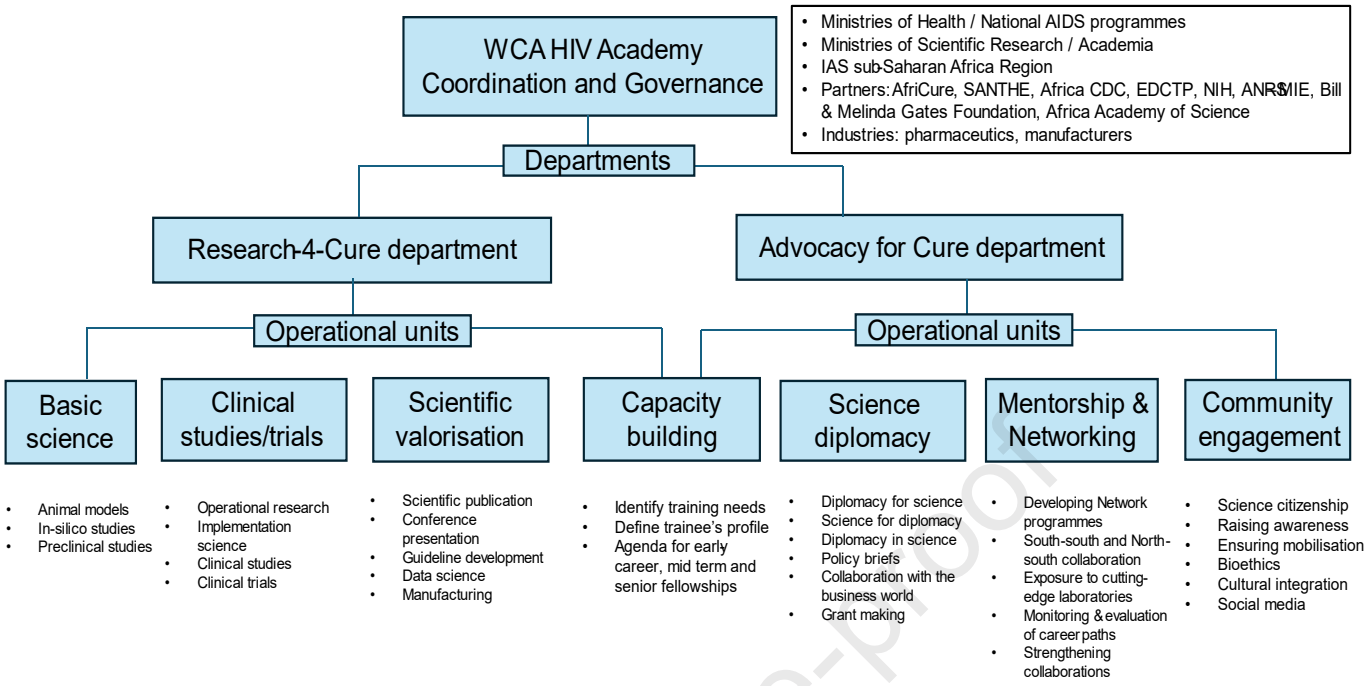

Legends: IAS: International AIDS Society; SANTHE: Sub-Saharan African Network for TB/HIV research Excellence; CDC: Centre for Disease Control and prevention; EDCTP: European and Developing countries Clinical Trial Partnership; NIH: National Institutes of Health; ANRS-MIE: Agence Nationale de Recherches sur le SIDA et les hépatites virales – Maladies Infectieuses Émergentes

284 Figure 2: Operational Framework of the WCA HIV Research-for-Cure Academy

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286 **HIV Cure Research Priorities for West and Central Africa**

287 To advance HIV cure research in WCA, seven priorities are identified for implementation (table 1).

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289 **Table 1: HIV Cure Research Priorities for West and Central Africa**

Research priorities	Key objectives
Measuring and characterizing the viral reservoirs	• Design of assay to quantify intact reservoirs for HIV non-B subtypes and associated recombinant forms. • Measurement of total and intact viral reservoirs. • Design of assay to characterize HIV integration sites • Evaluation of the expression of HIV proteins.
Immunology	• Evaluation of the efficacy and safety of broadly neutralizing antibodies across HIV circulating clades. • Assessment of the impact of HIV subtypes on immune response and natural viral control (elite controllers).

