CRISPR Gene Editing Drivers, Barriers and Prospects: A Comparative Study among Plant Scientists Globally

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Introduction

Global food production is under increasing pressure from multiple external factors, including climate change (Hasegawa et al., 2021; Müller et al., 2011; Ray et al., 2019; Rosenzweig et al., 2014), population growth (Charles et al., n.d.; Ray et al., 2013; Tilman et al., 2011; United Nations - Department of Economic and Social Affairs, 2019; van Dijk et al., 2021) and water scarcity (Dolan et al., 2021; Falkenmark, 2013; FAO, 2012). Weather and climate volatility are expected to increase with global climate change, resulting in the emergence and growth of new and existing viruses (Chakraborty & Newton, 2011; Chaloner et al., 2021; Karpicka-Ignatowska et al., 2021) and pests (Barford, 2013; Bebber et al., 2013; Ma et al., 2021), which have the potential to reduce agricultural productivity (FAO, 2020). The Intergovernmental Panel on Climate Change (IPCC) hypothesizes that heat thresholds for agriculture will be exceeded more frequently and for longer durations as temperatures globally are rising further threating agricultural production and global food security (Hasegawa et al., 2021; IPCC, 2021; Lesk et al., 2016; Verschuur et al., 2021).

Furthermore, the global population is expected to increase up to 9.7 billion people in 2050 (United Nations - Department of Economic and Social Affairs, 2019), increasing the demand for food globally between an estimated 36% and 56% between 2010 and 2050 (van Dijk et al., 2021). This increase, in combination with the external pressure from climate change, water scarcity and an increasing number of crop pests and diseases puts heavy pressure on agricultural production worldwide to keep up with demand. Especially seen in the light of food security, production solutions are needed to ensure a sustainable and sufficient agricultural production globally.

Between 720 and 811 million people suffer from chronical undernourishment globally in 2020, an increase of 118 up to 161 million people compared to 2019 and 9,9 percent of the global population. The FAO estimates that almost one-third of the global population did not have access to adequate food in 2020 (FAO, 2021). Plant breeding is seen as one of the most significant contributors to yield increases in agricultural production in the last decades and one of the greatest tools to decrease global food security (Qaim, 2016). According to Evenson and Gollin (2003), modern seed varieties contributed almost 21% to the agricultural production growth in developing countries, highlighting the importance of plant breeding in global food security. The Green Revolution was a period from 1960 to 2000 in which modern high-yielding crop varieties (MVs) were developed, to support developing countries in their objective to reduce food insecurity. The introduction of new high-yielding rice and wheat varieties led to up to tripled production numbers in Latin-America and Asia, resulting in increased food security in these areas (Evenson & Gollin, 2003; Pingali, 2012; Qaim, 2016). Despite the successes, critics argue that the Green Revolution also had negative impacts on the sustainability of agriculture, due to the intensive use of fertilizers, increased water consumption and degradation of the soil (Evenson & Gollin, 2003; John & Babu, 2021; Pingali, 1994, 2012).

New plant breeding techniques and their role in the future of agriculture

Currently, New Plant Breeding Techniques (NPBTs) are emerging as a response to both the increasing global food demand and increasing pressure on the environment (Enfissi et al., 2021; Qaim, 2020; Schaart et al., 2015; Shan-e-Ali Zaidi et al., 2019; Smith et al., 2021; Van de Wiel et al., 2018). These new breeding techniques consist of e.g. cisgenesis (Van de Wiel et al., 2018), induced early flowering (Schaart et al., 2015), agro-infiltration (Enfissi et al., 2021), genetic modification (Klümper & Qaim, 2014; Zilberman et al., 2015, 2018) and gene editing (Qaim, 2020; Shan-e-Ali Zaidi et al., 2019; Smith et al., 2021). Genetic modification (GM) of crops, has spread rapidly across major agricultural production areas in the last decades. In the 1980s the technology came up in the agri-biotechnology industry, quickly attracting the interest of the public (Barrows et al., 2014). Genetic modification of crops is described by the Food and Agricultural Organization of the United Nations (FAO) (FAO, 2011) as: ‘An organism in which one or more genes (called transgenes) have been introduced into its genetic material from another organism using recombinant DNA technology. For example, the genes may be from a different kingdom (such as from a bacterium to a plant) or a different species within the same kingdom (e.g. from one plant species to another)' (FAO, 2011). The technology allows that the DNA of an organism (e.g. food crops) can be manipulated and transferred to another organism. Through this transferring, preferred traits of an organism can be introduced into another organism (Raman, 2017). Some functions and benefits of GM include: pest resistance, biofortification of crops (Zilberman et al., 2018), herbicide tolerance (Klümper & Qaim, 2014) and improved resistance to insect pests and viral infections (Brookes & Barfoot, 2020). According to Brookes & Barfoot (2020), the introduction of GM has resulted in a 8.3% reduction in pesticide use worldwide and an almost 23 million kg reduction in carbon emissions in 2018 globally. Despite the perceived benefits, and GM already being deployed by more than 17 million farmers worldwide (Brookes & Barfoot, 2020), controversy surrounds the technology. Critics are concerned about the impact of GM on biodiversity and the ecology (Uzogara, 2000), biosafety and the health risks for consumers (Kumar et al., 2020), the effects on non-targeted organisms and the dominance of five multinationals (Monsanto, Syngenta, Bayer CropScience, Dupont & Limagrain) who own 70% of the GM seed market, which raises concerns about possible exploitation of farmers (Kumar et al., 2020). This criticism has led to mixed public acceptance of GM crops (Cui & Shoemaker, 2018) and strict regulation of genetically modified organisms, particularly in the European Union, raising the costs for commercialization significantly (Shew et al., 2018).

Gene editing (GE) technologies, allow plant scientists to alter, delete and/or add genetic material at site-specific locations in the gene of a living organism. Key differences between GM and GE are that GE technologies can make more accurate site-directed insertions in the DNA and that the insertion of foreign DNA from another organism (transgenesis) is less common in gene editing technologies (Ding et al., 2016; Martin-Laffon et al., 2020; Qaim, 2019; Ricroch, 2019). Examples of existing gene editing technologies are transcription activator-like effector nucleases (TALENs), Zinc-finger nucleases (ZFNs) and clustered regulatory interspaced short palindromic repeat (CRISPR). TALENs use engineered nucleases to make double-strand breaks (DSBs) at specific locations in the gene of a living organism. These breaks are repaired and sequence alterations can be created (Joung & Sander, 2013). ZFNs are programmable nucleases consisting of DNA-binding zinc-finger proteins, which are used to cut the DNA. ZFNs have relatively high off-target effects (M. Song et al., 2014).

Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) are found in the immune system of bacteria and archaea. This immune system, has the ability to find and exterminate unwanted DNA in a highly effective and specific manner (Li et al., 2016). CRISPR allows scientists to delete certain viruses from plants and make diseases inheritable for humans and animals (Jiang & Doudna, 2017; Manghwar et al., 2019; G. Song et al., 2016). Examples are the improved resistance again rice blast in China (Wang et al., 2016), the elimination of HIV-1 genomes from human cells using CRISPR (Kaminski et al., 2016) and the increase of the shelf-life of tomatoes (Yu et al., 2017). CRISPR is especially known for its simplicity and adaptability (R. K. Joshi et al., 2020). TALENs and ZFNs are protein-dependent DNA cleavage systems, whereas CRISPR falls under the RNA-dependent DNA cleavage systems category (K. Zhang et al., 2017). Also, variation introduced through CRISPR technology can be indistinguishable from variations that occur naturally, making it very difficult to know which crops have been edited using CRISPR gene editing (Chilcoat et al., 2017).

