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Potato crisps from CRISPR-Cas9 modification – Aspects of autonomy and fairness

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Abstract
Within the Swedish MISTRA Biotech research programme the quality of starch in potatoes has been changed by use of different technologies such as CRISPR-Cas9. The idea is to increase the level of amylose, both for health reasons and as a mean to investigate possibilities for replacing fossil based oxygen barriers in food packages, and so reducing the climate impact. The goals thus seem laudable to most, but the experience of introducing GMOs on the market shows that even though there might be agreement on the goals, the strategy of using biotechnology to achieve them can be ethically contested. We describe the intentions behind developing the new plants and analyse some of the ethical issues that the development and marketing of the gene-edited potatoes raise. We argue that the concepts of autonomy and fairness are useful tools to understand many of the conflicting ethical values in the discussions relating to gene-editing. From our perspective these concepts are interrelated and relevant in at least two ways: 1) Fairness in terms of both financial power and labelling as a means to ensure equal opportunities to make an autonomous decision as an individual ethical consumer and 2) Fairness in term of equal market power between autonomous market actors.

Key words: autonomy, fairness, potato starch, regulation

Introduction

Ever since A. L. Huxley's book Brave New World was published in 1932, reflections on engineered modifications of living beings have engaged a larger public and a wide range of ethical aspects have been scrutinized in both public and academic debates. According to a review of academic papers on ethical aspects of GMO a majority (84%) address consequences of cultivating GMO plants, often in terms of risks, the precautionary principle, sustainability and future generations, whereas 57% discuss the act of modification from a deontological perspective including definitions and the normative role of 'naturalness', and 43% of the philosophical papers focus on the agent along the lines of virtue ethics. They stress ideals such as trustworthiness, responsibility, wisdom, humility and care. In comparison, the review presents that laypersons (as mapped in academic studies) are similarly concerned with consequences, i.e. risks, and with naturalness in their judgement of the act. Although less focus on the actor, trustworthiness is described as an important virtue also by laypersons, and essential for establishing a dialogue between researchers and society (Gregorowius et al., 2012).

The relevance of discussing the above mentioned ethical aspects in relation to genetic modification (GM) and gene editing (GE) is obvious. We do, however, find that there are other important aspects when evaluating genetically modified organisms (GMOs) and gene edited organisms (GEOs) coming out of technologies such as CRISPR-Cas9, which in Gregorowius et al., 2012 are classified as "socio-economic concerns", but which in our perspective also have fundamental ethical dimensions. One example of such an issue concerns the difficulty of making autonomous decisions in a world offering constantly emerging new breeding possibilities and products, as well as the principles for 'fair distribution' of risks and opportunities and goods, among different stakeholders. A Swiss study of lay persons' perception of GM field trials confirm fairness is important, although the importance differ between outcome and process fairness and relates to whether one finds GM a morally important issue or not. (Siegrist et al., 2012).

Within the Swedish MISTRA Biotech research programme a changed quality of potato starch has been developed by use of novel biotechnologies (RNAi and CRISPR-Cas9). One project aims to contribute to lower fossil emissions by developing a potato starch 'plastic' to be used as oxygen barrier in packages (Muneer et al., 2016), another to improve storage qualities of potato starch (Andersson et al., 2017), and a third aims to alter starch qualities to be more beneficial from a health perspective, e.g. through lower glucose levels and insulin responses by higher diet fibre (Zhao et al., 2018). Introducing a GM/GE product on the market, especially for human consumption is, however, a complex undertaking, and neither fair distribution of possibilities or goods, nor requirements for autonomous choices are easily defined (see e.g. Siipi and Uusitalo, 2011). In order to show the relevance of issues such as fairness and autonomy, we begin by briefly describing the new potatoes followed by a description of the regulatory discussions and relate this to the question of the definition of GE. Based on this we analyse two aspects of fairness and autonomy in relation to the development and potential introduction to the market of the potatoes: 1) Fairness in terms of financial power and labelling as a means to ensure equal opportunities to make an autonomous decision as an individual ethical consumer and 2) Fairness in term of equal market power between autonomous market actors.

The case of gene-modified and gene-edited potatoes

Researchers connected to the Swedish MISTRA Biotech research programme have used CRISPR-Cas9 to combine potato starch with plant protein to create a composite material similar to plastic that can be used as an oxygen barrier in packages, and recycled as compost after usage (Muneer et al., 2016). They have further designed potatoes (*Solanum tuberosum*) with longer storing capacities thanks to a new starch composition (Andersson et al., 2017). Starch consists of two main components, and by eliminating the production of one of them, amylose, by site-directed mutagenesis, the gene edited starch instead consists of increased levels of amylopectin. This is interesting for the industry (which is co-financing the research) as short storing time of potato starch is an obstacle in the food production process. If the method is possible to apply on large scale, it could have an impact on the global production of about 40 million tonnes of starch per year, and according to the industry provide a 'more environmentally sustainable special ingredients to conscious consumers' (Sveriges Lantbruksuniversitet, 2016). Further, by use of classical GM-technology, a slightly different potato has been developed, which - after cooking - takes longer to digest, leading to a number of positive side-effect like slow carbohydrates and benign gut bacteria (Zhao et al., 2018). Contrary to the modified starch product, this potato can be prepared in a traditional way in everyday cooking (Sveriges Lantbruksuniversitet, 2018). This GM-potato, however, would have to be assessed according to EU Directive 2001/18/EC and labelled as a GM-food. It is therefore questionable, if it will reach consumers and whether they in turn will find it acceptable. The researchers are therefore

aiming at creating the same change by use of GE through CRISPR-Cas9 instead, as this is regulated as a traditional breeding technology in Sweden (Umeå University, 2015).

These new varieties of potatoes are interesting as they will be among the first CRISPR-Cas9 vegetables for industrial and consumption purposes in Sweden, but also because potato traditionally is the stable vegetable in the Scandinavian and Northern European kitchen and carries many cultural connotations. Considering potato chips and strips as well as the starch used in a large number of products, a wide range of producers and consumers would directly or indirectly come in contact with this new product.

Is CRISPR-Cas9 GMO? A regulatory challenge

When discussing autonomy and fairness in relation to GMOs and GEOs the legal status of CRISPR-Cas9 and other GE-techniques is important, as is the ensuing regulatory marketing framework. The EU Directive 2001/18/EC defines GMO as: ‘‘an organism with the exception of human beings, in which the genetic material has been altered in a way that does not occur naturally by mating and/or natural recombination” (Article 2(2)). Although specified in Annex I A part 1, the definition is regarded to be wide and unclear, but gains some clarity by the explicit exclusion in Annex I B of mutagenesis, cell fusion and certain other methods of exchange of genetic material used in traditional breeding (Zetterberg & Björnberg, 2017).

As new techniques develop the lack of a clear definition has lead to different interpretations in different Member States. In Sweden, gene editing through CRISPR-Cas9 is not considered GM but treated as conventional breeding whereas the EU-system still discusses whether the new methods of gene-editing should be considered GM or not. (Eriksson et al 2017). A decision is expected from the Court of Justice of the European Union in 2018. The Norwegian Biotechnology Advisory Board has proposed to differentiate regulation into three levels: changes that could be obtained through conventional breeding (1), intra-species modifications (2), and transgenic changes (3). The goal is to maintain control of GMOs and GEOs, but at the same time have a less demanding approval and control system for e.g. the potato plants described above (The Norwegian Biotechnology Advisory Board, 2017).

Arguments in favour of not defining GE as GM hold that GE involves no transgenesis (introducing a gene form a different species) and that the mutations could be reached by conventional breeding methods just requiring more time (Østerberg et al., 2016). Whether arguments like these will convince a European public highly sceptical towards GMOs remains to be seen (Mielby et al., 2013). Further, since 2015 each Member State in EU has the right to restrict or forbid cultivation of GM-crops within their own country according to the so called "opt-out" Directive 2015/412. Reasons to activate the Directive may refer to a range of aspects such as environmental, agricultural or public policies, territorial planning and land use, socio-economic impacts or risk of unwanted GMO presence i.e. cross-border contamination. The idea behind the Directive is described as twofold: to revise the often lengthy and non-conclusive decision-making process on GMOs by encouraging Member States to accept a GMO even if they will not cultivate it themselves, and to ensure that aspects other than those related to human or environmental risks can be taken into account (Eriksson et al., 2017). Hence, the Directive can be seen as a way to acknowledge that more than a strictly scientific perspective on what is perceived as a risk plays a role for public opinions on GMO (Gjerris, 2008).

However, some researchers have criticized the Directive for having neither improved the decision-making process, nor created the freedom of choice envisaged. In a ‘Corresponcence’ in the journal *Nature Biotechnology* they argue in favour of an ‘Opt in’-possibility, i.e. the right for each Member State to accept cultivating GMO-plants (Eriksson et al., 2018). This, it is said, would not change the opt-out possibility, but ensure freedom of act for Member States who are

in favour of GMO, but cannot allow it due to the need for a common agreement among all Member States. To what extent neighbouring Member States would have the possibility to veto such a decision based on the risk of GMOs reaching their territories is not discussed by the researchers, but remains to be solved.

On top of this arrives now the debate of whether or not to define new plant breeding technologies as GM-technologies. How the new plants are defined, both with regard to approval procedures and product labelling, will decide where they are grown and how much of a market-share they can obtain, and hence influence what choices farmers are "allowed" to make. It might also influence the level of citizen trust in the entire food system, as GMOs are covered by assessment and control but GEOs currently are not. Hence it seems the classical tension between autonomy (here on the level of each Member State's right to decide what to cultivate) and non-malefience will be important the coming years, as well as the issue of how to define the freedom to act (e.g. cultivate what you prefer) or the freedom not to have to act (e.g. not have to protect oneself from other's potentially harmful actions).

Fairness and autonomy

When considering the genetically altered potatoes described above and the unclear regulatory situation, it is relevant to discuss the connection between autonomy and fairness from the perspectives of 1) individual ethical consumers and 2) different market actors. Due to space limitations, we can merely highlight issues of relevance rather than discuss all relevant issues in depth.

Fairness in terms of financial power and labelling as a means to ensure equal opportunities to make an autonomous decision as an individual ethical consumer. It is uncontroversial to state that financially strong consumers have a wider range of purchase options compared to households with a more limited budget, and that one core element in practicing autonomy in everyday life is to choose what to eat, and ideally that food intake is based on one´s values. Given that food prices mirror whether they are produced with or without a certain technology, the ability to express one´s values regarding these technologies thus differ with budget limits. In the case of gene-edited potatoes a question could be, if they would outcompete conventional potatoes on the market. If so, consumers who do not wish to buy gene-edited potatoes (for whatever reason) will be forced to buy organic products which typically come with a higher cost. Further, if GE-potatoes are not legally considered GMOs, organic farmers can begin using GE-plants leaving consumers who do consider GE to be GM with little choice.

Another issue is how the political consumer runs the risk of being left on her own whether the potatoes are labelled or not. In a cacaphonic market-place filled with infomercials competing about consumer interest and usually not under-selling the merits of products (Gjerris et al., 2016) one can easily envision that the idea of an informed and autonomous choice by consumers about whether to by GE-potatoes or not will be under a lot of pressure both from those who criticise and those who support the technology. Further, whether one has the ability to gain relevant knowledge, and whether anyone is willing to provide it in a (as far as possible) neutral way, will shape the prerequisites for making autonomous choices. As the familiar discussion about GMOs show there is little agreement on this and as the discussion of e.g. off-targets effects of gene-editing are beginning to take off (Warmflash, 2017), there seems little doubt that ethical issues, including risks and benefits, will also be interpreted in a variety of ways concerning GE-plants.

Finally it is worth noting that attempts to define CRISPR-Cas9 as a conventional breeding tool primarily based on the technical fact that it is not transgenic, carries the risk of misunderstanding the discussion. Transgenesis is not the only reason that GMOs have been

opposed and the more proponents of GE seek to avoid substantial ethical discussions about concepts as power and naturalness the easier it is to see the GMO discussion repeat itself.

Fairness in term of equal market power between autonomous market actors. The first issue in this section concerns the different consequences of whether or not gene-editing such as CRISPR-Cas9 is defined as a GM. Historically, one point of criticism of GMOs points to the unfair competition between market actors, due to different financial strength between small-scale breeding companies and multinational companies, the latter having better chances coping with high regulatory demands (Raybould and Poppy, 2012). One may therefore expect that if CRISPR-Cas9 is regulated as GMO, it may exclude small companies from adopting the technology as the approval procedures will be too time-consuming and expensive. This is relevant not least from a fairness perspective. Creating fair competition is difficult since it raises questions of, for example, what kind of concerns are fair to formulate as assessment criteria for labelling a specific technology as GM or not. Envisaging future marketing of GE potato starch (for industrial purposes) the company developing the product would have an interest in high market shares, which they might lose if defined as GMO. Given it is defined as GMO, the suggested 'opt in' legislation would potentially open markets available also for smaller producers, although financial dimensions in handling legal process remain.

The last issue to discuss briefly in this section is that both the suggested opt-in possibility and the definition of GE as non-GM raises an issue with regard to organic farming. Since some of the consumer concerns regarding GMO relate to ideas about naturalness (Gregorowius et al., 2012) as does the choice of organic products, the risk of contamination followed by loss of 'naturalness' would be a serious challenge not least to the autonomy of organic farmers and consumers of their produce. Hence, one may expect that defining GE as conventional breeding and/or choosing a "liberal" approach for labelling might imply that the GM-free nature of organic farming could be compromised in the public eye.

Conclusion

Recent years have seen the advent of a number of biotechnologies such as CRISPR-Cas9 that carries great promise in relation to changing e.g. crops. Within the Swedish research project MISTRA Biotech, the methods have been used to produce various varieties of potatoes that could result in lower climate impact, higher food security and healthier diets. It is, however, debated, whether such technologies should be defined as GM-technologies or as conventional breeding tools. The choice of definition will make a huge difference both with regards to approval procedures, labelling and consumer acceptance. We show the relevance of linking this issue to the concepts of autonomy and fairness and highlight questions of fairness for the individual consumer in terms of financial strength to choose/de-select the new products and point to the difficulties of obtaining unbiased knowledge to make an autonomous decision for the average consumer in a marketplace filled with infomercials. Further we briefly discuss how different ways of defining the new technologies will have an influence on which companies will be able to utilize them. If GE is not classified as GM, the accessibility of the technique increases and opens to usage by small breeding companies, but might lead to a loss of trust in food regulation among some citizens. We also point to the problems that organic farming might face, if the technologies are accepted as conventional breeding technologies, thus running the risk of undermining the organic labels of GM-free quality in the eye of the part of the public who finds the distinction between conventional and GE important. We conclude that a wide range of issues falls under the heading of autonomy and fairness and therefore find that these concepts are a useful key to further analyse the current discussions of CRISPR-Cas9 and related technologies in connection with breeding of crop plants.

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