	• Exploration of the effect of cytotoxic T-lymphocyte and cytokine profile on viral replication (off versus on therapy). • Characterization of host markers such as human leucocyte antigens on HIV replication and control. • Exploration of immune checkpoint inhibitors. • Assessment of HIV tropism across age and viral clades.
Identification of and post treatment controllers	• Design of post-intervention control studies.
Manufacturing	• Development of point-of-care HIV DNA proviral load testing assays. • Design of assay to identify and detect biomarkers related to HIV functional cure. • Development of agents to silence or reverse latent reservoirs for a functional cure.
Therapeutic intervention	• Design of cost-effective gene therapy delivery methods.
Community / Stakeholder engagement and ethical consideration	• Development of the concept of citizen science for HIV cure-related research in LMICs. • Identification of barriers, facilitators and ethical considerations of successful community engagement • Formative research to inform the design and implementation of future trials. • Involvement of PLHIV in the design and the implementation of HIV cure related studies. • Development policies to facilitate the implementation of HIV cure research in WCA.
Capacity-building, mentorship and networking	• Establishment of a Research-for-Cure Academy for WCA.

1. Measuring and characterizing the viral reservoirs

Understanding the viral reservoir is crucial in informing cure strategies globally and most especially in WCA where limited data exists. As stated by IAS Global Scientific Strategy 2021, key research goals in this area include the measurement of total and replication-competent reservoir, the design of assay to characterize integration sites as well as to quantify the expression of HIV proteins and evaluate the link between residual plasma viremia and reservoirs [23]. In WCA, integrating longitudinal cohort studies to track reservoir evolution over time and under different ART regimens would provide invaluable insights into viral persistence. Importantly, the evaluation of HIV cellular reservoirs should take into consideration

cellular genomic factors such as APOBEC (to study the effect of defective viruses on HIV replication control) and HIV diversity (effect of pure subtypes, recombinants versus complex mosaic viruses on HIV replicative fitness and integration), the viral mutational patterns (wild-type versus multi-drug resistant viruses), age variability (key parameter in pediatric populations), gender/sex differences, and co-infections (i.e. oncogenic viruses, bacterial infections, tuberculosis and other opportunistic infections, etc.). Integration of reservoir studies with clinical, behavioral and demographic data in WCA could enhance predictive models for identifying individuals most likely to benefit from cure strategies. The WCA subregion therefore presents a unique opportunity to harvest several determinants for generalizability in HIV cure strategy at the global level.

In addition, the lack of region-specific data on the size and characteristics of intact HIV reservoirs in WCA populations, including pediatric and adolescent groups, represents a critical knowledge gap that must be addressed to inform tailored cure strategies [24].

2. Immunonology

To contribute to the development of effective and accessible functional cure in the context of high HIV genetic diversity like WCA, scientists of this geographical setting should investigate the impact of HIV subtypes on the immune response. This includes understanding immune escape pathways specific to subtypes circulating in the region. Moreover, examining the impact of cytotoxic T-lymphocytes and inflammatory profile on viral control or viral replication according to ethnicity diversity would be insightful. It would also be critical to investigate mucosal immunity, particularly in female populations, due to its role in viral transmission and persistence. Additionally, characterizing host markers, their variability and the potential implications on HIV persistence could contribute to designing effective immune therapies, especially the evaluation of the efficacy and safety of broadly neutralizing antibodies (bNAbs) in this highly heterogeneous setting. Another priority might be the exploration of the potential of immune checkpoint inhibitors in enhancing immune response against HIV clades circulating in this geographical setting. Recent advances in immunotherapies, including novel vaccine candidates and gene-editing approaches, should also be evaluated for their applicability and efficacy in the diverse immunogenetic backgrounds found in WCA. Studies should also explore combinations of immunomodulators tailored to host and viral characteristics of WCA populations.