CRISPR gene editing applications and controversy

Potential functions of CRISPR technology are herbicide resistance (Ricroch et al., 2017), drought resistance (Chilcoat et al., 2017), salt soil tolerance (Farhat et al., 2019), insect resistance (Zahoor et al., 2021), biofortification (Chilcoat et al., 2017; Jia & Nian, 2014; Ricroch et al., 2017), fungus resistance (Ricroch et al., 2017), virus resistance (Ali et al., 2016; Wang et al., 2016), increased shelf life (Yu et al., 2017), fertilizer use efficiency (Tiwari et al., 2020a) and improved cultivation of crops, all of which have potential to reduce global food insecurity and improve sustainability of agricultural production.

The technology has the potential to contribute to the solutions of problems encountered in food production globally, especially in developing countries. Feasible beneficiaries of CRISPR gene editing are reduced food insecurity (S. Ahmad et al., 2021; Georges & Ray, 2017b; Karavolias et al., 2021; Massel et al., 2021b; Y. Zhang et al., 2019; Zhu et al., 2020), reduced environmental damage in agricultural production (S. Ahmad et al., 2021; Biswas et al., 2021b; Georges & Ray, 2017b; Karavolias et al., 2021; Massel et al., 2021b; Y. Zhang et al., 2019; Zhu et al., 2020), increased nutritional value in crops (S. Ahmad et al., 2021; Biswas et al., 2021b; Karavolias et al., 2021; Zhu et al., 2020), increased producer profits (S. Ahmad et al., 2021; Van der Oost & Fresco, 2021) and increased yields and reduced yield variability (S. Ahmad et al., 2021; Biswas et al., 2021b; Georges & Ray, 2017b; Karavolias et al., 2021; Zhu et al., 2020).

Despite the perceived benefits of CRISPR, like GM, the technology has also caused controversy among consumers, policymakers and agricultural producers. Perceived risks and barriers of CRISPR gene editing implementation are policy/legal issues around CRSPR gene editing (Andoh, 2017; Menz et al., 2020; Purnhagen, 2018; Smyth et al., 2014), struggling to find competent delivery methods (F. Zhang et al., 2014), lack of fundamental knowledge on gRNA design (Masmitjà et al., 2019; Wilson et al., 2018), intellectual property right issues (Martin-Laffon et al., 2019; Mulvihill et al., 2017), lack of knowledge and misunderstanding among consumers (Ishii & Araki, 2016; Shew et al., 2018), the risk of off-target effects (N. Ahmad et al., 2020; Graham et al., 2020; X. H. Zhang et al., 2015), the creation of gene drives (Dolezel et al., 2020; Noble et al., 2017) and the high costs of the technology and subsequently underdeveloped infrastructure and technical expertise. This controversy, has led to the decision of the European Union (EU) to make CRISPR gene edited crops subject to strict GM regulations, limiting the applications of the technology and significantly increasing the costs of commercialization of CRISPR gene edited crops (Purnhagen, 2018; Purnhagen & Wesseler, 2020). Other countries like Argentina and the United States of America use a case-by-case judgement system to assess whether a CRISPR gene edited organism is GM or not. The United States Department of Agriculture (USDA) exempted 35 out of the 86 inquiries since 2010, using genome editing. Examples are genome edited canola and soybeans with modified oil composition using TALEN. In Argentina, a producer must proof the absence of a transgene in the crop in order to be exempted from GMO regulation (Menz et al., 2020).

Wageningen University & Research, one of the leading agricultural research institutes and universities, is the first institution to freely license its CRISPR patents as they believe it can play a pivotal role in fighting food insecurity and climate change (Van der Oost & Fresco, 2021). The potential of CRISPR to combat global food insecurity and its controversy amongst consumers, producers and regulatory bodies prior to its commercial release highlights the importance of better understanding where and how CRISPR could be implemented in commercial agriculture.

Literature gap in CRISPR research

The majority of current research on CRIPSR gene editing is either about the benefits, risks and barriers of the technology, or the consumer perceptions of (CRISPR) gene edited foods (Ishii & Araki, 2016; Shew et al., 2018). Plant scientists´ voices are heard, as they speak at conferences, join round tables with government officials and publish articles about the importance and/or risks of CRISPR gene editing. However, there lacks a holistic view on where the CRISPR gene editing sector is moving from plant scientists themselves. Therefore, this study aims to serve as the first step of reaching consensus among the global plant science community, about the potential and barriers of the CRISPR gene editing technology, and where and how CRISPR may emerge in commercial agriculture. This study will elicit the perceptions among plant scientists globally about what the major benefits, barriers and prospects of the technology are. These insights can be specified up to continent-, crop-and sector- (public/private) level which can help governments and the plant science industry to implement tailored strategies to overcome the challenges and mitigate the risks of CRISPR gene editing in order to improve food security and make food production more sustainable.

Research questions

In order to fill this literature gap, six research questions were formulated. All results will be specified to region (Africa, Asia, Europe, North America, Oceania and South America) and sector level (private and public).

1. What percentage of the current research and development budgets of plant research institutes/universities/private companies will be invested in CRISPR gene editing?
2. What will be the main functions of CRISPR gene editing?
3. What are, looking at the whole market (both producers and consumers), the main barriers of CRISPR gene editing adoption?
4. Which crops will benefit the most of CRISPR gene editing?
5. Who and/or what will be the main beneficiaries of CRISPR gene editing adoption?
6. Will the CRISPR gene editing sector be public or private sector dominated?

Research methodology and sampling

Target population

The target population of the survey consisted of plant scientists globally. Thus, any scientist active in the field of plant science with working knowledge on plant biology, plant pathology and/or plant breeding were targeted for this survey. Although the targets were heterogeneous in their disciplines (ranging from private to public institutions, working in different regions and on many different crops) they all were assumed to have fundamental technical knowledge on plants and crops and could assess the best what the implications of implementing a technology such as CRISPR are and will be in the food production sector. This assumption was made based on where the contact details of the targeted respondents were collected, at plant science faculties, research institutes, plant science associations and private companies active in plant sciences and biotechnology globally. Importantly, we wanted to target plant scientists across the globe, working in as many crops and cropping regions dealing with different (external) factors such as the climate, consumer acceptance, regulation, and food demands possible.

Sampling

To grasp the opinion of these many experts, the research method requires a wide reach as well as quantifiable data in order to answer the research questions. The research participants were targeted through stratified purposeful sampling, which is a form of non-probability sampling (Sandelowski, 2000). This form of sampling is chosen, as the target population of this study has specific traits; they are required to be knowledgeable about plant sciences and the CRISPR gene editing subject. Contact details of plant scientists were derived by conducting extensive online research. The websites of plant scientist platforms, societies, universities and private companies worldwide were (manually) scraped for contact details and listed. Also, the contact details of scientists who published about CRISPR gene editing technology were obtained from the Web of Knowledge database, regardless of whether they were predominantly positive or negative about the gene editing technology. This approach resulted in a database of 6294 e-mail addresses of plant scientists, to whom the survey was distributed using Microsoft Word´s mail merge option. All contact details were publicly available, which likely biased our sample towards the public sector as many private companies do not list individual e-mail addresses. Furthermore, in the e-mail we asked to further distribute the survey to colleagues active in the field of plant sciences, a form of snowball sampling (Leighton et al., 2021). The survey was also shared on LinkedIn by professors and other contacts aligned to Ghent University and the University of Arkansas, using hashtags (#) such as CRISPR, gene editing, new plant breeding techniques and CRISPRCas9.

