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Africanizing genome editing for food sustainability

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ABSTRACT

Genome editing has great potential to alleviate the persistent food insecurity in Africa. However, achieving this goal is faced with a myriad of challenges. We describe components that we envisage are crucial in positioning Africa for an early commercial agricultural genome editing take-off. We review the evolving genome editing technologies based on CRISPR/Cas systems. We then present the status of research in genome editing to improve food sustainability in Africa, and its potential commercialization in the short-term.

1. Background

1.1. What is genome editing and how does it differ from other breeding technologies?

Genome editing (GEd) is a suite of tools that breeders use to make specific alterations within a genome of a target organism. This is an advancement from other breeding technologies because it is faster and more efficient. Fig. 1 is used to illustrate differences in breeding technologies in developing disease resistant crop varieties. In all cases, the improved variety is produced by changing its genetic makeup. Classical breeding achieves this by crossing together an elite disease susceptible variety with a donor disease resistant variety and selecting the offspring with the desired combination of characteristics. To maintain the desired characteristics of the elite variety, the breeder performs 5–7 backcrosses. This process can take up to 10 years for most crops (Fuente et al., 2013; Gao, 2020). In mutation breeding, a disease susceptible crop variety is mutagenized using radiation or chemicals followed by selecting and backcrossing of the mutants to fix the trait. This process also takes 8–10 years (Gao, 2020). In transgenic technology, the breeder adds a new gene to the genome of an elite disease susceptible variety. The gene must be added in embryonic cells – in most cases callus tissue – and then regenerated in tissue culture to produce a disease resistant plant variety. For most crops, this process takes 8–12 years because of strict regulations (Gao, 2020). To achieve the same goal of imparting disease resistance using GEd, a breeder can inactivate (edit) a disease susceptibility gene in a disease susceptible variety. In most applications, GEd is also performed in embryonic cells like callus followed by regeneration of disease resistant variety. On average, this process takes 2–5 years (Gao, 2020). The shorter time in GEd is because for targeted mutagenesis, no backcrossing is required and some GEd applications are not transgenic greatly shortening regulatory approval.

1.2. The current status of genome editing technology and its potential application for food sustainability in Africa

The general mechanism of GEd works by target locus location in the genome of the organism undergoing editing through DNA/RNA complementarity using a short probe followed by cleavage of the DNA to induce a double stranded break (DSBs). The DSB is then repaired by the endogenous non-homologous end-joining (NHEJ) or homology-directed repair (HDR) pathways. While NHEJ is an error-prone repair process and often results in the introduction of mutations, such as small insertions and deletions (INDELs), HDR results in a precise repair of DSBs. Such

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editing can be achieved using different GEd tools including: (1) clustered regularly interspaced short palindromic repeats (CRISPR)-CRISPR-associated protein 9 (Cas9) (Cong et al., 2013; Jinek et al., 2012; Mali et al., 2013), (2) transcription activator-like effector nucleases (TALENs) (Christian et al., 2010), (3) zinc-finger nucleases (ZFNs) (Bibikova et al., 2002), and (4) homing endonucleases or meganucleases (Bogdanove et al., 2018). Of these, CRISPR/Cas9 is the most widely used GEd tool – because of its relative simplicity, versatility, and precision. This review will focus on GEd using CRISPR/Cas technology and refer readers to excellent reviews for other GEd applications (Bartsevich et al., 2016; Joung and Sander, 2012; Paschon et al., 2019).

In its basic application, the nuclease enzyme Cas9 associates with CRISPR RNA – a guide RNA (gRNA) designed to recognize a target site for editing. Once the Cas9/gRNA complex recognizes target DNA, Cas9 causes knicks on DNA upstream of a site called the protospacer adjacent motif (PAM). The PAM is a three-nucleotide sequence that serves as a recognition site for Cas9 to start editing upstream (Jiang and Doudna, 2015). It is usually NGG or NAG, where N is any nucleotide (Fig. 2A).

CRISPR/Cas technology has been used in improvement of many crops for disease resilience, nutrition, heterosis, and other agronomic traits. Notably, the first CRISPR-edited food, the GABA-enriched tomato, was commercialized in Japan in 2021 (Nonaka et al., 2017; Waltz, 2022). This tomato was engineered to help lower blood pressure and promote relaxation.

But even as new products are developed, CRISPR/Cas system GEd has undergone significant refinements and advances (Wang and Doudna, 2023). At the heart of these advances is CRISPR multiplexing, based editing and prime editing.

Multiplexing – Reviewed in [(Abdelrahman et al., 2021; Najera et al., 2019)] (Fig. 2B) involves targeting numerous gRNAs. This is a good way to edit crops that carry multiple copies of the same gene – as was shown in the case of hexaploid wheat – where enhanced resistance to powdery mildew was realized when three copies of the disease susceptibility gene *Mildew Locus O1* (*MLO1*) were targeted (Zhang et al., 2017). Another demonstrated potential application of multiplex CRISPR is the case for accelerated domestication of crops where several genes are required to change a wild crop relative to a high yielding domesticated crop. As an example, Li et al. (2018) imparted domestication traits into four stress tolerant wild tomato accessions by CRISPR engineering genes associated with morphology, flower and fruit production, and ascorbic acid synthesis. Multiplex CRISPR has also found application in cases where multiple genes in a pathway require inactivation. For example, Vernet et al. (2022) showed that CRISPR inactivation of three genes – *Mitosis instead of Meosis* (*MiMe*) genes (d'Erfurth et al., 2009; Mieulet et al., 2016) and simultaneous expression of the developmental gene *BABY-BOOM* (*BBM*) in egg cells produced seeds that could be propagated asexually. This technology referred to as synthetic apomixis has great potential to increase rice production in Africa because farmers will be able to regrow their own hybrids for multiple generations without loss of hybrid vigor.

Base editing – Reviewed in (Bharat et al., 2020; Gürel et al., 2020; Mishra et al., 2019) enables generation site-specific and precise point mutations without DSBs, eliminating the need for repair templates and limiting undesired by-products during editing (Fig. 2C). The editing machinery – CRISPR base editor – is made up of a fusion between a variant of Cas9 that produces a single stranded break instead of the usual double stranded break; like Cas9 nickase or a catalytically inactive Cas protein e.g. dCas9 and an enzyme that catalyzes a nucleobase deamination reaction [reviewed in (Porto et al., 2020; Rees and Liu, 2018)]. Editing is achieved when the sgRNA directs the nCas9-deaminase fusion to the genomic target, where deamination occurs leading to a base mismatch. The mismatch is subsequently repaired through cellular DNA repair mechanisms. In plants, the common base editors are Cytosin and Adenine editors that produce C to T and A to G conversions (Gaudelli et al., 2017; Komor et al., 2016; Li et al., 2018). These have found widespread applications in crop improvement including nutritional

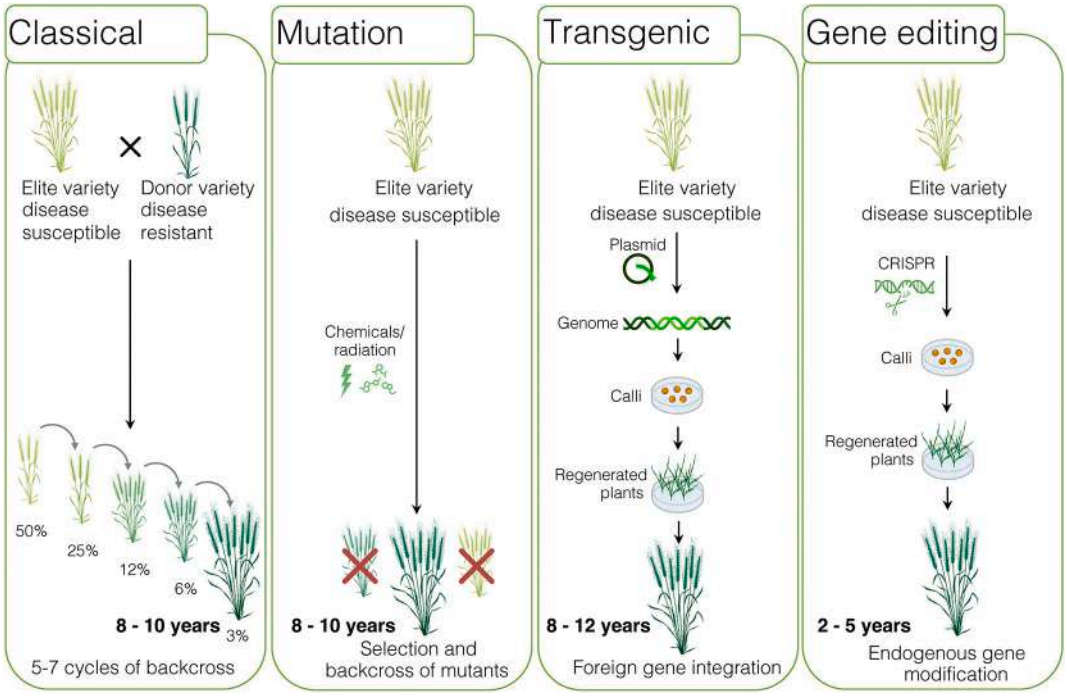


Fig. 1. Comparing genome editing with other breeding technologies using disease resistant rice as an example. Classical breeding (8–10 years) involves crossing a disease susceptible elite variety with a disease resistant donor variety followed by backcrossing to eliminate undesired traits. Mutation breeding (8–10 years) involves mutagenizing an elite variety followed by selection of the desired trait and backcrossing. Transgenic approach (8–12 years) involves insertion of a foreign gene conferring resistance in embryonic cells followed by tissue culture-based regeneration of the improved plant. Genome editing (2–5 years) involve specific alteration of an endogenous gene in embryonic cells followed by regeneration. Figure is constructed based on Gao, 2020 and created using resources from BioRender.com.

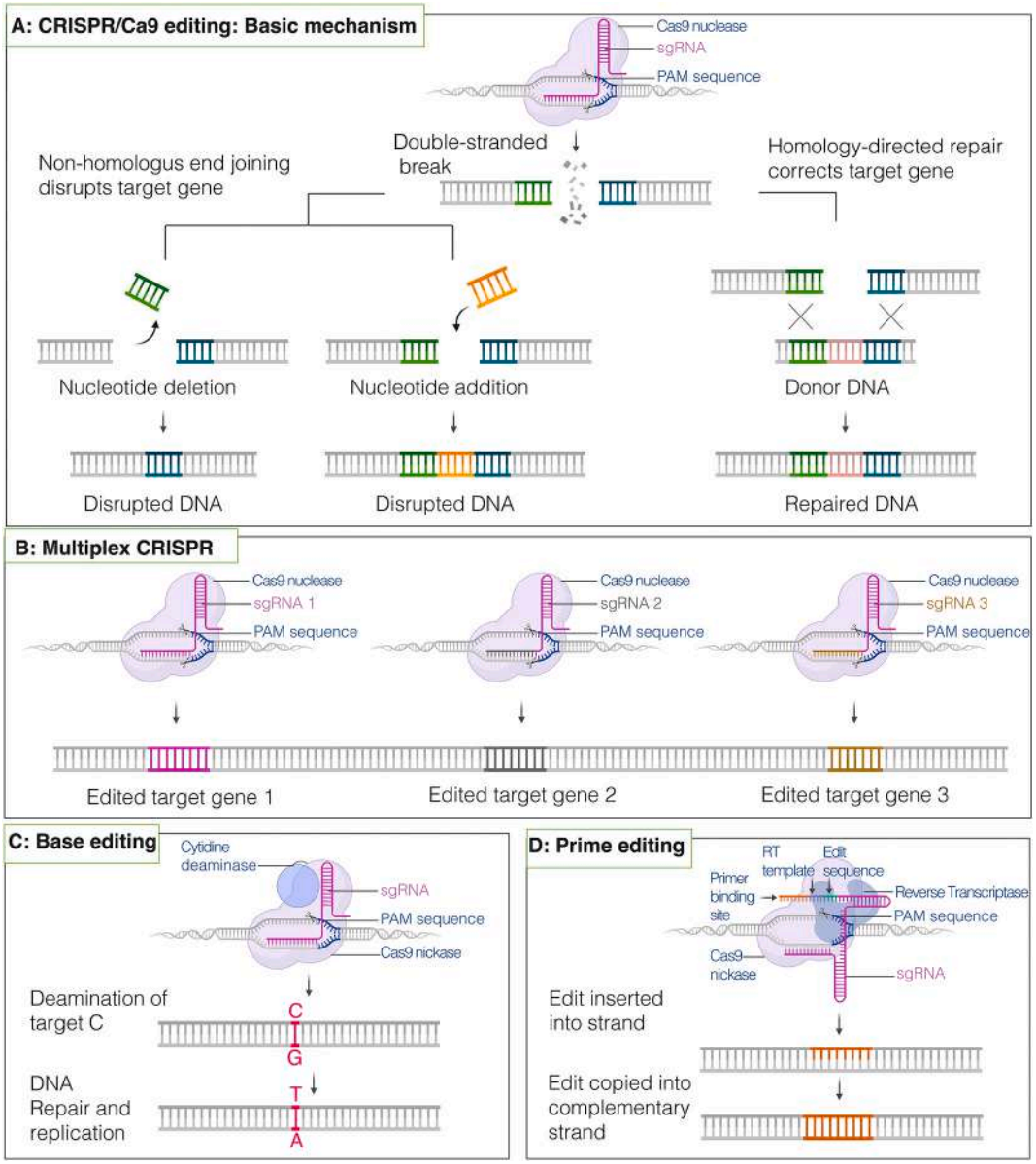


Fig. 2. Genome editing using CRISPR/Cas technology. (A) Basic mechanism of CRISPR/Cas9 editing (Jiang and Doudna, 2015) describing induction of double stranded breads of DNA that are repaired using either non homologues end joining (causing deletions and additions) or homology directed repair (leading to insertion of a DNA segment). Advances in CRISPR/Cas editing illustrated by: (B) Multiplex CRISPR (Najera et al., 2019) where multiple guide RNAs (gRNAs) can be used with Cas9 to simultaneously edit multiple targets in a genome; (C) Base editing (Komor et al., 2016) consisting of a Cas9 nickase that causes single stranded breaks instead of double stranded breaks. Cas9 nickase is linked to a deaminase that causes site-specific base modifications; (D) Prime editing (PE) composed of Cas9 nickase, reverse transcriptase and a repair strand (Anzalone et al., 2019). PE allows editing of more bases within a target site. Created with BioRender.com.

enhancement, disease resistance, nitrogen use efficiency and herbicide resistance. For example, Zhang et al. (2019) developed transgene free wheat germplasm with mutations that imparted tolerance against sulfonylurea, imidazolinone and aryloxyphenoxy propionate-type herbicides by base editing the acetolactate synthase (ALS) and acetyl-coenzyme A carboxylase genes (Zhang et al., 2019). Potentially, African staple cereals like maize, sorghum, and millets whose yields are diminished by parasitic weeds could be CRISPR modified to be herbicide tolerant.

Prime editing (Anzalone et al., 2019) – still in its infancy, is an advancement of HDR and base editing that allows for precise modification of more bases within a target site. In prime editing (PE), it is possible to introduce base-to-base conversions and to make small insertions/deletions, without the need for DSBs or donor DNA templates. Prime editors consist of nCas9 fused to a reverse transcriptase (RT) and a prime editing gRNA (pegRNA) that serves both to direct nCas9 to the target site and encode the desired edit (Fig. 2D). In plants, PE has been demonstrated in rice (Butt et al., 2020; Hua et al., 2020; Li et al., 2020; Lin et al., 2020; Tang et al., 2020; R. Xu et al., 2020; W. Xu et al., 2020), wheat (Lin et al., 2020), maize (Jiang et al., 2020), and tomato (Lu et al., 2021). In the work reported by Butt et al. (2020), PE was used to precisely introduce herbicide tolerance in rice by a G to T substation. This change converted a critical tryptophan residue to a leucin; and a further G to A substitution that destroyed the PAM site to prevent further editing by the PE machinery (Butt et al., 2020). While PE needs further optimization to boost efficiency, existing evidence suggests that it can overcome the drawbacks of GEd, such as low HDR frequency and off-target mutations.

2. Harnessing genome editing for food sustainability in Africa: what will it take?

Beyond the engrained African problems (Asongu, 2015) such as poor transport infrastructure, poverty and gender inequity that disfavor development, adoption of agricultural biotechnology in Africa is also constrained by fundamental science advancement issues like: (i) lack of capacity in modern biotechnology among African scientists to develop and deploy "home-grown" biotech solutions, (ii) poor conversion of upstream science in advanced countries to translational research that can solve real-life problems in Africa (Delmer, 2005), (iii) low confidence with biotechnology because of the long-held perception of multinational push (Mmbando, 2023), (iv) highly precautionary approach to agri-biotechnology regulation.

While overcoming deep-seated hurdles of development in Africa is important and must be dealt with for Agribiotech to thrive, in this article we chose to focus on tackling a specific, concrete problem and propose a model on how Africa can maximize gains from science-based solutions. Below, we provide a systematic analysis of four issues that we deem critical in such a model: (i) leveraging strategic partnerships to develop demand-driven GEd products that meet societal needs, (ii) developing human and physical science infrastructure to facilitate development of home-grown GEd products, (iii) developing appropriate regulatory, stewardship, and licensing models for commercialization of GEd products, and (iv) fostering reliable and trust-worthy public communication on GEd.

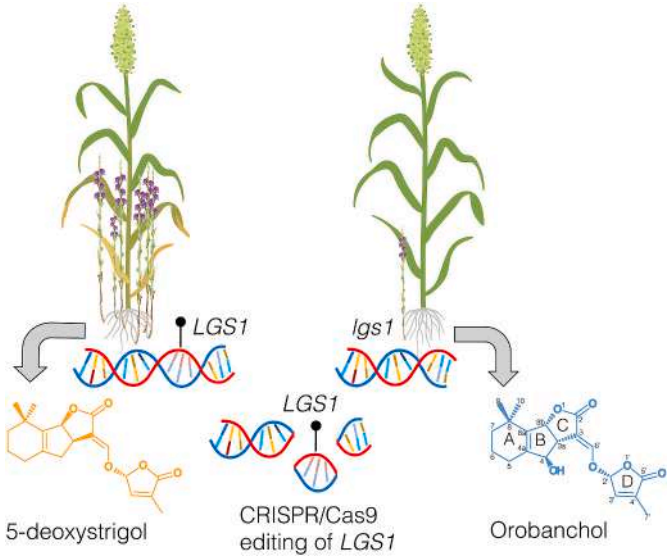
2.1. Leveraging strategic partnerships to develop demand driven genome edited products that meet societal needs

Active research and development on GEd products in America, Europe and Asia are a result of advances in science, technology, and innovations (STI). This process typically begins with basic research to identify suitable GEd targets, which are then validated through proof of concept experiments. Once validated, the research advances to translational studies to develop GEd crops with beneficial traits. Despite great advances in STI elsewhere, Africa has remained behind (Abkallo et al., 2024; Kahn, 2022). And most advances abroad have not been developed into translational products specific for Africa; mostly because developers of such innovations are not aware of the problems unique to Africa (Delmer, 2005). Indeed, a recent University-Industry Demonstration Partnership (UIDP) Workshop (Clark, 2021) emphasized that current partnership models do not work well for developing countries.

As such, it is incumbent upon African scientists to devise new

Box 1
Principle behind Feed the Future *Striga*-Smart Sorghum for Africa (SSSfA)

As an obligate parasite, the lifecycle of *Striga* – a parasitic plant that greatly diminishes yields if cereals in Africa – is intricately coupled with its host (Runo and Kuria, 2018). But tight synchronization biology is also the parasite's Achille's heel. Researchers at Pennsylvania State University (Penn State) and Corteva Agrisciences partnering with Kenyan scientists provided proof of concept experiments demonstrating that *Striga* can be controlled by interfering with the "information exchange" between the host and the parasite at germination. The theoretical premise of the work hinged on the fact that *Striga* relies on host derived chemical signals – strigolactones – to germinate and initiate its lifecycle (Matusova et al., 2005). Some natural genotypes of sorghum do not effectively induce germination of the parasite because of genetic mutations that cause a loss of function in the *LOW GERMINATION STIMULANT 1* (*LGS1*) locus, and specifically the sulfotransferase gene involved in strigolactone biosynthesis (Hess and Ejeta, 1992; Mallu et al., 2021; Mohemed et al., 2018). These are described as *Striga* resistant. In contrast, wild type sorghum genotypes produce 5-deoxystrigol, a powerful inducer of *Striga* germination which makes the sorghum *Striga* susceptible. By mimicking this natural mutation, Corteva Agriscience researchers developed *lgs1* mutant lines (Bellis et al., 2020) using CRISPR/Cas technology (Jinek et al., 2012; Najera et al., 2019) in a popular, high yielding but *Striga* susceptible African sorghum variety called Macia. Subsequent molecular and *Striga* resistance screening assays showed that the GEds were largely resistant to *Striga* (Bellis et al., 2020). Encouraged by this success, the SSSfA consortium sought to expand the findings and build a sustainable model for developing home-grown GEd *Striga* resistant sorghum. The goal was to initiate commercialization of the first GEd, *Striga* resistant sorghum in the background of the popular African sorghum cultivar, Macia, and further develop other *Striga* resistant sorghum varieties adaptable to local environment and preferred (food and feed) by smallholder farmers, and the industry in Ethiopia and Kenya.

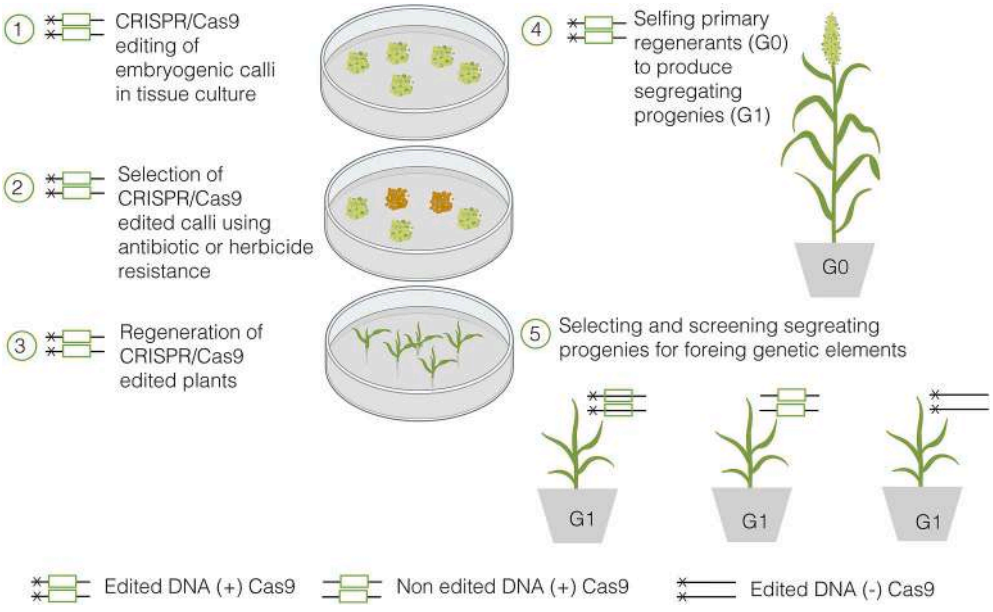


strategic partnerships, ideally with more African engagement. In such partnerships, the African scientist brings to the table first-hand knowledge on agricultural constraints while the overseas partner presents basic biology and advanced technology knowledge. The resulting partnership then seeks to leverage on advances in STI to tailor-make solutions to the identified constraint. To illustrate this concept, we use the example of the Feed the Future *Striga*-Smart Sorghum for Africa (SSSfA) consortium that is developing GEd solutions to manage one of the most intractable problems of African agriculture, the parasitic plant *Striga* (Box 1).

Alongside similar partnerships, Corteva Agriscience is developing maize lethal necrosis (MLN) resistant maize in partnership with the Kenya Agricultural and Livestock Research Institute (KALRO) and the International Centre for Maize and Wheat Improvement (CIMMYT) (https://www.cimmyt.org/content/uploads/2020/02/MLN-gene-editing-project-brief-2019-11.pdf). Corteva Agriscience also partnered with the Danforth Centre and the Ethiopian Institute for Agricultural Research (EIAR) to develop lodging resistant GEd teff, *Eragrostis tef* (Beyene et al., 2022). Other notable pioneering efforts include the development of GEd bacterial wilt-resistant rice, which is currently undergoing field evaluation in Burkina Faso (Sprink et al., 2022) made possible through a partnership between local and international partners. If successful, these products will soon be commercialized and form the first wave of GEd products in Africa. Numerous groups have also reported GEd product development that have gone past the proof of concept stage of product development. The Consultative Group of International Agricultural Research (CGIAR) and other partners have developed GEd bananas with resistance to viruses (Tripathi et al., 2019) and bacterial diseases (Tripathi et al., 2021), GEd bacterial leaf blight resistant rice (Schepler-Luu et al., 2023), GEd vaccines against African swine fever and *Theileria parva* (Karembu, 2021), and trypanosomiasis resistant goat (Karembu, 2021). Additionally, there are efforts from African national agricultural research institutes (NARIs) developing drought tolerant wheat (Mohr et al., 2022), and low cyanide cassava (Bicko et al., 2021). Successful demonstration of efficacy of these products will lead to a second wave of commercial GEd products in Africa in the short term. A third wave of GEd products is also in sight resulting from ongoing research on optimization of GEd protocols for recalcitrant African indigenous crops. For example, Syombua et al. (2021) developed an efficient GEd protocol for yam (*Diascorea* spp.) paving way for development of disease resistant, and improved nutrition as described in (Tripathi et al., 2022). Likewise, Odipio et al. (2017) showed proof of concept for editing local cassava varieties with a future goal of altering flowering time. It is also expected that products developed elsewhere using emerging CRISPR technologies will soon find their way in Africa. For example, there are already efforts in Kenya to evaluate herbicide tolerant sorghum developed using base editing. There is also ongoing research in Germany (Duseldof University) and France (L'institut Agro Montpellier) to impart African rice germplasm with resistance against rice yellow mottle virus (Arra et al., 2024). Future GEd products will also include synthetic hybrids, as projected by ongoing research. For example, a consortium led by The University of Queensland is developing sorghum and cowpea synthetic hybrids for Africa (https://hy-gain.org/article/2020/06/rewiring-plant-reproduction-higher-seed-yields). Additionally, recent innovations in rice apomixis (Vernet et al., 2022; Wei et al., 2023) will likely drive research into synthetic hybrid rice production for the African market. Theses waves of GEd product development are depicted in Fig. 3 alongside the current regulatory landscape in Africa.

Box 2
Production of transgene free genome edited products

The most common approach for removing transgenes (foreign genetic elements) is selecting null segregants by Mendelian segregation. In this approach the CRISPR/Cas9 cassette is introduced as DNA in embryonic cells called calli (step 1). CRISPR/Cas9 edited calli are then selected based on antibiotic or herbicide resistance (step 2); then regenerated into plantlets (step 3). Initial CRISPR/Cas9 edited plants (G0) are then grown to maturity and crossed to obtain G1 progenies (step 4). In the G1 progenies, the transgene (CRISPR/Cas9 encoding, and selectable marker genetic elements) segregate according to the Mendelian law of segregation with outcomes of desired null segregants in which the plants have undergone editing but do not contain the transgene (step 5). Figure created with resources from BioRender.com



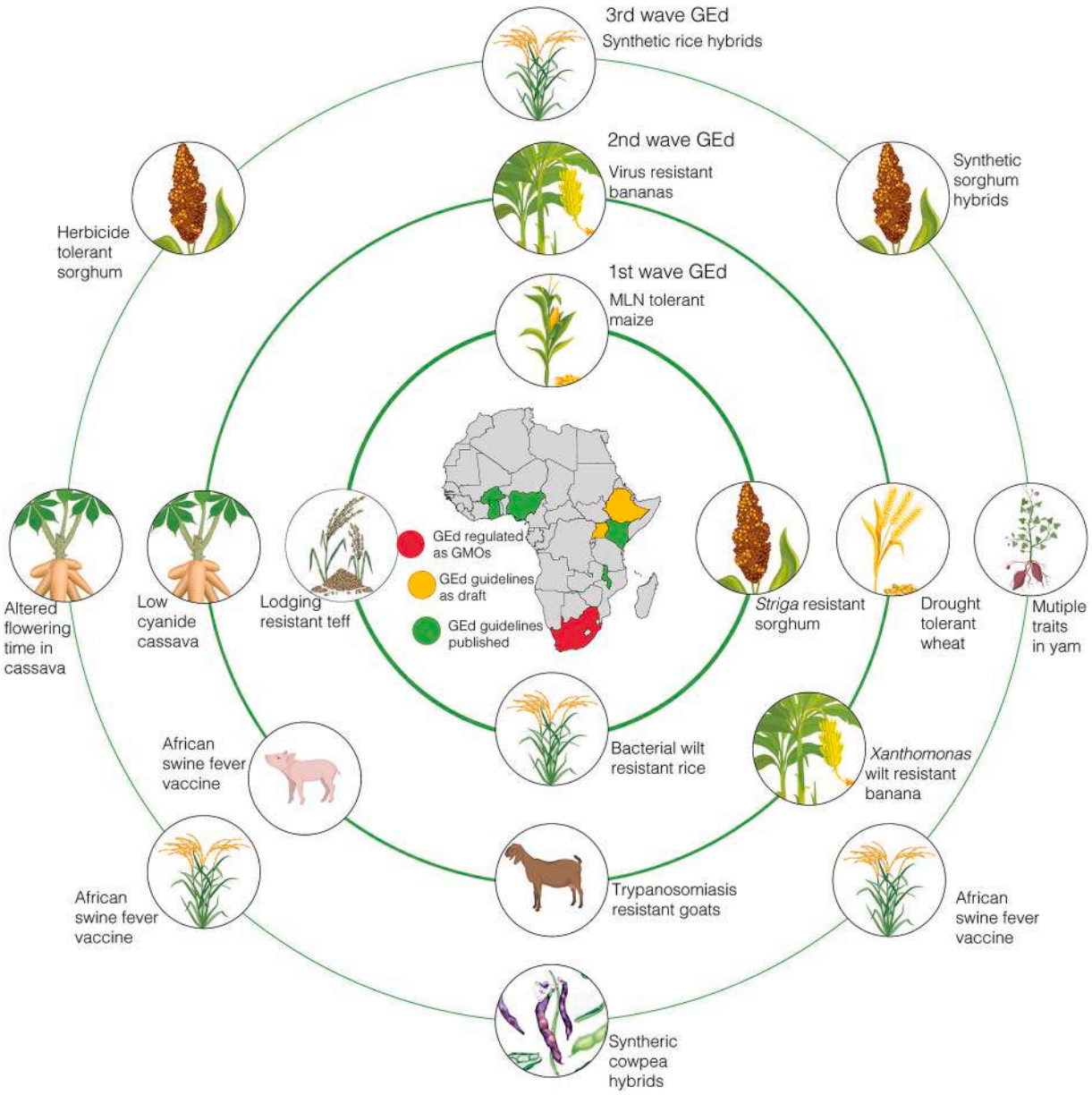


Fig. 3. Status of genome editing of agricultural products and regulation in Africa. Inner circle describes the regulatory status of genome editing (GEd) in Africa. The red area (South Africa) represents countries that regulate GEd crops as genetically modified organisms (GMOs). Orange areas (Ethiopia and Uganda) represent countries where discussions are ongoing on development of GEd specific guidelines. Green areas (Burkina Faso, Ghana, Kenya, Nigeria, and Malawi) represent countries that have published GEd specific legislation that exclude products of GEd that do not carry foreign genetic material from GMO regulation. Concentric circles show current research status and possible future commercialization of GEd agricultural products in Africa. 1st wave are products whose field evaluations have either commenced or awaiting regulatory policy promulgation; 2nd wave are products that have gone past proof of concept or under laboratory stage of development and 3rd wave are products awaiting production or evaluation in Africa. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

2.2. Developing human and physical science infrastructure to facilitate development of home-grown genome edited products

Successful partnerships are based on the ability of local (African) scientists to communicate at the same level as their peers abroad. After partnerships are formed, local scientists must have the science and infrastructure wherewithal to help implement the partnership goals. Logically, Africa will need technically skilled personnel and sound research capability. This will help spur STI for GEd research and provide an ecosystem to uptake future technologies.

Regarding personnel, we propose the view that this is a powerful aspect that has potential to drive GEd innovations in Africa with far-reaching implications. To add context, much of the great agri-biotech advancement in Asia is attributable to training of a cadre of local scientists and leaders described as community change-agents in the report by USAID (https://www.usaid.gov/sites/default/files/2022-05/USAID-Legacy-in-Agricultural-Development.PDF). During the Green Revolution, Asian governments and development partners established agricultural institutions and trained many students at the PhD level. These investments kept pace with the innovative breeding technologies that Norman Borlaug and other crop scientists were producing at the time (Evenson and Gollin, 2003). As a result, Asia's agri-biotech industry took off due to well-trained group of scientists who were able to sustain the momentum of the Green Revolution for subsequent technological breakthroughs.

It is encouraging to see African-led initiatives training the next

generation of biotechnologists and molecular biologists e.g. the Pan African University of Science Technology and Innovation (PAUSTI). Also inspiring is the African Union Development Agency-New Partnerships for Africa's Development (AUDA-NEPAD) which is on the forefront of advocating for use of GEd to mitigate against hunger and malnutrition (https://assets.au-apet.org/knowledge-products/genome-editing/Policy%20Framework%20for%20Applications%20of%20Genome%20Editing.pdf). International research communities too have played a strong role. To give an example, PlantGENE (https://plantgene.atlassian.net/wiki/spaces/PH/overview) is a network of scientists involved in use of genetic transformation for translational research, funded by grants from the United States' National Science Foundation (NSF). The network seeks to break technical barriers in plant genetic transformation and GEd through a series of seminars, workshops and in-person trainings. This network has a special focus on improving the genetic transformation capability in Africa. Another example is the training of African scientists via the African Orphan Crops Consortium (AOCC). Through their program African Plant Breeding Academy, the consortium, which was initiated by the, University of California, Davis, the Innovative Genomics Institute at Berkeley, CA, and funded by the Foundation for Food and Agricultural Research (FFAR) (Jamnadass et al., 2020) trains African scientists in advanced genomics and GEd technologies for breeding.

Regarding infrastructure, researchers, national programs, and universities in Africa should take ownership and responsibility and create centers of excellence in plant biotechnology established strategically in as many locations in Africa as is practically possible. The hubs can serve as one-stop shops for technology development where GEd protocols can be customized to suit local needs and market. There already exist such hubs and the model can be expanded. To name a few, the Kenyatta University Plant Transformation Laboratory in Kenya is licensed to carry out research in genetic transformation. The modest facility has been instrumental in training regional scientists in biotechnology. Others are the Institute of Bio and Emerging Technologies (BETiN) in Ethiopia that has received support from the federal government to support research. It is also encouraging to see further support for biotechnology research infrastructure in Africa via the international research community. For example, the International Centre for Genetic Engineering and Biotechnology (ICGEB) is set to establish an advanced research facility at Egerton University in Kenya. The facility which will be co-funded by the government of Kenya will also serve as a regional hub for ICGEB African member states. Such hubs, strategically established in Africa, will not only spur innovation but also retain African scientists trained abroad and attract international scientists keen on translational research. These efforts are examples of African ownership and responsibility in action.

2.3. Developing appropriate regulatory, stewardship, and licensing models for commercialization of genome edited products

Advancing GEd products developed through partnerships to commercialization require appropriate regulation, stewardship, and licensing, – often called freedom to operate. Each of these issues is explained in the analysis below.

Regulation: African countries need risk-appropriate and harmonized legal framework for regulation of GEd products, bearing in mind that there is a growing global consensus for a more permissive regulation of GEd products compared to genetically modified organisms (GMOs) (Jenkins et al., 2021, 2023; Menz et al., 2020). Such regulation must be grounded in science and product based. GEd products that do not contain foreign genetic material (from sexually incompatible species) could occur in nature or be developed through traditional breeding – thus, their risks are no different, and they should be regulated no differently. Globally harmonized regulatory frameworks based on this premise are currently in development (Jenkins et al., 2021, 2023). It is encouraging to see that this understanding is also being adopted in Africa. A look at the GEd guidelines in Burkina Faso, Ghana, Kenya, Nigeria, and Malawi reveal that GEd products that do not lead to introduction of foreign genetic material will not be regulated as GMOs. This is to say that for GEd product developers in Africa, removal of foreign DNA material (CRISPR/Cas encoding and selectable marker genetic elements) in the final products will greatly simplify the path to commercialization. A general scheme for producing foreign DNA free GEd products is explained in Box 1. Other methods are based on Cas9 free delivery systems using ribonucleoproteins (RNPs) (Reviewed in (Jang et al., 2020; Mazurov et al., 2023; Zhang et al., 2021).

But disparities in regulation of GEd exist even within African countries in the same trading block. For instance, Kenya has a strong and efficient regulatory system for GEd products and encourages use of new technologies to combat adverse effects of climate change and sustain food security (Mmbando, 2023). But contrastingly, EAC block member Tanzania is yet to develop GEd specific guidelines. The country has few research studies on GMO and GEd; and prohibit importation of GMO (Mmbando, 2023). In neighboring Uganda, there are good biotechnology research facilities in national agricultural research institutions owing to an early start and significant investments in biotechnology by development partners (Kedisso et al., 2022). Additionally, Uganda has well trained scientists who have initiated discussions on development of GEd specific guidelines (Kedisso et al., 2022). However, in 2022, the Ugandan President declined to assent to the Genetic Engineering Regulatory Act (GERA) creating uncertainty around application of GM and GEd technologies in the country.

Such disparities present challenges of upscaling technologies across boundaries. To put it in perspective, Kenya, Uganda, and Tanzania have common agricultural constraints – including pests, diseases, and drought – meaning that crop varieties developed for improvement in one country would be useful across the region. But without harmonized regulatory framework, such scale up is not possible.

Stewardship: To safeguard product quality and integrity, ensure sustainable access to good quality seeds by farmers and comply with regulations in neighboring or export market countries, a robust stewardship plan is crucial. Further, stewardship is critical in adoption as well as promoting consumer confidence. During the development and delivery of the proposed GEd, stewardship considerations should encompass identity preservation, trait performance, pathogen resistance management, good agricultural and agronomic practices (GAP), marketing, labeling, and consumer acceptance. As most GEd start as GMO before subsequent segregation, stewardship is especially critical at this stage (Pixley et al., 2022).

To foster trust, developers of GEd products in Africa must set stewardship requirements and ensure best management practices. Institutions are encouraged to form affiliation with Excellence Through Stewardship (ETS); a global industry-coordinated organization that promotes the adoption of stewardship programs and quality management systems for the full life cycle of biotechnology-derived plant products (https://www.excellencethroughstewardship.org/our-members).

Licensing: It is critical that crops developed with GEd technology are commercialized in a manner that does not infringe the contractual, intellectual property (IP) or other proprietary rights of third parties. Because Africa is entering the GEd foray when other countries have made significant investments in research and development, it is fair to assume creative solutions to existing IP will be needed to commercialize GEd products. Therefore, African partners will need to carefully evaluate and negotiate with technology developers to obtain appropriate licensing for commercialization of products in Africa. Oner way is to leverage on expertise and experience of international non-profits that have worked on approaches to minimize or eliminate licensing barriers for biotech products intended for commercialization in Africa on licensing and IP. As an example, in 2006, The Rockefeller and McKnight Foundation facilitated the Meridian Institute to establish the Public Intellectual Property Resource for Agriculture (PIPRA) initiative (https://merid.org/case-study/public-intellectual-property-resource-for-agr

iculture-pipra/). By leveraging IP technologies from the public sector, PIPRA developed a public IP assets database, established best practices to guide development of research innovations, and created specific, pooled public sector IP technology packages to facilitate humanitarian and special use objectives. In all cases, IP and licensing must be thought through carefully, and thoroughly to find appropriate models for Africa.

After licensing agreements have been negotiated, partners will need to agree on appropriate ways of handling the potential for liability arising from the development, production, and use of agricultural GEd products. Differences in regulatory systems underscores the need to manage potential liabilities. For instance, GEd products can cross over to countries where they are regarded as GMOs leading to potentially expensive legal processes. This necessitates, African institutions working with international partners to put in place appropriate safeguards to cover liabilities. One approach is to agree to indemnify – agree by contract to protect a partner from financial loss. That way, the international partner can donate their technology on humanitarian use without liability risk. Other options that African partners can explore are appropriate insurance coverage and cost recovery models (Boadi, 2009).

2.4. Fostering reliable and trust-worthy public communication on genome editing

Genome editing is establishing itself against the background of misconceptions and emotional perceptions of GMO food. The first challenge is therefore to address the mistakes from the GMO debate and challenge the "technology victim mentality" that has previously been peddled in Africa by anti-technology activists over the last two decades, and thereby nurture an enabling environment for GEd.

One way is by incorporating shared values, trust factors and appropriate messaging in a language understood by broad stakeholders. One approach greatly applied in global biotechnology and biosafety programs is the "3Is" strategy: Integrity > Inspire > Inform.

Integrity: This acts as a main element for building trust and a positive reputation. Failure to manage stakeholder expectations may compromise these efforts, and in this case, diminish the support and interest needed for creation of an enabling environment. To avert such an outcome, GEd developers in Africa must engage the public in an open and honest bidirectional dialogue, including not only stakeholder benefits but also their (GEd) potential limits, myths, and pitfalls.

Inspire: To succeed, GEd products must have the political goodwill of the African governments. One approach is to hold workshops where regulators, technology developers and other stakeholders meet to learn from international experiences and draw consensus on future actions. To foster adequate and harmonized regulatory approaches to ease adoption and implementation of GEd technologies across Africa, regulators can leverage on the African "comradery" and continental bodies such as AUDA-NEPAD and expertise from international organizations such as Program for Biosafety Systems (PBS) administered through the International Food Policy Research Institute (IFPRI) to develop and inform and policies in neighboring African countries. It is encouraging to note that Africa Union has recognized GEd technologies as crucial pillars to deliver on its STI agenda further drawing support and trust from member states.

Inform: Rather than the common practice of general communication approaches, developers of GEd products in Africa can consider adopting a data driven communications strategy based on stakeholders' information and knowledge needs. A proven approach that has worked is to identify key players through a participatory stakeholders net mapping analysis. The network's high ranking societal trust and credibility will contribute towards building public confidence and obtaining "social license to operate" for GEd technology in Africa.

Still, achieving widespread acceptance of GEd and shedding the GMO label will be challenging and may require additional strategies not covered here. Each African country has its own unique and complex issues. It's also unrealistic to assume that a country's stance on emerging technologies is static, as these positions can shift due to political influence.

3. Conclusions and perspectives

As seen in the examples given here, Africa is making steady progress in development of demand driven GEd products aimed at solving some of the continent's most intractable constraints of food security. Significant progress is also being made in policy and legal frameworks and communication strategies to enhance acceptance and technology uptake. Yet a greater sense of urgency is needed; climate change, global conflict and political unrest, and a large, fast-growing, and more prosperous population in Africa are creating severe stress on value chains and food security. Africa must act quickly to overcome the bottleneck of low science strength, enact capability training, and harmonize GEd policies and nurture an enabling environment for utilization of GEd products.

CRediT authorship contribution statement

Steven Runo: Writing – review & editing, Writing – original draft, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Conceptualization. **Margaret Karembu:** Writing – review & editing, Writing – original draft, Software, Resources, Project administration, Funding acquisition, Conceptualization. **Francis Nan'gayo:** Writing – review & editing, Writing – original draft, Investigation, Funding acquisition. **Firew Mekbib:** Writing – review & editing, Writing – original draft. **Teklehaimanot Haileselassie:** Writing – review & editing, Writing – original draft, Investigation, Funding acquisition. **Kassahun Tesfaye:** Writing – review & editing, Writing – original draft, Investigation, Conceptualization. **Jesse R. Lasky:** Writing – review & editing, Writing – original draft, Conceptualization. **Huirong Gao:** Writing – review & editing, Writing – original draft, Investigation, Formal analysis, Data curation, Conceptualization. **Todd Jones:** Writing – review & editing, Writing – original draft, Supervision, Resources, Data curation, Conceptualization.

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

No data was used for the research described in the article.

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