3. Identification of post-treatment controllers

In the absence of necessary markers to identify post-treatment controllers, analytical antiretroviral treatment interruption (ATI) might be an essential tool to evaluate HIV cure research intervention in WCA. However, ethical frameworks and risk mitigation strategies tailored to local settings are essential for safe

ATI implementation. In this frame, designing and implementing ATI studies within WCA in accordance with the recommendations for ATI in HIV clinical trials would be of paramount importance in advancing cure research [25, 26]. Moreover, investigating the role of host genetics including human leucocytes antigens (HLA), immune responses, and viral factors in achieving post-treatment control might be of interest in these settings. Of note, sub-Saharan African countries are still among the most under-represented populations in terms of human genetic studies and more specifically HLA characterization. Despite hosting highest broad genetic diversity globally, there is limited evidence regarding HLA typing by ethnicities. Therefore, establishing HLA-genotype databases by ethnicity in WCA could guide personalized interventions. In the context of epidemiological transition in LMICs, diseases of public health importance such as the interactions between communicable (Tuberculosis, emerging infections) or non-communicable diseases (cancers, metabolic disorders), vaccination and responses to vaccines that could be related to HLA typing using polymorphism analysis in WCA will be of interest [27]. Special attention with careful ethical considerations should be given to paediatric and adolescent populations, who remain underrepresented in post-treatment control studies despite representing a significant proportion of PLHIV in WCA [24].

4. Manufacturing

WCA can benefit from accessible and relevant manufacturing of essential tools to enhance cure strategies locally. To facilitate the monitoring of HIV therapeutic responses when conducting cure research, it is crucial to invest in the development of low-cost point-of-care viral load testing assays (especially proviral DNA) and adapt these assays for diverse HIV subtypes. This includes the development of region-specific reagents and platforms adapted to low-resource settings. Ensuring availability and accessibility of such assays will be key to supporting equitable progress in HIV cure research in WCA. The development of protocols for full length sequencing of viruses from the reservoirs would contribute to the understanding of the viral dynamics toward HIV cure strategies. Furthermore, technology transfer and local production of diagnostic and therapeutic tools are essential to reduce costs and ensure sustainability of cure research efforts in resource-limited settings [28]. Establishing public-private partnerships with local biotech start-ups could catalyze innovation and manufacturing autonomy.

5. Therapeutic interventions

Gene therapy, as a groundbreaking field will contribute substantially towards the eradication of HIV reservoirs. Considering the high diversity of subtypes in WCA, designing gene therapies that are effective on a broad range of HIV subtypes will be great interest. Even though gene therapy holds enormous

promise, there are still challenges including safety and cost-effectiveness (delivery and accessibility) to overcome especially in LMICs including WCA countries. Therefore, the priorities in this field for these regions should be feasibility assessment of implementing gene therapy (CRISPR-cas) as well as the development of simplified and cost-effective gene therapy delivery methods. It is also critical to assess the ethical, social, and regulatory implications of gene therapy in WCA, ensuring that future interventions are both acceptable and accessible to local populations. Pilot programs in selected WCA research centers could help assess early outcomes and safety signals.

Moreover, the local development of immunotherapy such as bNAbs, the design of affordable assays specific for the detection and quantification of biomarkers related to cure, will scale-up interventions on HIV clades circulating in WCA. The development of agents to permanently silence or reverse latent reservoirs will contribute to targeting diverse proviruses.

Engagement with regulatory bodies in WCA will also be essential to develop ethical guidelines and approval pathways for future therapeutic interventions.