Survey method

The complete survey is found in *Appendix 1*. The survey begins with a general introduction asking about the background of the plant scientist in terms of academic level (High school, BSc, MSc, Ph.D., Postdoc, Professorship, Other), activity in the public/private (or both) sectors, years of experience in the plant science sector and the activity in the fundamental or applied sciences. Respondents were then asked which regions their research and development activities of their respective research group/department primarily focuses on (Africa, Asia, Europe, North America, Oceania, South America), and whether their research group/department is active in CRISPR research and development, and if yes, beginning when.

Research and development budget allocation

The respondents were asked to indicate the percentage of the total research and development budget, which their research group or academic department currently allocates towards CRIPSR gene editing, as well as the percentage they envision to be allocated in three, five and ten years in the future. The results of this question can provide insight in the (relative) investments in CRISPR gene editing technology in different regions, among different crops and in the public and private sector. When funding research and development, there are different risks concerning the success of the new technology, such as market risk (competition, low demand, changing market conditions) and technological risk (technology fails to deliver expected results). Therefore, the level of investment in a new technology could provide insight in the level of confidence a program has in the technology (Bodner & Rouse, 2007). Current and anticipated future budget allocations in CRISPR gene editing technology, provide insight in the level of involvement plant scientists, research institutions and biotechnology companies currently have and are estimated to have in CRISPR gene editing. This question is intended to elicit where and by whom, we will see the largest growth in CRISPR funding.

Functions CRISPR gene editing

Participants were then asked about which functions of CRISPR gene editing could have the greatest impact in their region of expertise. The options that participants could choose from were herbicide resistance (Ricroch et al., 2017), drought resistance (Chilcoat et al., 2017), salt soil tolerance (Farhat et al., 2019), insect resistance (Zahoor et al., 2021), biofortification (Chilcoat et al., 2017; Jia & Nian, 2014; Ricroch et al., 2017), fungus resistance (Ricroch et al., 2017), virus resistance (Ali et al., 2016; Wang et al., 2016), increased shelf-life (Yu et al., 2017), fertilizer use efficiency (Tiwari et al., 2020b) and improved cultivation of crops. Because these benefits are not exhaustive, respondents were allowed to add additional functions in the ´Other´ box. Subsequently, the respondents were asked the question:

> *Given your research activities, how do you rate the probability of successful development and implementation of the following possible functions of the CRISPR gene editing technology in your region of expertise?*

This question was asked for each region separately, thus if a respondent indicated that he or she was active in multiple regions they would answer this question for each specific region they are active in. The respondents rated each function on a Likert scale from 1 (low probability) to 7 (high probability), where 8 represented the *´I do not know´* option. The Likert scale was chosen, as it is easy to construct, easy to interpret and complete. Contrary, a weakness may be the that participants avoid extreme responses (Taherdoost, 2019). A seven-point Likert scale was used, which is common in social research, provides nuance in the respondents' answers while at the same time seven attributes is also the maximum a human mind can distinguish at a time (A. Joshi et al., 2015). The results from this question can provide insights in which functions of the CRIPSR gene editing technology could be the most beneficial for each region worldwide and which function could have the highest likelihood of success, between crops and between the public and private sector.

Barriers of adoption CRISPR gene editing

The next section, aimed to elicit which barriers of adoption plant scientists think are the most binding across their region and sector for CRISPR gene editing implementation. The survey questions were again asked separately for each region, and the same Likert scale from 1 (strongly disagree) to 7 (strongly agree) was used. The question was asked as:

> *Given your research activities, please give your opinion about what the major barriers are that impede the large-scale implementation of CRISPR gene editing in your region of expertise.*

The barrier choices were policy/legal issues around CRSPR gene editing (Andoh, 2017; Menz et al., 2020; Purnhagen, 2018; Smyth et al., 2014), struggling to find competent delivery methods (F. Zhang et al., 2014), lack of fundamental knowledge on gRNA design (Masmitjà et al., 2019; Wilson et al., 2018), intellectual property right issues (Martin-Laffon et al., 2019; Mulvihill et al., 2017), lack of knowledge and misunderstanding among consumers (Ishii & Araki, 2016; Shew et al., 2018), the risk of off-target effects (N. Ahmad et al., 2020; Graham et al., 2020; X. H. Zhang et al., 2015), the creation of gene drives (Dolezel et al., 2020; Noble et al., 2017) and the high costs of the technology and subsequently lack of infrastructure and technical expertise. An ´*Other*´ option was not provided for this question as the questions were asked in statement form, see *Appendix 1* for examples. Results from this question can provide the scientific community a better understanding of barriers of adoption of CRISPR gene editing by region and differences between the public and private plant science community.

Benefits for specific food crops

The plant scientists were asked in which food crops they are active, multiple answers were possible. The list of food crop choices in the survey was based on the production data of food crops globally from the Food and Agricultural Organization (FAO, 2019), resulting in the following list of crops: *wheat, maize, soybean, rice, potatoes, cassava, sorghum, millet, yams, plantains, vegetables, fruits, legumes and other*.

For *vegetables, fruits, legumes* and *other* there was a text box available, in which the respondent was asked to specify the crop in more detail. As such, the respondents were asked which crops would benefit the most in their opinion from CRISPR gene editing in their region of expertise. The question was formulated as:

> *What is in your opinion the likelihood of the following crops to benefit significantly from CRISPR gene editing technology in your region of expertise?*

The respondents were asked to rate all crops (same crop choices as for the question which dealt with the question in which crop the respondents works) on a Likert scale from 1 (extremely unlikely) to 7 (extremely likely). The respondents were also provided with an *´I do not know´* option. With the results of this question, an assessment could possibly be made on which crops will benefit the most of CRISPR gene editing in a specific region according to the global plant science community.

Beneficiaries CRISPR gene editing

The next portion of the survey dealt with eliciting who and/or what anticipated beneficiaries of CRISPR gene editing would be. Respondents were asked to rate the possible beneficiaries of CRISPR gene editing, by the region of their expertise, on a seven-point Likert scale from 1 (no beneficiary) to 7 (major beneficiary). The question was formulated as:

> *What are (or will be) the major beneficiaries of CRISPR gene editing adoption in your region of expertise?*

The possible beneficiaries, based on previous literature research, were listed as follows: reduced food insecurity (S. Ahmad et al., 2021; Georges & Ray, 2017a; Karavolias et al., 2021; Y. Zhang et al., 2019; Zhu et al., 2020), reduced environmental damage in agricultural production (S. Ahmad et al., 2021; Biswas et al., 2021a; Georges & Ray, 2017a; Karavolias et al., 2021; Massel et al., 2021a), increased nutritional value in crops (S. Ahmad et al., 2021; Biswas et al., 2021b; Karavolias et al., 2021; Zhu et al., 2020), increased producer profits (S. Ahmad et al., 2021; Van der Oost & Fresco, 2021), increased yields and reduced yield variability (S. Ahmad et al., 2021; Biswas et al., 2021a; Georges & Ray, 2017a; Karavolias et al., 2021; Zhu et al., 2020). The answers to this question, could possibly give insight in what the perceived beneficiaries of CRISPR gene editing adoption are and in what regions they will emerge according to the plant scientists. It assists in answering the research question about what the main drivers for CRISPR gene editing adoption are.

Industry consensus on CRISPR gene editing subjects

The public funding of research and development in the agricultural industry, has been reduced in many countries and particularly in the United States (Nature Food, 2020). An exception in this regard, is China where a significant increase of patents can be observed, held and funded by the public sector (Cai et al., 2020). Contrary, private sector investments in the plant science industry globally rose from $5.1 billion to almost $16 billion in the period from 1990 till 2014 (Fuglie, 2016). Some scientists argue that this is an undesirable trend, as the access to new technologies will mainly be for those who can afford it as private companies have a profit orientation (Tripp & Byerlee, 2000; Van der Oost & Fresco, 2021). Currently, the majority of the CRISPR gene editing patents are owned by the United States, China, Japan and multiple European countries. Thirty-three percent of these patents are owned by private companies (Martin-Laffon et al., 2019). Wageningen University & Research has taken the first steps to make the CRISPR gene editing sector more inclusive, by licensing their CRISPR patents free of charge to those who aim to support food security in low-income countries with it (Van der Oost & Fresco, 2021). There exists a debate in the plant science sector on where the gene editing sector should be moving. Thus, insights in where the respondents foresee the technology moving could be of interest for policymakers, agronomists and stakeholders in the industry.

The final part of the survey consists of multiple statements which aim to measure on a seven-point Likert scale from 1 (strongly disagree) to 7 (strongly agree) if the CRISPR gene editing sector is moving into the direction of private sector/multinational dominance or if smaller companies and public institutions like universities can play a significant role, what the main dangers are of CRISPR gene editing adoption and if the technology will be available in developing countries or remains mainly for the biotechnology sector in developed countries. The statements asked to the respondents were:

1. *CRISPR gene edited foods should be subject to Genetically Modified Organisms regulation*
2. *CRISPR gene editing can be one of the major contributors to the solutions of environmental and food insecurity issues*
3. *CRISPR gene editing technology is currently too expensive to make it a feasible option for developing countries*
4. *Off-targeted editing is a significant threat for CRISPR gene editing in plant breeding*
5. *Potential negative side-effects of CRISPR gene editing, have not yet been investigated thoroughly enough to bring gene edited food crops to the market*
6. *CRISPR gene editing patents will primarily be owned by large plant breeding multinationals*
7. *In 25 years, the majority of food crops grown globally will be edited using CRISPR gene editing technology*
8. *The private sector will dominate the CRISPR gene editing market in terms of patents and edited crops on the market, rather than the public sector*
9. *The CRISPR gene editing market will be dominated by multinationals, startups and scaleups will play a minor role*
10. *CRISPR gene editing will remain an expensive technology and therefore primarily be applied in developed countries*

Data analysis and statistical testing

After collecting the responses, statistical analyses were performed on the different variables of the survey questions. All questions were answered on a scale from one to seven and consequently a mean score could be derived from every variable in the survey, separated by region and sector. All descriptive statistics were extracted from Qualtrics and compared. Two tests are common to use for Likert-scale data: t-tests and Mann-Whitney tests. Both tests have nearly equivalent Type-I error rates and power (de Winter & Dodou, 2010). Thus, pairwise t-tests were used for further analysis. The statistical analysis focused on the four key questions: functions of CRISPR, barriers of CRISPR implementation, crop benefits and beneficiaries of CRIPSR adoption. The answers to these questions, contain the information to answer the research questions. Also, they lend themselves well for statistical comparison, as all the crops, barriers, functions and beneficiaries received different scores from the respondents which can be compared.

For each variable, a weighted average mean was calculated of all the scores given by the respondents, per region and sector. We chose to use a weighted average mean, because there were differences in number of responses among variables within all questions. Because of the fact this survey contained many variables per question, the decision was made to compare each variable score to the weighted average mean using a pairwise t-test instead of comparing each variable to every other variable in the question. In this way outlying scores could be detected, scores which significantly differ from the weighted average of all scores of e.g. barriers of CRISPR adoption in Africa or the beneficiaries of CRISPR in North America. By this, we could assess whether the respondents rated certain functions, barriers, crop benefits and beneficiaries higher or lower than others, separated by region and sector. Also, some questions contained up to eleven variables, making it almost impossible to test every variable against each other while still being able to draw up comprehensible results.

These tests, show which functions are expected by plant scientists to be successfully or less successfully developed with CRIPSR, which barriers are perceived more or less impeding, which crops will benefit the most from CRISPR gene editing and who or what the main beneficiaries of CRISPR will be. A significance level of five percent was used for all tests. Pairwise t-tests were only run within a region or sector, as comparing between regions and/or sectors is difficult, due to major context differences. However, this research draws a picture on where the major difficulties, opportunities and beneficiaries of CRISPR gene editing lay per region and sector.

Results

Survey responses

The sampling and distribution efforts resulted in 1040 unique responses, of which 669 were usable. Of the entire sample, 371 responses were deleted, for two reasons. Given the length of the survey and thought which was required, any responses under 120 seconds were deleted (47 responses). Also, responses with a completion rate lower than 90 percent were deleted (324 responses).

Research and development budget allocation towards CRISPR gene editing

The survey results, visualized in *Table 2,* show an interesting development of the investments in CRISPR gene editing technology, according to plant scientists globally. The question which was asked to the respondents was:

> *Could you indicate for your research group/department, what percentage of the total research and development budget is/will be currently/in 3 years/in 5 years/in 10 years allocated to CRISPR gene editing research and development?*

Table 2: Budget allocation towards CRISPR gene editing (in % of the total research and development), separated by region and sector

	Current	**in 3 years**	**in 5 years**	**in 10 years**
All respondents	26,27%	25,05%	29,15%	33,55%
Africa	21,18%	21,77%	27,87%	34,73%
Asia	26,63%	26,76%	32,06%	35,23%
Europe	20,63%	21,29%	24,81%	28,96%
North America	26,08%	23,18%	26,17%	30,62%
Oceania	32,25%	28,06%	34,82%	34,31%
South America	16,53%	19,76%	26,84%	34,12%
Public	26,64%	25,84%	30,39%	34,87%
Private	15,58%	14,17%	20,29%	28,33%

The mean current research and development budget allocation towards (in % of the total research and development budget) CRISPR gene editing according to all respondents who answered the question is slightly higher than a quarter of their total budget, 26,27%. Interestingly, according to the plant scientists participating in this survey this percentage will drop to 25,05% in 3 years. In 5 years the mean allocation of budget towards CRISPR gene editing increases again to 29,15% and reaches 33,55% in 10 years, which equals a more than 7% relative investment increase in CRISPR gene editing globally in the next ten years. While interpreting these results it is important to realize that the presented numbers are relative (% of total research and development budget) and no assumptions about the size of the absolute CRISPR gene editing investments can be derived from the data.

Research and development budget allocation towards CRISPR – Regional trends

Looking at the regional distribution of current and future budget allocations in *Table 2*, multiple differences can be observed. South America (16,53%), Europe (20,63%) and Africa (21,18%) denote the lowest current budget allocations towards CRISPR gene editing technology, whereas the allocations of North America and Asia are around 26,08% and 26,63% respectively with the current allocation in Oceania being the highest with 32,25%. Interestingly, the envisioned budget allocations in 3 years drop in North America (23,18%) and Oceania (28,06%) compared to their current budget allocations. There is likely selection bias in these numbers in that participants who choose to answer the survey are likely active in gene editing and would represent research groups with higher than average budgets allocated to CRISPR.

The budget of the other regions increase minimally, only South America denotes an increase to 19,76%. The 5 years allocation of budgets increases, compared to the 3 years allocations, with increases across all regions ranging from 2,99% (North America) to 7,08% (South America). In 10 years, African (34,73%), Asian (35,23%), Oceanian (34,31%) and South American (34,12%) plant scientists expect to allocate over more than one-third of their total budget towards CRISPR gene editing technology. North America and Europe remain slightly behind, with allocations of 30,62% and 28,96% respectively. Overall, all budget allocations increase over a ten-year timespan. The highest relative increases between now and ten years in budget allocation towards CRISPR gene editing emerge in South America (17,59%) and Africa (13,55%). The budget allocation in Asia increases 8,6%, in Europe 8,33%, in North America 4,54% and in Oceania 2,06%. It is important when interpreting these results, that these are relative allocations (in % of the total research and development budget)

Research and development budget allocation towards CRISPR – Public/private trends

Table 2 presents the sectoral differences of the allocation of research and development budgets towards CRISPR gene editing. The average current budget allocations were reported at 26,64% for the public sector and 15,58% for the private sector. The allocation decreases in 3 years for both the public sector (25,84%) and the private sector (14,17%), after which the allocation increases in 5 years, a similar pattern as observed earlier in the regional comparison. In 5 years, public sector budget allocation reaches 30,39% and private sector allocation was reported to be on average 20,29%. According to the survey respondents, relative budget allocations towards CRISPR gene editing reach 34,87% for the public sector and 28,33% in the private sector in 10 years. Overall, looking at the difference between the current and in 10 years budget allocations, the growth is 8,23% for the public sector and 12,75% for the private sector according to the survey data. Again, it is important to interpret these results in terms of relative changes and not absolute spending. Since the base amount spent on CRISPR was not asked there is no way to derive total increase in dollars from these estimates.

Functions of CRISPR gene editing

Table 3 highlights the mean scores on the potential of successful implementation of possible functions of CRISPR gene editing can be found, separated by region and sector. Respondents rated the functions on a Likert-scale from 1 (low probability) to 7 (high probability). The question asked was:

> *Given your research activities, how do you rate the probability of successful development and implementation of the following possible functions of the CRISPR gene editing technology in your region of expertise?*

Functions of CRISPR – A regional comparison

African plant scientists rate *drought resistance*, *insect resistance*, *fungus resistance* and *virus resistance* as the functions of CRISPR gene editing with the highest probability of successful implementation in their region, statistically compared to the weighted mean of all functions in Africa of 3,89. The scores of these functions are significantly higher (P < 0,05) than the weighted average of all functions in Africa. Contrary, *salt soil resistance*, *fertilizer use efficiency* and *improved cultivation* were rated significantly lower as possible successful functions of CRISPR in Africa. These non-significant scores do not indicate the specific function is not important, just unlikely to be successfully implemented. Successful implementation could be due to targeted funding, the severity of an issue or the number of plant scientists working on said issue. The survey did not set out to explain why an issue was important but rather what issue(s)/function(s) plant scientists thought would be successfully addressed via CRISPR.

In Asia, *fungus resistance and virus resistance* are the highest rated functions, whereas *fertilizer use efficiency* is seen as least viable function of the CRISPR technology in the Asian context according to plant scientists active in the region. All functions were statistically compared to the weighted mean of all functions in Asia of 3,95.

Plant scientists with research programs focusing on European agriculture, see *drought resistance*, *insect resistance*, *fungus resistance* and *virus resistance* as the most likely functions to be successfully implemented, statistically compared to the weighted mean of all functions in Europe of 3,56. Interestingly, all other functions score significantly lower than the weighted average mean, ranging from 2,28 to 3,28.

North American plant scientists indicated that *herbicide resistance* will likely be the most successful function with a score of 5,02, the only function score exceeding five across all regions and sectors. *Fungus resistance* and *virus resistance* reported significant higher scores as well, with 4,96 and 4,74, respectively. On the other end *salt soil resistance*, *biofortification*, *fertilizer use efficiency* and *improved cultivation* score significantly lower than the weighted average function score in the North American region. All functions in North America were statistically compared to the weighted mean of all functions, 4,00.

Oceania and South America denoted no significant differences compared to the weighted average function score of their regions. Again, this lack of statistical difference does not indicate that CRISPR would have low probability of success/adoption in these areas, rather that there is no obvious function in which CRISPR may be targeted.

Overall, four regions (Africa, Asia, Europe and North America) denoted significant higher scores for *fungus resistance* and *virus resistance* and significant lower scores on *fertilizer use efficiency* as possible function of CRISPR gene editing. *Drought resistance* and *insect resistance* seem to be viable functions of CRISPR in Africa and Europe, where *herbicide resistance* appears to be dominant in North America according to plant scientists.

Barriers of CRISPR adoption

Table 4 shows the perceived barriers of CRISPR gene editing implementation, across different regions and sectors. The survey participants rated nine barriers on a Likert-scale from 1 (strongly disagree) to 7 (strongly agree) which resulted in a mean score for every barrier. The question asked was:

> *Given your research activities, please give your opinion about what the major barriers are that impede the large-scale implementation of CRISPR gene editing in your region of expertise.*

Barriers of CRISPR adoption – A regional comparison

African plant scientists, foresee multiple barriers as significantly more impeding than others*. Policy/ legal issues* was rated the highest with a score of 5,80, closely followed by *lack of infrastructure/technical expertise* (5,71). *High development costs* and *consumer perceptions/knowledge* gap were the other two barriers that scored significantly higher than the weighted mean, with a score higher than five. Conversely, *off-target effects, gene drives* and *gRNA design* were scored significantly lower than the weighted average of all barriers of CRISPR gene editing implementation in Africa. All barriers in Africa were statistically compared to the weighted mean of all barriers in Africa, being 4,97.

In Asia, *policy/legal issues* are considered as the most impeding barrier of CRISPR gene editing implementation, followed by *consumer perceptions/knowledge gap*. *Intellectual property rights issues* is another barrier considered as more impeding than the weighted average of all barriers in Asia (4,24). *Off-target effects*, *gRNA design* and *lack of infrastructure/technical expertise* are considered less impeding than the weighted average of all barriers in Asia.

European plant scientists who were surveyed rated *policy/legal issues* as the most impeding barrier of CRISPR gene editing implementation, with a score of 6,72 it is the highest rated barrier across all regions and both the public and private sector. *Consumer perceptions/knowledge gap* denoted a significant higher score than the weighted average with 5,91 as well, followed by *intellectual property rights issues*. Interestingly, all other barriers were rated significantly lower than the weighted average mean of all barriers (4,12) by plant scientists with expertise in European agriculture.

North American plant scientists rate *policy/legal issues*, *consumer perceptions/knowledge gap* and intellectual property rights issues significantly higher than the weighted mean of all barriers in the North American region (3,98). The other barriers were all rated significantly lower than the weighted average of all barriers in the region, except for *high development costs* and *delivery methods* for which no differences from the weighted average were found.

In Oceania *policy/legal issues* and *consumer perceptions/knowledge gap* were considered as the most impeding barriers of CRISPR gene editing implementation, with scores of 5,22 and 5,18 respectively. The only significant lower score than the weighted mean was found for *gRNA design*. All barriers in Oceania were statistically compared to the weighted mean of all barriers in Africa, being 3,98.

Respondents with expertise in South America, rated *consumer perceptions/knowledge gap* and *high development costs* as the biggest impediments of CRISPR adoption in the region. *Off-target effects* are considered as least impeding in the South American plant science industry. The weighted mean of all barriers in South America was 4,10.

Across all regions, *consumer perceptions/knowledge gap* is considered as a significant more impeding barrier than the weighted average of all barriers in the corresponding region. *Policy/legal issues* is rated significantly higher than the weighted average of the corresponding region in all regions, except South America. *Intellectual property rights issues* is rated as highly impeding in Asia, Europe and North America. Not surprisingly, we see that *high development costs* is considered as a barrier in Africa and South America. Contrary, *off-target effects* scores significantly lower in all regions, except Oceania. The barrier *gRNA design* denotes low scores as well in all regions, except in South America. *Lack of infrastructure/technical expertise* denotes low scores in the most developed regions in terms of CRIPSR gene editing, Asia, Europe and North America.

Barriers of CRISPR adoption – A public/private comparison

Plant scientists active in the public sector listed, in this order, *policy/legal issues, consumer perceptions/knowledge gap* and *intellectual property rights issues* as significantly most impeding barriers of CRISPR gene editing. All other barriers score significantly lower than the weighted average barrier score of the public sector, except for *delivery methods* and *high development costs* for which no differences from the weighted mean were found. All barriers were tested against the weighted mean of 4,31.

In the private sector, *policy/legal issues*, *consumer perceptions/knowledge gap* and *intellectual property rights issues* are considered as most impeding. Unlike the public sector, the private sector also considered *high development costs* as significantly more impeding than the mean of all barriers. All other barriers are scored significantly lower than the weighted average mean, being 4,09.

The public and private sector plant scientists exhibited similar patterns when it comes to the perception of barriers of CRIPSR gene editing adoption. The key difference is that the private sector considers *high development costs* as a more impeding barrier compared to other barriers as well, where the public sector does not. Also, no differences were found for *delivery methods* in the public sector, where the private sector scores this barrier as significantly lower than the weighted average mean of all barriers in the private sector.

	Africa (σ=4,97) **		Asia (σ=4,24) **		Europe (σ=4,12) **		North America (σ=3,98) **		Oceania (σ=3,98) **		South America (σ=4,10) **		Public (σ=4,31) **		Private (σ=4,09) **	
Barriers	Mean	# of responses	Mean	# of responses	Mean	# of responses	Mean	# of responses	Mean	# of responses	Mean	# of responses	Mean	# of responses	Mean	# of responses
Policy/legal issues	5,80	169	5,45	99	6,72	307	4,48	201	5,22	18			5,70	561	5,65	217
Delivery methods					3,88	295									3,58	217
gRNA design	4,59	169	3,15	97	2,88	296	3,29	197	2,50	18			3,45	561	3,15	217
Intellectual property rights			4,80	94	4,46	299	4,45	198					4,57	561	4,38	217
Consumer perceptions/ knowledge gap	5,46	167	4,98	96	5,91	301	5,29	198	5,18	17	5,04	51	5,51	561	5,40	217
Off-target effects	3,83	167	3,75	96	3,43	295	3,37	200			3,14	50	3,56	561	3,37	217
Gene drives	3,87	168			3,37	299	3,55	199					3,62	561	3,46	217
High development costs	5,67	166			3,58	298					4,78	51			4,36	217

Lack of infrastructure/ technical expertise	5,71	170	3,79	98	2,75	297	3,30	199					3,78	555	3,45	217

Table 4: Plant scientists' opinions on the barriers of CRISPR gene editing technology, rated on a scale from 1 (strongly disagree) to 7 (strongly agree)

* The presented values denote an issue of the corresponding variable which was statistically (P<0.05) higher (green font) or lower (red font) than the weighted average of all barriers of CRISPR implementation of the corresponding region/sector. An empty cell denotes no statistical difference was found

** The σ denotes the weighted average of the aggregated barriers of the corresponding region/sector

Benefits of CRISPR gene editing for specific crops

In *Table 5,* the results on the benefits for specific crops are presented by region and sector. Respondents rated eight crops (respondents could introduce additional crops through the *Other* option) on a scale from 1 (extremely unlikely) to 7 (extremely likely). The question asked was:

> *What is in your opinion the likelihood of the following crops to benefit significantly from CRISPR gene editing technology in your region of expertise?*

Crop benefits – A regional comparison

African plant scientists, rate three crops as the (significant) likeliest to benefit from CRISPR gene editing in their region*. Maize* is the rated the highest compared to the other crops, with a score of 5,98. *Soybean* (5,13) and *cassava* (4,97) were also statistically higher than the average of all crops likely to benefit from CRISPR. One crop is rated significantly lower than the weighted average score of all crops in Africa (4,46), which is *plantains*.

Respondents with expertise in the Asian region, see the most potential in (in this order): *rice*, *soybean*, *maize*, *wheat* and *potatoes*, respectively. *Rice* received the score of 6,33, which is the highest score of all crops across all regions. All other crops in Asia were rated significantly lower than the weighted average score of 4,21.

For the European region, four crops scored significantly higher than the weighted mean of all crops (3,40): *wheat*, *maize*, *potatoes* and *soybean*. All other crops received a significant lower score, except for *rice* for which no statistical difference from the weighted mean was found.

In North America, five crops were indicated as most likely to benefit from CRISPR gene editing. *Maize*, *soybean*, *wheat*, *potatoes* and *rice* scored statistically higher than the weighted average of all crops in North America. Not surprisingly, *cassava* and *plantains* scored significantly lower.

In Oceania, no statistical different scores from the weighted average mean of 3,32 were observed.

In South America, *soybean* was expected to benefit significantly from CRISPR gene editing with a score of 6,26. *Maize*, *rice* and *wheat* were also expected to benefit significantly more from the technology than other crops. All other crops are predicted to benefit less, except for *potatoes* for which no statistical differences from the weighted mean of 3,80 were found.

Overall, a clear trend can be observed regarding the crop benefits. In all regions except Oceania, *maize* and *soybean* are expected to benefit significantly more than other crops from CRISPR gene editing. *Wheat* scores significantly higher in all regions, except for Africa and Oceania. Furthermore, *rice* is expected to benefit significantly more compared to the other crops in Asia, North America and South America. *Potatoes* are expected to benefit in Asia, Europe and North America, whereas *cassava* is only expected to benefit from CRISPR gene editing in Africa. *Plantains* is not expected to benefit exceptionally from the technology in any of the regions. Also, *other* crops were not rated significantly higher in any of the regions.

Crop benefits – A public/private comparison

Looking at sectoral level, comparable results between the public and private sector were found. In both sectors *wheat*, *maize*, *soybean* and *potatoes* scored significantly higher than the weighted average crop benefit score of the corresponding sector (3,98 for public, 3,66 for private). Also, *cassava*, *plantains*, *sorghum* and *other* scored significantly lower in both sectors. The only difference between the two sectors is the fact that a significant higher result emerged for *rice* in the public sector, whereas in the private sector no statistical differences were found for *rice*.

Beneficiaries of CRISPR gene editing

Table 6 presents the results on the perceived beneficiaries of CRISPR gene editing according to plant scientists globally. Six answer options were provided to the respondents as well as an *Other* option. These options were rated on a scale from 1 (no beneficiary) to 7 (major beneficiary). The question asked was:

> *What are (or will be) the major beneficiaries of CRISPR gene editing adoption in your region of expertise?*

Beneficiaries of CRISPR – A regional comparison

Analyzing the results of the beneficiaries question, it can be observed that little statistical differences were found across all regions. In Africa, only *yields* is rated higher than the weighted average of 3,76 of all beneficiaries in the region. In Europe and North America, *food insecurity* scores statistically lower than the weighted average, whereas *yields* scores significantly higher than the weighted mean in both regions. All beneficiary scores were statistically compared to the weighted mean of all beneficiaries in the corresponding region, being 3,94 for Europe and 3,96 for North America. In Asia, Oceania and South America, no statistical differences were found, meaning that all beneficiary options were scored highly comparable.

Beneficiaries of CRISPR – A public/private comparison

In both the public and private sector *yields* denoted significant higher scores than the weighted average scores of the corresponding sector (3,98 for the public sector, 3,66 for the private sector). For the public sector, *producer profits* denoted a statistically higher score as well, whereas *reduced food insecurity* denoted a significant lower score than the weighted mean. In the private sector no statistical differences were found for these two variables.

Table 6: Plant scientists' opinions on the beneficiaries of CRISPR gene editing technology, rated on a scale from 1 (no beneficiary) to 7 (major beneficiary).

	Africa (σ=3,76) **		**Europe** (σ=3,94) **		**North America** (σ=3,96) **		**Public** (σ=3,98) **		**Private** (σ=3,66) **	
Beneficiaries	**Mean**	**# of responses**	**Mean**	**# of responses**	**Mean**	**# of responses**	**Mean**	**# of responses**	**Mean**	**# of responses**
Reduced food insecurity			3,33	295	3,25	186	3,39	540		
Environmental damage agriculture										
Increased nutritional value in crops										
Producer profits							4,16	535		
Increased yields	4,16	171	4,33	293	4,39	187	4,33	540	4,24	207
Yield variability										
Other****										

* The presented values denote an issue of the corresponding variable which was statistically ($P<0.05$) higher (green font) or lower (red font) than the weighted average of beneficiaries of CRISPR implementation of the corresponding region/sector. An empty cell denotes no statistical difference was found

** The ơ denotes the weighted average of the aggregated beneficiaries of the corresponding region/sector

*** No significant differences from the weighted average mean were found for Asia, South America and Oceania, therefore these results are not included in Table 6

**** Other consists of answers the respondents were allowed to put forward themselves, examples are: *improved quality of produce*, *reduced biotic stresses* and *reduced use of agro-inputs*

Industry consensus on CRISPR gene editing subjects

Table 7, shows the scores on different statements concerning multiple topics such as CRISPR regulation, CRISPR market structures and risks of CRISPR gene editing that were asked to the survey respondents. These statements were rated on a seven-point Likert scale from 1 (strongly disagree) to 7 (strongly agree). No statistical tests were performed on these variables. However, multiple trends can be observed. The first statement compared CRISPR gene edited and GM crops, which was formulated as:

> *CRISPR gene edited foods should be subject to Genetically Modified Organisms regulation*

Across both sectors and all regions, scientists score the statement lower than three, except for Africa with a score of 3,31. This corresponds with a result between *disagree (2)*, *somewhat disagree (3)* and *neither agree nor disagree (4)*.

Another statement with high scores across all regions and sectors, was the statement regarding the potential of CRISPR gene editing to be a major contributor to the solutions of food insecurity and environmental issues. It was formulated as:

> *CRISPR gene editing can be one of the major contributors to the solutions of environmental and food insecurity issues*

Scores ranged across all regions and sectors between 5,86 and 5,98. This corresponds with a result between *somewhat agree (5)* and *agree (6)*. On average, respondents agree across all regions and sectors that CRISPR gene editing can be one of the major contributors to the solutions of these issues.

The last statement that will be highlighted, is concerning the private sector dominance in the CRISPR gene editing market. It was formulated as:

The private sector will dominate the CRISPR gene editing market in terms of patents and edited crops on the market, rather than the public sector

Scores ranged between 4,90 (Asia and Oceania) and 5,45 (private sector) across all regions and sectors. This corresponds with a result of *neither agree nor disagree (4), somewhat agree (5)* and *agree (6)*. There seems to be consensus among plant scientists globally, that the private sector will be the more dominant actor in the CRISPR gene editing market in terms of patents and edited crops on the market, rather than the public sector.

Overall, these statements indicated that plant scientists globally are reluctant to the idea of CRISPR gene editing being regulated in a similar way as GM crops, have confidence in the hypothesis that CRISPR gene editing can be one of the major solutions to environmental and food insecurity issues and believe that the private sector will be the more dominant player in the CRISPR market rather than the public sector.

	Africa	Asia	Europe	North America	Oceania	South America	Public	Private
	Mean	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**	**Mean**
CRISPR gene edited foods should be subject to Genetically Modified Organisms regulation.	3,31	2,90	2,52	2,86	3,00	2,76	2,88	2,88
CRISPR gene editing can be one of the major contributors to the solutions of environmental and food insecurity issues	5,98	5,90	5,97	5,86	5,95	5,92	5,89	5,94
CRISPR gene editing technology is currently too expensive to make it a feasible option for developing countries	4,41	3,90	3,40	3,69	3,57	3,94	3,85	4,18
ff-targeted editing is a significant threat for CRISPR gene editing in plant breeding	3,87	3,50	3,15	3,29	3,38	3,03	3,42	3,63
Potential negative side-effects of CRISPR gene editing, have not yet been investigated thoroughly enough to bring gene edited food crops to the market	3,63	3,60	2,91	3,05	3,43	3,00	3,28	3,31
CRISPR gene editing patents will primarily be owned by large plant breeding multinationals	5,03	5,00	4,78	4,76	4,90	4,60	4,90	5,01
In 25 years, the majority of food crops grown globally will be edited using CRISPR gene editing technology	4,79	4,90	4,92	4,75	4,67	4,92	4,83	4,88

The private sector will dominate the CRISPR gene editing market in terms of patents and edited crops on the market, rather than the public sector	5,36	4,90	5,20	5,33	4,90	5,22	5,33	5,45
The CRISPR gene editing market will be dominated by multinationals, startups and scaleups will play a minor role	5,02	4,50	4,56	4,61	4,19	4,49	4,77	4,68
CRISPR gene editing will remain an expensive technology and therefore primarily be applied in developed countries	3,97	3,50	3,41	3,58	3,19	3,40	3,69	3,70

Table 7: Plant scientists' opinions on multiple statements concerning CRISPR gene editing technology, rated on a scale from 1 (strongly disagree) to 7 (strongly agree)

Discussion and conclusions

While the scientific community worked to increase the potential of CRISPR gene editing to contribute to food security and sustainability of agricultural production, the consensus on which crop(s), which trait(s) and which region(s) will benefit the most is still nebulous. Despite its potential, CRISPR has not been widely implemented as gene editing tool across agricultural industries globally due to a litany of barriers of adoption and dissemination. CRISPR gene editing in food crops, specifically staple crops, faces multiple barriers such as low consumer acceptance, regulatory issues and lack of (technical) infrastructure in different regions. The majority of existing scientific studies on CRISPR gene editing focus on small scale regions which focus on the perspectives of consumers on the technology, barriers of adoption, possible functions of the gene editing tool and what problems the technology can help to solve. Yet, no study has provided an empirical, global elicitation on the opinions of plant scientists worldwide on the subjects of barriers, functions, investments, beneficiaries and benefits for specific crops of CRISPR. This study has gathered scientific opinions across each potential region CRISPR could be deployed, both the private and public sector and over fourteen crops in order to provide an aggregated view on the major drivers, barriers and prospects of CRISPR gene editing. A better understanding of the potential of CRISPR from those on the ground floor of its evolution can help provide a better idea of its future.

Our results show that relative investments in CRISPR gene editing are envisioned to grow across all regions and both in the public and private sector over a ten-year timespan. The data emphasizes that plant scientists globally predict that CRISPR gene editing will receive a relative higher part of the total research and development budgets, across all regions and sectors. It appears that CRISPR gene editing will become a growing portion of research across the global plant science industry.

Fungus resistance and *virus resistance* were rated as the most likely functions of CRISPR gene editing to be successfully developed and implemented in agricultural production across four regions (Africa, Asia, Europe and North America). Only African plant scientists rated *drought resistance* as a likely function to be successfully implemented using CRISPR, not surprising given the decreasing amounts of fresh water available for agricultural production across many parts of Africa. *Insect resistance* was rated as third likeliest amongst all functions, with significant higher results than the weighted mean in both Africa and Europe. *Herbicide resistance* was voted to be the highest function across rated functions in North America, which should not be surprising given the large percentage of adoption of Roundup Ready crops available currently across North America. At the sectoral level, both the public and private sectors thought *fungus resistance*, *virus resistance* and *insect resistance* were rated the most likely functions to be implemented via CRISPR. Public sector scientists expect *herbicide resistance* and *drought resistance* likely to be implemented as well, next to the aforementioned functions. Across all regions and sectors the plant scientists seem to think *fungus resistance* and *virus resistance* will likely be the most successfully implemented functions using CRISPR, with *insect resistance* as third likeliest.

Multiple barriers of adoption denoted significant higher scores than the weighted mean of the corresponding sector/region in the results. Thus, and likely most frustrating to plant scientists, *consumer perception/knowledge gap*, was thought to be the most impeding barrier of CRISPR adoption. *Policy/legal issues* scored significantly higher than the weighted mean across all regions, except for South America. This could be explained due to the fact that multiple South American countries have allowed genome edited crops to be grown, such as the production of high oleic soybeans (edited using TALEN gene editing) in Argentina (Menz et al., 2020). Europe, denoted the highest score for *policy/legal issues* out of all regions and both sectors. One potential explanation for this high score of Europe on *policy/legal issues* could be, that the European Union has the strictest regulations for CRISPR gene edited crops by making them subject to GM regulations (Purnhagen & Wesseler, 2020). *Intellectual* *property rights issues* denoted significant higher results than the weighted mean in Asia, Europe and North America, the regions which hold the most CRISPR patents in the market (Martin-Laffon et al., 2019). One potential explanation for this is that given the large amount of CRISPR patents, there is likely a large amount of copyright infringement or money spent on legal matters protecting that intellectual property. *High development costs* are seen as a barrier by African and South American scientists, both regions are populated with a high number of developing countries which likely are plagued by lower relative research and development budgets. Overall, across all regions the education of consumers about CRISPR and creating an understandable comprehensive regulatory framework seem to be large impediments of commercial adoption of CRISPR gene editing. In high-income countries, a clear framework for intellectual property rights of CRISPR patents is needed, whereas funding and lack of investment is an impediment in developing countries. In both the public and private sector, *consumer perceptions/knowledge gap* and *policy/legal issues* seem to be the most impeding barriers of CRISPR adoption, followed by *intellectual property rights issues*. In the private sector, scientists see *high development costs* as an issue that impedes the adoption of CRISPR adoption.

This study indicated that *maize* and *soybean* are expected to benefit the most from CRISPR gene editing across all regions, except for Oceania. *Wheat* (Asia, Europe, North America and South America), *rice* (Asia, North America and South America) and *potatoes* (Asia, Europe and North America) are other crops in which plant scientists globally see potential to benefit from the CRISPR technology. In both the public and private sector, scientists believe that *maize, soybean, wheat* and *potatoes* are most likely to benefit from CRISPR gene editing technology. The only difference between these two sectors is, that public scientists score *rice* as significantly higher than the weighted mean as well. This may not be surprising given the large role public breeding still plays in *rice* unlike *soy* and *maize.*

Little differences were found regionally on whom and what the main beneficiaries of CRISPR will be. *Reduced food insecurity* was scored significantly lower than the weighted average in Europe and North America, not surprising since neither region is plagued with high food insecurity rates. The biggest beneficiary of CRISPR adoption was estimated to be *increased yields*, for scientists in Africa, Europe and North America. Interesting, as the yield gap is relatively small in Europe and North America (Hengsdijk & Langeveld, 2009). Little significant results were found in the public and private sector as well, where both sectors denoted high scores for *increased yields*. Also, for the public sector *producer profits* is seen as a (possible) beneficiary of CRISPR gene editing technology. The variables in this question (*reduced food insecurity*, *environmental damage in agriculture, increased nutritional value in crops, producer profits, yields and yield variability*) very much intertwine with each other in the agricultural sector, e.g. if yields increase, food insecurity is likely to decrease as well. This could be one of the potential explanations for the low number of significant results found in this question, as each variable is tested to the weighted mean.

The survey statements indicate that plant scientists are highly reluctant to the idea of CRISPR gene editing being regulated in a similar way as GM crops. Furthermore, the sector believes that CRISPR technology can be one of the most important solutions of environmental and food insecurity issues. Lastly, plant scientists indicated that the sector sees the private sector dominating the CRISPR market.

While diverse, there are some limitations to the participants of the survey itself. The first is, that the North American sample is dominated by American scientists with little representation from either Mexico or Canada. Furthermore, the Oceanian and South American sample was relatively small compared to the other four regions, with 21 and 64 respondents respectively.

Also, it is important to consider that all results of the functions, barriers, crop benefits and beneficiaries, were tested against the weighted mean of all functions/barriers/crop benefits/beneficiaries of their own region/sector. This means, that significant results only emerge when the test is significantly different from this weighted mean. This does not imply that significant lower results or results that were not different from the mean, are not of importance. The results in this study only show differences at region and sector level, whereas the situation can look different on national and local level.

Another limitation of this study is the sampling. The total amount of plant scientists per region and sector is unknown, therefore it is difficult to assess whether this study includes a representative sample for each region and sector. The results of this study are biased towards Europe and North America, as well as the public sector. Private sector plant scientists contact details are rarely publicly available and therefore this target group was more difficult to reach.

In order to better understand drivers, barriers and prospects of CRISPR at national and local level, similar research should be conducted at a more granular level. Also, at crop level it could be that major differences between the perceptions of barriers, beneficiaries and functions of CRISPR exist, for instance, maize production for livestock vs maize production for human consumption. This study can be of use for the plant science sector, policymakers and agronomists in the sense that it draws a picture on what the major perceived barriers and prospects of CRISPR are, and what differences at regional and sectoral level are. At national and local level, policymakers could test the hypotheses raised from this study to design tailored regulations and investments in the CRISPR sector. Also, plant scientists globally can use this study to see what other scientists active in different regions foresee as the most important functions, risks and implications of the technology, to seek collaboration and take the development of the technology forward.

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