6. Science citizenship for community/stakeholder engagement, socio-behavioral sciences and ethical considerations

Following the citizen science approach including community, stakeholder engagement, ethical committees as well as socio-behavioral sciences, this would serve as a critical component in shaping HIV cure research, its understanding, acceptability and adaptation within the WCA context [29]. In the start-up of this research academy, inclusion of community members (especially PLHIV) and ethical committees alongside researchers in the design and the implementation will ensure that their priorities and perculiarities are not left behind. However, in WCA, community involvement has historically been limited as HIV cure related research remains scarce. Developing culturally adapted education tools and promoting participatory research models will enhance trust and involvement. Of note, the community is the key determinant of successful research planning, implementation, result analysis and interpretation, as well as the dissemination strategy to stakeholders and to the scientific community [29, 30]. Therefore, through formative research, it is pivotal for investigators of these subregions to identify barriers, facilitators and ethical considerations of successful community engagement considering the population diversity in terms of ethnicities, religiosity and cultures. Digital platforms, including WhatsApp groups, local radio, and influencer-based engagement, could be leveraged for community dialogue. Importantly, stakeholders should review existing strategies and innovate new ones for implementation. This will catalyze and enhance the engagement of community members in all aspects of HIV cure related research in WCA, including policymakers, traditional leaders, religious leaders, as well as influencers on social media.

Increased efforts should also be made to address stigma, misinformation, and to build trust between researchers and affected communities, which are crucial for the success of future cure trials.

7. Capacity building and networking

As demonstrated earlier, scientists from French-speaking SSA settings are less involved in HIV cure research (figure 1). To catalyze basic research and clinical studies/trials in the field of HIV cure research in these highly affected settings with diverse viral clades, capacity-building of early/mid-career researchers is of paramount significance. This requirement would be chiefly implemented through the establishment of an academy with a bilingual (French and English) communication that might significantly improve the initiation and the advancement of cure related research in these settings, develop specific mentorship scheme between same language senior-scientists versus early career investigators, set-up network through the local senior scientific leader's connectivity, and finally draft local grants with international collaborations identified within the network. Encouraging inter-institutional mobility and research exchange programs among French-speaking countries will strengthen regional expertise. Beyond the current European and USA collaborative networks established with WCA institutions, extending collaboration with the Chinese Academy of Science (preliminaries through Diana Boraschi) and Europe (EU2Cure HIV Symposium) and Canada (CANcure) could also give a broader umbrella to the success of this initiative in WCA. This strategy, if successfully implemented, will lead to the generation of local evidence from WCA that will contribute substantially to addressing the global challenges on HIV cure.

It is also crucial to secure increased and sustained funding, both international and domestic, to address current disparities in research capacity and treatment access, particularly in WCA countries which lag behind their counterparts in HIV response and innovation. Strengthening South-South and North-South collaborations, as well as adapting existing research networks to the specific needs of WCA, will further accelerate progress in the region.

Conclusion

The establishment of an HIV cure academy in WCA emerges as a transformative strategy to equitably advance HIV cure research in SSA and in other LMICs. By providing a platform for education, capacity building, advocacy, and networking, with the development and evaluation of context-adapted therapeutic interventions locally, the academy will play a pivotal role in shaping the trajectory of HIV cure research in the sub-region, serving as "Think-thank" of HIV cure in WCA inspired by the Research-for-cure academy of the IAS to contributing to HIV cure strategies at the global level. Ultimately, bridging the gaps in research infrastructure, capacity, and funding will not only benefit WCA but also contribute to global HIV cure efforts by ensuring that strategies are effective and applicable across diverse populations and viral landscapes. WCA's unique virological, immunological, and socio-cultural context positions it as a vital player in the global fight to end HIV if investments, collaborations, and inclusive approaches are robustly supported.

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References

1. The Joint United Nations Programme on HIV/AIDS (UNAIDS). Global HIV Statistics. Fact Sheet 2023. 2023;

2. Castro-Gonzalez S, Colomer-Lluch M, Serra-Moreno R. Barriers for HIV Cure: The Latent Reservoir. AIDS Research and Human Retroviruses. 2018;34(9):739–59.

3. Pitman MC, Lau JSY, McMahon JH, Lewin SR. Barriers and strategies to achieve a cure for HIV. The Lancet HIV. 2018;5(6):e317–28.

4. Foka, F.E.T.; Mufhandu, H.T. Current ARTs, Virologic Failure, and Implications for AIDS Management: A Systematic Review. Viruses 2023, 15, 1732.

5. Mbirimtengerenji ND. Is HIV/AIDS epidemic outcome of poverty in sub-Saharan Africa? Croatian Medical Journal. 2007;48(5):605–17.

6. Nyindo M. Complementary factors contributing to the rapid spread of HIV-I in sub-Saharan Africa: a review. East Afr Med J. 2005;82(1):40–6.

7. Bajunirwe F, Akakimpa D, Tumwebaze FP, Abongomera G, Mugyenyi PN, Kityo CM. Persistence of traditional and emergence of new structural drivers and factors for the HIV epidemic in rural Uganda; A qualitative study. PLoS ONE. 2019;14(11):1–15.

8. UN Joint Programme on HIV/AIDS (UNAIDS). Seizing the moment:Tackling entrenched inequalities to end epidemics. Global Aids Update. 2020;14.

9. Tatoud R, Jones RB, Dong K, Ndung T, Deeks S, Tiemessen T. Advancing HIV cure research in low- and middle-income countries requires empowerment of the next generation of scientists. Journal of Virus Eradication. 2024;10(1):100364.

10. Dubé K, Mthimkhulu D, Ngcobo W, Mindry D, Maphalala L, Pillay V, Tran W, Korolkova A, Ndung'u T, Dong K. 'With this study, we have hope that something is coming': community members' perceptions of HIV cure-related research in Durban, South Africa - a qualitative focus group study. HIV Res Clin Pract. 2023 Jul 29;24(1):2243046.

11. Kanki PJ, Hopper JR, Essex M. The origins of HIV-1 and HTLV-4/HIV-2. Ann N Y Acad Sci. 1987;511:370-5. doi: 10.1111/j.1749-6632.1987.tb36265.x. PMID: 2894192

12. Barr L, Jefferys R. A landscape analysis of HIV cure-related clinical research in 2019. Journal of Virus Eradication. 2020;6(4):100010.

13. Williams A, Menon S, Crowe M, Agarwal N, Biccler J, Bbosa N, et al. Geographic and Population Distributions of Human Immunodeficiency Virus (HIV)– 1 and HIV-2 Circulating Subtypes : A Systematic Literature Review and Meta-analysis (2010 – 2021). The Journal of Infectious Diseases. 2023;228(11):1583–91.

14. Godwe C, Goni OH, San JE, Sonela N, Tchakoute M, Nanfack A, Koro FK, Butel C, Vidal N, Duerr R, Martin DP, de Oliveira T, Peeters M, Altfeld M, Ayouba A, Ndung'u T, Tongo M. Phylogenetic evidence of extensive spatial mixing of diverse HIV-1 group M lineages within Cameroon but not between its neighbours. Virus Evol. 2024 Sep 2;10(1):veae070.

15. Sarabia I and Bosque A. HIV-1 Latency and Latency Reversal: Does Subtype Matter? Viruses. 2019 Nov 28;11(12):1104.

16. Ka'e AC, Fokam J, Togna Pabo WLR, Ngoufack Jagni Semengue E, Yagai B, Nka AD, et al. Evaluation of archived drug resistance mutations in HIV-1 DNA among vertically infected adolescents under antiretroviral treatment in Cameroon: Findings during the COVID-19 pandemic. HIV Med. 2023;

17. Ka'e AC, Nka AD, Yagai B, Kammogne ID, Ngoufack Jagni Semengue E, Nanfack AJ, et al. The mother-to-child transmission of HIV-1 and profile of viral reservoirs in pediatric population: A systematic review with meta-analysis of the Cameroonian studies. PLoS ONE. 2023;18(1 January):1–19.

18. Ka'e AC, Nanfack A, Santoro M, Yagai B, Ambada G, Sagnia B, et al. Characterisation of HIV- - 1 reservoirs in paediatric populations : protocol for a analysis systematic review and meta- -. 2023;1–5.

19. Kfutwah AKW, Tejiokem MC, Ateba FN, Ndongo JA, Penda IC, Ngoupo PAT, et al. Seronegativation in early treated HIV-infected infants: Frequency and potential implications on care and follow-up in a resource-limited country. Journal of Acquired Immune Deficiency Syndromes. 2011;58(2):43–6.

20. Fokam J, Mpouel Bala ML, Santoro MM, Takou D, Tala V, Beloumou G, et al. Archiving of mutations in HIV-1 cellular reservoirs among vertically infected adolescents is contingent with clinical stages and plasma viral load: Evidence from the EDCTP-READY study. HIV Medicine. 2021;(June):1–10.

21. Directives nationales sur la prise en charge du VIH - Coordination de la résistance du VIH-1 aux antiretroviraux (VIROFORUM). Available on https://www.differentiatedservicedelivery.org/wp-content/uploads/Directives_version-finale-05-aout-2021_Cameroon.pdf

22. IAS-International AIDS Society. IAS-Fellowships [Internet]. IAS. Available from: https://www.iasociety.org/taxonomy/term/343

23. Deeks SG, Archin N, Cannon P, Collins S, Jones RB, de Jong MAWP, et al. Research priorities for an HIV cure: International AIDS Society Global Scientific Strategy 2021. Nature medicine. 2021;27(12):2085–98.

24. Rakhmanina N, Foster C, Agwu A. Adolescents and young adults with HIV and unsuppressed viral load: where do we go from here? Curr Opin HIV AIDS. 2024 Nov 1;19(6):368-376.

25. Julg B, Dee L, Cannon P, Ananworanich J, Barouch DH, Bar K et al. Recommendations for Analytical Antiretroviral Treatment Interruptions in HIV Research Trials – Report of a Consensus Meeting. Lancet HIV. 2019;6(4): e259–e268.

26. Ka'e AC, Santoro MM, Duca L, Chenwi CA, Ngoufack JSE, Nka AD et al. Evaluation of HIV-1 DNA levels among adolescents living with perinatally acquired HIV-1 in Yaounde, Cameroon: A contribution to paediatric HIV cure research in Sub-Saharan Africa.

Journal of Virus Eradication. 2024; 10 (2024) 10036.

27. Pagkrati I, Duke JL, Mbunwe E, Mosbruger TL, Wasserman J, Dinou A, et al. Genomic characterization of HLA class I and class II genes in ethnically diverse sub-Saharan African populations: A report on novel HLA alleles 2024;102:192–205.

28. Nakaziya OG. Leveraging Technology Transfer for Self-Reliance in HIV/AIDS Management in Africa: Policy Frameworks and Sustainable Partnership Models. Eurasian Experimental Journal of Public Health. 2025; 7(1).

29. Lo YR, Chu C, Ananworanich J, Excler JL, Tucker JD. Stakeholder Engagement in HIV Cure Research: Lessons Learned from Other HIV Interventions and the Way Forward. AIDS Patient Care STDS. 2015 Jul;29(7):389-99.

30. Tucker JD, Rennie S; Social and Ethical Working Group on HIV Cure. Social and ethical implications of HIV cure research. AIDS. 2014 Jun 1;28(9):1247-50.

Declaration of interests

☒ 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.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: