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REVIEW ARTICLE

Challenges facing European agriculture and possible biotechnological solutions

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Abstract

Agriculture faces many challenges to maximize yields while it is required to operate in an environmentally sustainable manner. In the present study, we analyze the major agricultural challenges identified by European farmers (primarily related to biotic stresses) in 13 countries, namely Belgium, Bulgaria, the Czech Republic, France, Germany, Hungary, Italy, Portugal, Romania, Spain, Sweden, UK and Turkey, for nine major crops (barley, beet, grapevine, maize, oilseed rape, olive, potato, sunflower and wheat). Most biotic stresses (BSs) are related to fungi or insects, but viral diseases, bacterial diseases and even parasitic plants have an important impact on yield and harvest quality. We examine how these challenges have been addressed by public and private research sectors, using either conventional breeding, marker-assisted selection, transgenesis, cisgenesis, RNAi technology or mutagenesis. Both national surveys and scientific literature analysis followed by text mining were employed to evaluate genetic engineering (GE) and non-GE approaches. This is the first report of text mining of the scientific literature on plant breeding and agricultural biotechnology research. For the nine major crops in Europe, 128 BS challenges were identified with 40% of these addressed neither in the scientific literature nor in recent European public research programs. We found evidence that the private sector was addressing only a few of these ''neglected'' challenges. Consequently, there are considerable gaps between farmer's needs and current breeding and biotechnology research. We also provide evidence that the current political situation in certain European countries is an impediment to GE research in order to address these agricultural challenges in the future. This study should also contribute to the decision-making process on future pertinent international consortia to fill the identified research gaps.

Keywords

Automated literature analysis, biotic stress, breeding, cisgenesis, marker-assisted selection, oligonucleotide directed mutagenesis, patent, text mining, transgenesis

History

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Introduction

Agriculture is facing many challenges, which have been intensified in recent years by the deceleration of crop yield increases caused by pests, diseases and abiotic stresses (Grassini et al., 2013). Extreme conditions (e.g. droughts and floods) limit production and lead to high prices worldwide. The world population is expected to grow to 9 billion (ca. 30%) by 2050. So investment to improve agricultural production and productivity is needed to meet these challenges (FAO, 2012). In addition, climate variability will exacerbate food insecurity (Challinor et al., 2014; Wheeler & von Braun, 2013) and could also affect harvest quality (e.g. by increased mycotoxin contamination from proliferating

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saprophytic fungi). Climate-driven disease emergence may occur (Altizer et al., 2013) and invasive species represent a threat to both agricultural productivity and biodiversity (Pyšek & Richardson, 2010). Consequently, the appearance and spread of new pests and diseases in novel cultivation areas are expected to increase. Examples of invasive species already causing considerable economic damage are those from the *Striga* and *Orobanche* genera (Parker, 2009). These parasitic weeds are present in several European countries such as Spain, France, Greece and Italy, but they have also been reported in Romania, Bulgaria, Portugal, Germany and several other Mediterranean countries.

In Europe, which is used as a case study in this review, economic constraints such as high fuel costs and the pressure to reduce use of pesticide are also important (Tester & Langridge, 2010). European farmers face increasing pressure to produce in a more sustainable way and, at the same time, need to adapt to strong competition from other regions of the world for both internal consumption and export. In addition, protein-rich crop production occupies only 3% of arable land in the European Union (EU) and supplies only ca. 30% of the total crop protein demand. Hence, there is a strong reliance on soybean import into the EU, mostly for feed production. Responding to this is a challenge for European agriculture as, for example is the enhancement of the quality of soybean products (Krezhova, 2011).

Thus, definitive changes in agricultural production are needed in order to improve crop productivity and crop management. Genetics can significantly contribute to addressing these issues. Transferring desirable genetic traits into a crop from the same species or from wild relatives can take a long time with conventional methods, even when aided by marker-assisted selection (MAS). On the other hand, genetic engineering (GE) is much faster, but is currently delayed by specific regulatory constraints and costs. To prepare for the future and to increase food production in the next 25 years, advanced agricultural research, utilizing all the available genetic resources (McCouch et al., 2013) and plant breeding techniques, must now be promoted. Here, we examined whether this is currently occurring in Europe. Currently, there is intense debate throughout the continent on ways to overcome the bottleneck for the approval of GE products and also over the regulation of products from new plant breeding technologies. Therefore, it is timely to examine whether Europe is adequately addressing agricultural challenges and whether there are obstacles impeding progress.

Thirteen countries were included in this study, namely Belgium, Bulgaria, the Czech Republic, France, Germany, Hungary, Italy, Portugal, Romania, Spain, Sweden, UK and Turkey. Turkey was included because it is the seventh largest agricultural producer in the world and an associate member of the EU. These countries are representative of four European regions: Southern, Central, Western and Northern Europe. We addressed the following questions in the European context:

- What are the main agricultural challenges identified by farmers?
- What is the state of art in the scientific literature focusing on these challenges?
- Is European research addressing these challenges?
- Does the private sector adequately focus on these challenges?
- Is there any bias for or against using GE in European agricultural research?

The main challenges faced by European farmers

The share of farmed area (in %) for each major crop across Europe (considering only the above-mentioned 13 countries), is shown in Figure 1(a). The distribution of these major crops per country is presented in Figure 1(b) (see also Panel 1 and the details in Panel 2 in Supplementary Material 1). Wheat occupies the largest areas in the 13 selected countries, with the exception of Portugal, followed by maize and barley. Oilseed rape (OSR) is of major importance in France and Germany. Some countries are rather specialized like UK or Germany having three or four major crops. Others such as Italy divide their agricultural area among several crops. Sunflower is grown in similar percentages in six countries, namely Bulgaria, France, Hungary, Romania, Spain and Turkey, while potatoes are cultivated in all the countries. Rice, olives and soybean are limited to a few, mostly southern, countries.

To identify challenges faced by farmers and the research programs involving agricultural biotechnology which address them, we used a bottom-up approach from farmers to researchers through national surveys. A questionnaire with nine key questions was sent to agricultural specialists, farmer organizations and researchers in the selected countries (see Tables S1 and S2 in Supplementary Material 2). The questionnaire also included questions related to public and private research, and funding for research. In a second step, participants also completed a table containing biotic stress (BS) challenges for each crop (fungal and viral diseases, insect pests or weed and parasitic plants) and included qualitative (i.e. whether the disease is present in their country or not) and quantitative information (i.e. how much area of the crop is affected by the disease).

Farmers identified BSs (a total of 128 of them – see Supplementary Material 3) as their major challenges, followed by drought, frost and nutritional enhancement in nine major crops, namely barley, beet, grapevine, maize, OSR, olive, potato, sunflower and wheat. Most BS related to fungi or insects, such as wheat leaf rust or European corn borer. Also, viral diseases, bacterial diseases and even parasitic plants also impact on yields and harvest quality. Some crops are impacted by more diseases than others – 16 were reported for beet, whereas potato is affected by only 8. However, each disease has a varying impact on the crop. For example, Septoria leaf blotch causes damage to half of the wheat area in the Czech Republic, France and Sweden, whereas golden nematode affects less than a quarter of potato crop areas.

State of art of the scientific literature focusing on BS challenges

Scientific articles concerning the identified BS challenges were analyzed over the period between January 2007 (when articles using RNAi first appeared) and January 2014. The CAB (Commonwealth Agricultural Bureaux), FSTA (Food Science and Technology Abstracts), PubMed

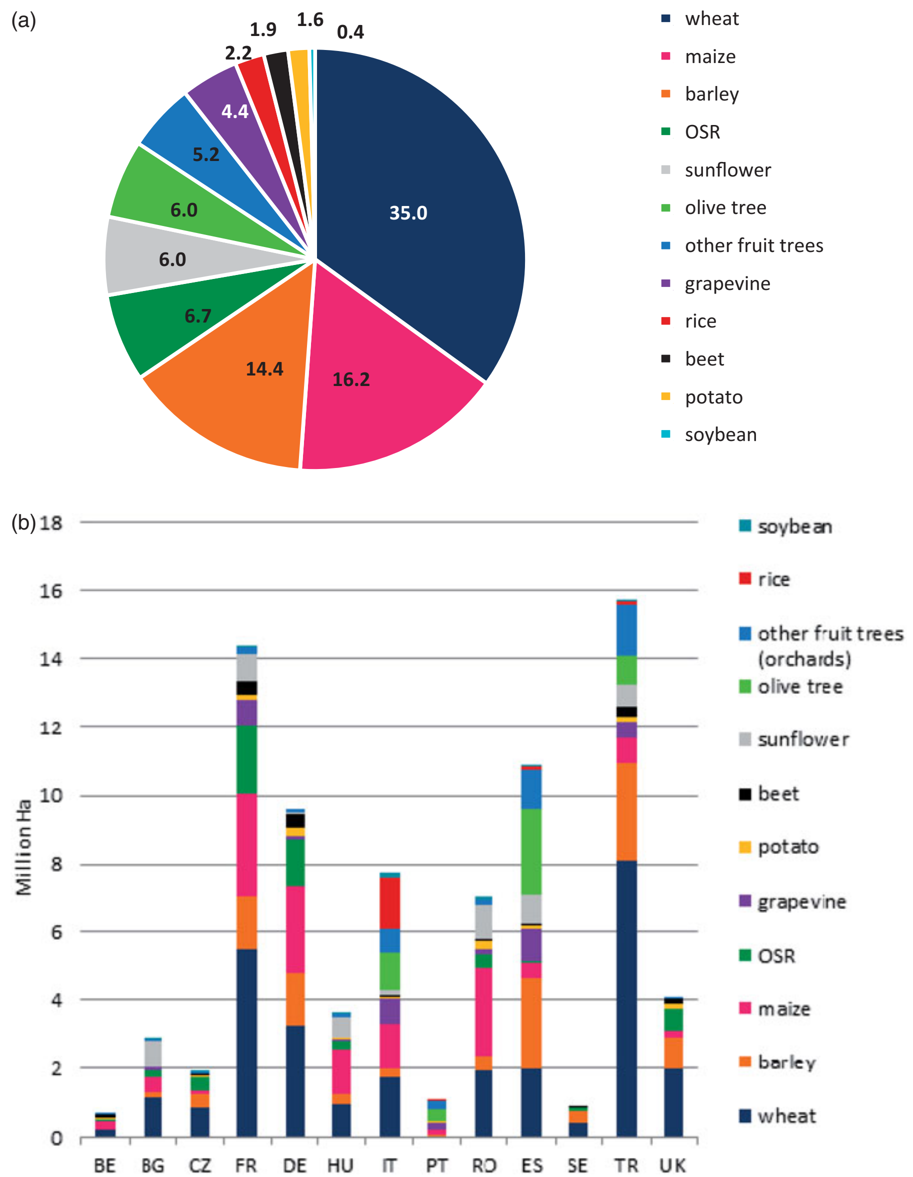

Figure 1. Agricultural areas of major crops in 13 representative European countries.

(National Center for Biotechnology Information) and Web of Science (Thomson Reuters) databases were screened using queries built for each BS/crop pair (Table S3a in Supplementary Material 2) as well as for terms corresponding to plant breeding techniques (Table S3b) by using synonyms, Boolean and proximity operators and truncations. The results were exported to the bibliographic management software EndNote (Thomson Reuters) and then classified into thematic groups based on BS/crop pair. We then used a new text-mining software (Luxid® Content Enrichment Platform), developed by the company Temis, which has been adapted to agricultural research and biotechnology purposes. Using Luxid®, publications were sorted according to plant breeding technique (e.g. transgenesis or other plant breeding methods), BS and crop.

Different GE categories, namely transgenesis, cisgenesis or RNAi, were treated individually, even though not all differences between them may be meaningful from a scientific point of view as well as from a regulatory point of view. For instance, some consider cisgenesis less risky and thus (ethically or generally) more acceptable than transgenesis (Schouten, 2014). Reviewing this issue, EFSA (2012) concluded that cisgenic plants would have similar hazards associated with them to conventionally bred plants. Plants containing RNAi constructs (be they transgenic or cisgenic) are likely to be as safe as conventionally bred plants, as they are expected to contain loss of function or knock down alleles of endogenous genes.

To the best of our knowledge, this is the first report of this type, namely, text mining of the scientific literature on plant breeding and agricultural biotechnology research. After removing duplicates, scientific papers were processed to the highlight pertinent data by filling tables containing the plant, the studied trait and the name and location of the research laboratory (Supplementary Materials 4 and 5).

In total, 12 647 articles related to the 128 BS challenges in nine crops were collected. From these, 763 articles (Supplementary Material 4, a–h) dealt with breeding techniques aiming to build BS resistance in crops (molecular markers to tag resistance genes and MAS 78.8%; transgenesis, T 9.2%; RNAi/silencing including stable and transient assays 5.9%; conventional breeding 2.9%; other transient assays

Table 1. Distribution of published breeding studies per crop and per technique, and the share of Europe compared to the rest of the world.

			Worldwide		Europe	
Crop	Number of studies for crop (%) worldwide	Share of Europe: number of studies (% within crop)	Share of T + C + RNAi: number of studies (%)	Share of MAS + conv.: number of studies (%)	Share of T + C + RNAi: number of studies (%)	Share of MAS + conv.: number of studies (%)
Wheat	639 (68.2)	164 (25.7)	53 (8.3)	580 (90.8)	17 (10.4)	145 (88.4)
Potato	104 (11.1)	57 (54.8)	49 (47.1)	51 (49.0)	19 (33.3)	36 (63.2)
Barley	78 (8.3)	40 (51.3)	16 (20.5)	61 (78.2)	13 (32.5)	26 (65.0)
Grapevine	47 (5)	34 (72.3)	13 (27.7)	34 (72.3)	8 (23.5)	26 (76.4)
Sunflower	19 (2.0)	4 (21.0)	1 (5.3)	17 (89.5)	0 (0)	4 (100)
Maize	17 (1.8)	6 (35.3)	4 (23.5)	13 (76.5)	1 (16.7)	5 (83.3)
Beet	17 (1.8)	14 (82.3)	4 (23.5)	13 (76.5)	4 (28.6)	10 (71.4)
OSR	16 (2)	4 (25.0)	9 (56.2)	5 (31.2)	1 (25.0)	3 (75.0)
Total	937	323 (34.5)	149 (15.9)	774 (82.6)	63 (19.5)	255 (78.9)

C, cisgenesis; Conv, conventional breeding; MAS, marker-assisted selection; T, transgenesis; RNAi, RNA interference. Data were compiled from Supplementary Material 5. GE techniques subjected to a heavy regulatory burden (and political opposition) are grouped (T + C + RNAi, including transient assays); MAS and conventional breeding grouped separately. Studies describing mutagenesis or resistance gene cloning are not included in the column ''worldwide'' and ''Europe'' (which explains that the sum of individual frequencies does not always add up to 100%).

1.7%; cloning 0.8%; cisgenesis, C 0.4%; *in vitro* and *in vivo* mutagenesis 0.4%). Among these articles, 71 (9.3%) were published in collaboration with at least one private laboratory.

Some articles contain several studies and their distribution per crop and per BS is shown in Supplementary Material 5 (937 studies in total). Wheat, the most cultivated crop in the world (215 Mha in 2014 according to FAO), also dominates the selected literature (68.2% of studies; Table 1, first row). Among the 20 BS compiled for wheat (Supplementary Material 5), 17 are dealt with, although, some only by a single publication. Studies on fungal diseases predominate, while those on insect pests are rarer. Pest insects are strikingly the least dealt with (papers on ground beetle, frit fly and chloropid gout fly are absent, and limited in number for sunn pest, grain aphid and leaf beetle). All the breeding techniques were used against fungal and viral diseases and insect pests, but MAS dominated. Barley ranked third (8% of studies in Supplementary Material 5; 9 out of 16 BS), and fungal disease studies using MAS predominated as well, with no studies on six insect challenges. It is striking that maize (159 Mha worldwide) is poorly represented in this literature survey (1.8% of studies; 6 BS out of 16). An explanation may be that maize resistance to insects has been largely developed in the private sector (47 patents registered, see Supplementary Material 8). Similarly, for OSR and sunflower, very few breeding papers were published: 5 BS out of 20 and 6 BS out of 14, respectively. Although half of the identified BS in OSR are caused by insects, resistance breeding to these pests is almost absent from our literature compilation. In the sunflower, no paper was recorded on insect resistance, and for fungal diseases MAS was the predominant technique. In grapevine, among 11 BS, only two fungal resistance (downy and powdery mildew) studies were recorded, and a limited number of studies on resistance to viruses. In potato, which ranks second (11.1%) in this literature survey, the recorded resistance breeding concerned almost all pests and diseases, with most research on late blight resistance. All the techniques were used, with T being the main approach for insect and early blight resistances. In beet, efforts against a viral disease (rhizomania) are dominant using mainly MAS, while no studies were recorded for the seven insects or two nematode challenges. No breeding study was identified in the case of olive.

In summary, fungal resistance was investigated in 819 studies, i.e. 87.4% of the studies collected in Supplementary Material 5. This is primarily due to the identification of resistance genes which can be introgressed using MAS. The success of this approach is illustrated by the control of wheat stem rust (*Puccinia graminis*), which is no longer identified as a challenge in our survey (see Supplementary Material 3), although a new virulent wheat stem rust, Ug99, does pose a significant future threat. On the other hand, resistance to some fungal diseases was not represented in our survey (e.g. grey mould in grapevine and leaf spot in beet). Concerning insect resistance (38 studies, i.e. 4.1%), a lack of breeding studies is obvious. Strikingly, 71 BS out of 128 are not referred to in these 937 studies.

A total of 323 breeding studies among the 937 (34.5%) listed in Supplementary Material 5 were published by 21 countries in Europe (plus 4 by Turkey). Table 1 shows the crop by technique distribution of these studies in the world and the relative share of European laboratories. It appears that in Europe, wheat and sunflower research is underrepresented (at least in this literature compilation), while beet and grapevine research has a higher share of this worldwide compilation. Regarding the techniques, it seems that European research has not avoided the use of T, C or RNAi, according to the published literature. The use of these novel breeding techniques is slightly higher in Europe (19.5%) compared to worldwide (15.9%). Since this situation may be rapidly changing, hereafter, we also examine current research programs in these 13 representative European countries.

The use of GE in current European public research programs to address agricultural challenges

The methodology used to identify which challenges are addressed by recent research programs involved a combination of data collection tools and included several phases: some research programs are available on the Internet, some information was obtained by directly contacting national

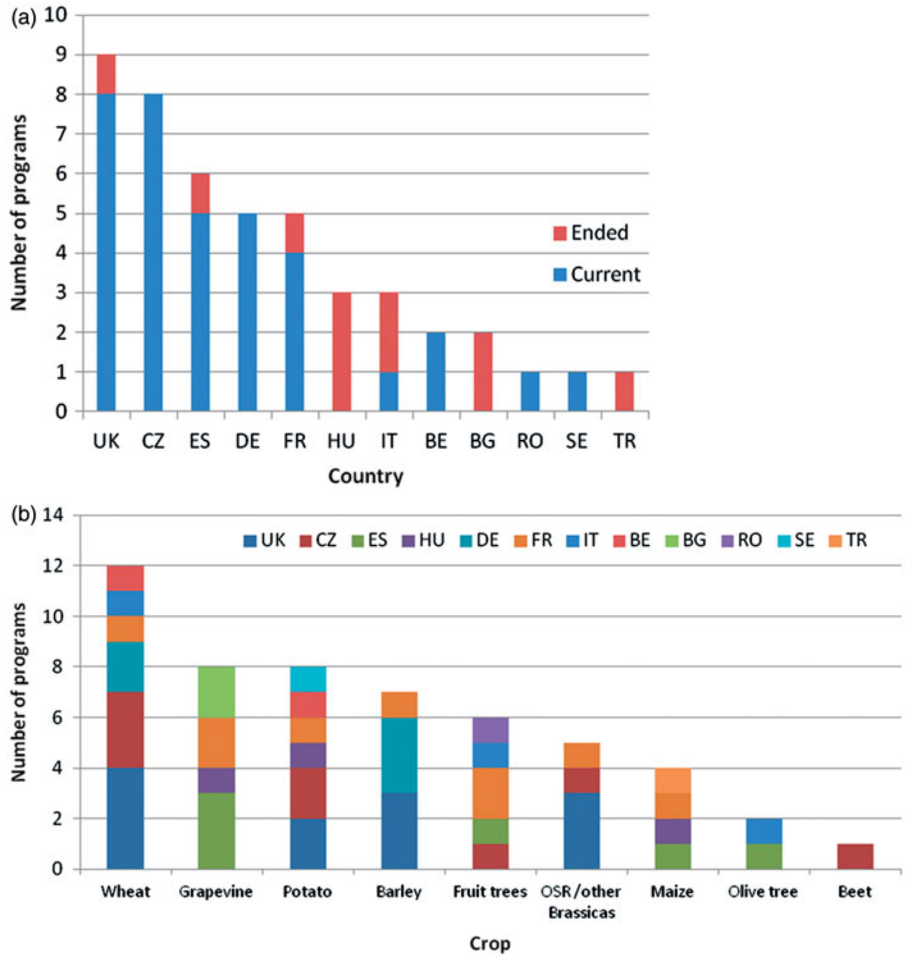

Figure 2. Number of recent European plant-breeding programs using genetic engineering to deal with biotic stress challenges. (a) Per country. The total number of programs is 46 (35 current). Some of these programs used both MAS and GE. Concluded programs (11) are shown in red. (b) Per crop, with the breakdown per country. The total number of programs on a per crop basis is 53 as some programs dealt with more than one crop.

laboratories. As plant breeding research is organized very differently in a variety of European countries, the depth of the data may differ between these countries. Therefore, the obtained quantitative data set may not fully represent comparable absolute values. Nevertheless, they give a broad overview of plant breeding activities using GE in Europe. Only research programs directly relevant to addressing the BS challenges identified in this study were included.

Regarding all BS challenges identified by our questionnaire concerning major crops, 46 recent research programs using GE (mostly T) were recorded in 12 representative countries (Figure 2a; see details in Supplementary Material 6). The United Kingdom has the most research programs using GE. Countries in which cultivation of commercial GE crops is possible (Spain, the Czech Republic) tended to have a higher share of such programs with respect to the relative importance of their agricultural economy in Europe. However, no program was reported in Portugal.

Eight Member States (Austria, Bulgaria, France, Germany, Greece, Hungary, Italy and Luxembourg) currently apply national bans on approved transgenic events (essentially MON810 maize), on the basis of alleged environmental effects (for more information, see, http://greenbiotech.eu/eu-gm-crops/). Agricultural areas of major crops. France and Germany have fewer research programs using GE than UK as a comparator. Italy has just one current program, while Hungary has none and in 2012 new field trials with transgenic varieties were effectively suspended. Bulgaria had two research programs related to BS using T, but field trials have been banned for >6 years and all programs have stopped as a consequence.

Public research breeding efforts using GE are unequally divided between crops (Figure 2b). For example, similar numbers of research programs using GE are conducted on grapevine, potato and barley, despite differences in cultivated areas. This could be explained by the severity of some fungal diseases that affect grapevine and potato (see Supplementary Material 3). Only research programs concerned with BS and using GE or new techniques were included. However, many pests and diseases are not considered in these programs irrespective of the technique used (Supplementary Material 6 highlights programs using all the techniques). Other relevant programs, not captured in this study, may exist however, when also considering the scientific literature (Supplementary Materials 4 and 5), it appears that 51 BS challenges (out of the 128 identified in the present survey) are insufficiently dealt with by genetic approaches. Among these ''neglected'' challenges, a few are particularly worrying: 10 BS affect >50% of the crop's cultivated area, 23 BS affect <25% of crop areas but are present in all the countries.

Public research programs were also found to deal with other challenges such as abiotic stresses and nutritional quality. However, these were not considered further in the current study although it is recognized that much basic research is carried out in these areas. Some early-stage programs also focus on new technologies for targeted insertion of genes into plant genomes using site-specific nucleases or targeted modification of plant genes using CRISPRs, Clustered Regularly Interspaced Short Palindromic Repeats (see Table S2 in Supplementary Material 2).

Involvement of the private sector in research on BS challenges

For commercial reasons, private companies could not answer our questionnaire. To circumvent this problem, we examined field trials of GE varieties (for commercial authorization) and patents relevant to resistance to BS. Data on field trials of GE plants, developed by private and/or public laboratories were collected in all 28 European countries including the representative countries of this study. Data from the European Register (Deliberate release and placing on the EU market of GMOs – GMO register. http://gmoinfo.jrc.ec.europa.eu/gmp_browse.aspx) were examined from 2003 to 2013. In Turkey, because of earlier restrictive regulations, and the total ban on growing GE plants by the Biosafety Law in 2010, no field trial was implemented after 2003. Key details are displayed in Supplementary Material 7 (year of the start of the trial, the country where the trial took place, the crop and the trait under study).

Field trials declined sharply in the EU from 2000 (Marshall, 2014) as a consequence of vandalism (Kuntz, 2012) and other political or social pressures. Therefore, field trials in Europe do not perfectly reflect current breeding programs as they may be performed elsewhere. Between 2003 and 2013, 888 field trials of GE plants were registered (34 were withdrawn during the same period). Only 25 trials were registered in 2013, of which 16 were in Spain. More than 80% of the field trials in Europe are performed by the private sector, mostly dealing with events for which market authorization either for import or cultivation is sought. For example, in Spain, the distribution for 2013 is as follows: eight maize trials (five private vs. three public), four cotton (all private), three sugar beet (all private) and one wheat trial (public). A total of 41 field trials (Supplementary Material 7) were related to 8 of the 128 BS challenges. Among the 51 ‘‘neglected’’ BS challenges not identified in the current European public research programs or in the recent literature search (Supplementary Material 3), only one is addressed by these field trials (see Supplementary Material 7): resistance to corn cutworms (*Agrotis* sp.).

Patents related to the identified BS challenges according to pests/diseases, crops and techniques were queried in the Questel Orbit Patents database (see queries in Table S4 in Supplementary Material 2). Three hundred and fifty patents concerning these challenges were found, and 84 of them were European patents (see details in Supplementary Material 8). Patents related to these BS challenges involve both public and private laboratories. Most of European patents concern maize (34), potato (20) and Brassica (8). For all the crops, the proportion of European patents, compared with the total number, exceeds 25%, except for wheat, which is under represented (2% of total patents). Four crops are highly represented in European patents (Beet: 57%; Potato: 48%; Brassica: 40% and Maize: 39%). Supplementary Material 3 shows the distribution of European/non-European patents according to BS challenges per crop. Among the 51 ‘‘neglected’’ BS challenges not identified in the current European public research programs or in the recent literature search, 11 are covered by European or non-European patents.

Conclusions

It is clear from our bottom-up approach that European farmers need solutions to deal with a number of challenges, the biggest of which are BS. GE could provide at least part of the solution by allowing direct gene transfer to produce a resistance factor via transgenesis or the use of RNAi techniques to reduce expression of target endogenous genes or plant pest genes (Zhang et al., 2015). Cisgenesis has rarely been used so far but may also have a future role. However, for BS as for other challenges, GE is not the only option and conventional plant breeding techniques must also be considered, in particular in combination with GE. MAS is the method of choice in many cases and is reflected in our literature survey but MAS, like other conventional breeding techniques, can only work with the gene pool available within the species or in sexually compatible relatives. In addition, plants generally require distinct arsenals of genes to durably combat pests or diseases. GE could provide unique means to expand the list of useful genes/traits. In some cases, GE may be the superior or the sole available solution and it can often provide broader options for insect or virus resistance.

Wheat is harvested in almost all the European countries and dominates the selected literature. However, fungal diseases and insect pests, together with other factors, contribute to generally decreasing wheat yields. Gains from conventional breeding are becoming smaller over time and it is expected that further yield growth will be generated from genomics research. This will be an important component in successfully addressing the challenge to double global crop production by 2050 (Ray et al., 2013). The current rate of increase in global production must be accelerated to meet demand because crop yield growth has been shown to be an effective tool in reducing global poverty and undernourishment (Dwivedi et al., 2007).

Although not considered in detail here, the impact of abiotic stresses are not negligible. Heat waves and drought in 2003 significantly reduced crop productivity in Southern European countries (e.g. maize yield in Northern Italy was 36% less; Ciais et al., 2005). Since Mediterranean countries normally have dry and hot summers, both irrigation and cultivation of drought-tolerant species could help in reducing the impact of climate changes. Rain fed agricultural production in other parts of Europe will likely be more affected by frequent heat waves and droughts. In Turkey, e.g. in 2014, wheat and barley yields were reduced 13.8% and 20.8%, respectively, compared to the previous years due to drought.

Public research efforts involving GE differ from country to country. We were interested in the influence of the political situation on this research. A bias against GE is not apparent in the recent scientific literature when Europe is compared to the rest of the world. This compilation suggests Europe has a strong potential capacity to use GE for plant breeding efforts. However, a bias is clearly visible when current research programs in various European states are compared. In the countries with strong opposition to ''GMOs'', funding for public research programs using GE, especially for those involving field trials with GE plants, is very limited. Our survey provides quantitative evidence that the political context in Europe, allegedly based on the precautionary principle, is currently inhibiting European research using GE, and consequently potential solutions to address European farmer challenges.

Several other issues concerning both European Member States' policies (Katzek, 2014; Kuntz, 2014; Sabalza et al., 2011) and structures at the highest levels of European policy making Institutions (Davison, 2010) are relevant to this discussion. These are for example: (1) an inability to implement its own legislation to approve GE plants for cultivation (the Amflora potato cultivation dossier took 13 years from submission to approval), (2) a failure to remove illegal national bans, (3) a zero tolerance for products not yet approved (Wager & McHughen, 2010) and (4) an inability to protect EFSA from pressures exerted by activists and some Member States (EPEC, 2011). Therefore, the notion that ''risk in the EU context is no longer about science-based assessment, but is now a political accountability issue'' (Smyth & Phillips, 2014) is a reality! During the final preparation stages of this article, the European Parliament adopted the possibility for individual Member States to ban the cultivation of GM crops approved at EU level, based on a set of vague criteria. This means a *de facto* de-harmonization of a European market, and a serious erosion of decision-making processes based on evidence and science. For GE events that are approved and therefore, by scientific criteria, safe for cultivation, a number of EU member states may now legally be able to deny their farmers the freedom of choice, blocking development and creating unfair internal competition within the EU. In addition, the case of soybean clearly highlights the contrast between EU policies on the import and cultivation of GE crops. While the overwhelming majority of soybean imported by the EU (see ''Introduction'' section) is GE, its cultivation is not allowed. This contrast is directly relevant for the decision-making processes of product developers and investors. This decision is indirectly damaging for the formulation of long-term research strategies in the European innovation sector.

Another issue is raised by the rapid progress in new plant breeding techniques (NPBTs) including genome editing. A recent publication demonstrates the use of genome editing to confer resistance to powdery mildew in wheat (Wang et al., 2014), thus highlighting the potential of such NPBTs. However, there is debate within the EU about the regulatory status of such plants (i.e. whether plants developed by NPBTs will be considered to be ''GMOs'' or not). The regulatory status of such plants in the EU could strongly delay possible commercial availability of these crops (Brüller et al., 2012) and severely hamper the development of not only European small and medium-sized plant breeding companies but also the whole of European agriculture.

The European Commission (2013) published its proposal to upgrade protective measures against plant pests in 2013. This is an important initiative not only because of the spread of existing pests and diseases but also because of the increasing threats due to climate variability (Fisher et al., 2012). Pesticides cannot provide long-term solutions to pests and diseases, and a decrease in pesticide use is highly desirable for both economic and environmental reasons. Therefore, plant breeding will remain essential for crop protection and food security. Precise breeding techniques such as MAS, T and NPBTs are important approaches where quick responses to emerging threats are required. However, the success of T and NPBTs will depend on developments in legislation. There is a need to change the ''GMO'' regulatory system and its recent European alterations to ensure that approval relies on a science-based framework regulating traits and products, not the technology employed (EASAC, 2014). Also, true freedom of choice for farmers needs to be defended as a basic policy principle. Paradoxically, the constraints of the regulatory system are one reason for continuous development of new methods in order to introduce desirable traits into crops (Leyser, 2014). Science is taking new routes to overcome the illogical hurdles created by an inappropriate regulatory system.

The EU budget for 2014–2020 marks a decisive shift toward Research and Development and Innovation (R&D&I) with a 30% real terms increase in the budget for Horizon 2020. A further EUR 83 billion is expected to be invested in R&D&I as well as SMEs through the new European Structural and Investment Funds (European Commission, 2014). Further opportunities exist under the new European Common Agricultural Policies (CAP), where innovation is also one of the top funding priorities. Efficient use of these resources, however, is not possible when prejudice excludes technologies for non-scientific reasons. There is potential in Europe for better alignment of farmers' and agricultural policies' needs, creating synergies between the need to protect crops against pests, the need to be more environmentally friendly and the need to help farmers obtain a better harvest and lower production costs. The latter are important in the context of the CAP in which different markets are becoming less protected and competition among farmers is becoming more important. Programs that finance agricultural research should take into account these different needs and stimulate the development of plants that will make the life of European farmers easier and more rewarding. This can be best achieved when public research institutions join their efforts with farmers' organizations in defining aims and approaches that will most likely result in innovative solutions to pressing needs.

Research is often limited by financial resources. Therefore, rationalization of limited means is necessary for ensuring relevant and coordinated public research (EASAC, 2014). The data presented here could enable decision-makers from different countries to pool resources in the most pertinent breeding research projects (i.e. most related to the needs of farmers). Figure 3 shows graphical visualization of cultivated areas for a given crop by country superimposed with the severity of selected diseases thus suggesting ways to build international research consortia. In the first example (*Cercospora* leaf spot in beet), France, Germany, Turkey, Italy and Belgium should have the greatest interest in implementing a consortium against this disease. However, only one scientific paper was identified in our study. The second example of grey mould in grapevine highlights

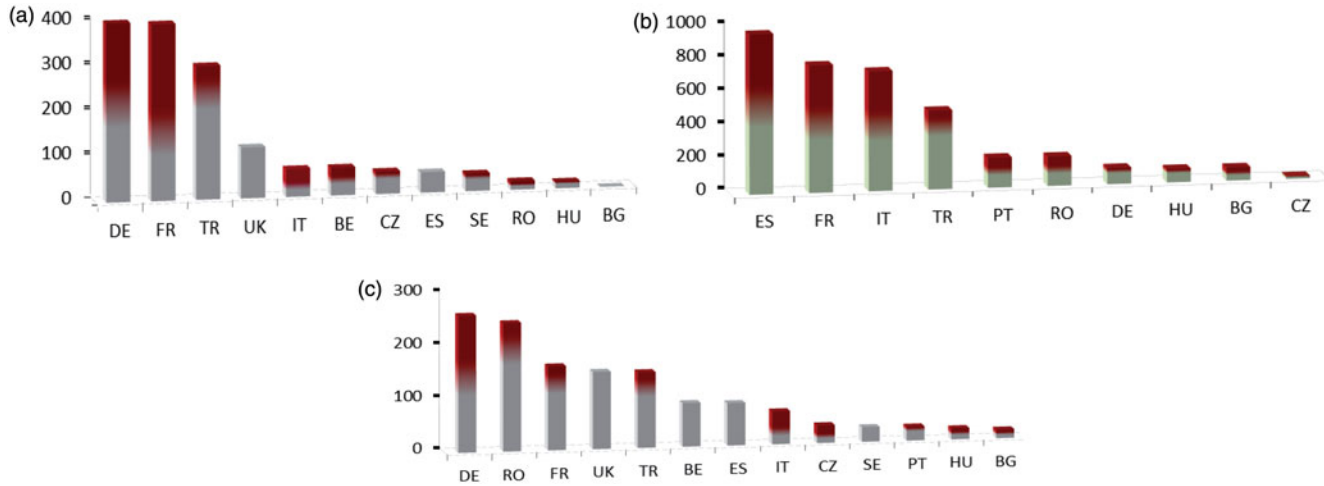

Figure 3. Graphical visualization of the severity of challenges related to bioaggressors for European farmers. The bars show cultivated area (×1000 ha) in the various representative countries. The severity of the disease is shown in red according to the estimations presented in Supplementary Material 3. (a) Cercospora leaf spot in beet, (b) grey mould in grapevine and (c) Potato virus Y in potato.

a case where 10 countries might be interested in embarking on joint research projects. The third example concerns a potato viral disease for which resistance is described in a number of publications, using various approaches (transgenic and non-transgenic). In this case, efforts could concentrate on providing farmers with a range of resistance genes for durable control of this virus.

Collaboration of the private and public sector is evident in most European countries (Supplementary Material 2, Table S2, Question 8) and the private sector has, through seed distribution, a more direct connection to farmers than public research institutions. Financial mechanisms that stimulate such developments should play an important part of future development of the CAP, but at least in the field that we are investigating here, no financial mechanisms could outweigh a regulatory system that efficiently suppresses innovation and development.

In conclusion, we have identified 128 serious challenges for farmers (39 currently neglected in terms of research effort, i.e. not identified in current European public research programs, or in recent research literature and not covered by patents or field trials). For some pests and diseases, only biotechnological approaches will lead to solutions, and researchers within Europe have the expertise to use new technologies for maximum impact. However, politics is preventing them from deploying the most appropriate technologies to address the challenges. Decision-makers have two choices when designing ways to meet these challenges, either to change an inappropriate regulatory system for GE plants or to fund plant science to a much higher level in order to compensate for the political restrictions on research efficiency.

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References

Altizer S, Ostfeld RS, Johnson P, et al. (2013). Climate change and infectious diseases: from evidence to a predictive framework. Science, 341, 514–9.

Brüller W, Hartmann J, Hochegger R, et al. (2012). Cisgenesis. A report on the practical consequences of the application of novel techniques in plant breeding. Bundesministerium für Gesundheit, Sektion II, Vienna, Austria. Available from: http://bmg.gv.at/cms/home/attachments/6/6/0/CH1052/CMS1352183689337/cisgenesis_20121105.pdf.

Challinor AJ, Watson J, Lobell DB, et al. (2014). A meta-analysis of crop yield. Nat Climate Change, 4, 287–91.

Ciais P, Reichstein M, Viovy N, et al. (2005). Europe-wide reduction in primary productivity caused by the heat and drought in 2003. Nature, 437, 529–33.

Davison J. (2010). GM plants: science, politics and EC regulations. Plant Sci, 178, 94–8.

Dwivedi SL, Crouch JH, Mackill DJ, et al. (2007). The molecularization of public sector crop breeding: progress, problems, and prospects. Adv Agron, 95, 163–318.

EASAC. (2014). Risks to plant health: European Union priorities for tackling emerging plant pests and diseases. EASAC policy report 24. German National Academy of Sciences Leopoldina, Halle Germany. Available from: http://www.easac.eu/fileadmin/PDF_s/reports_statements/EASAC_24_RisksPlantHealth_FullReport.pdf.

EFSA Panel on Genetically Modified Organisms. (2012). Scientific opinion addressing the safety assessment of plants developed through cisgenesis and intragenesis. EFSA J, 10, 2561.

EPEC. (2011). Evaluation of the EU legislative framework in the field of cultivation of GMOs under Directive 2001/18/EC and Regulation (EC) no 1829/2003, and the placing on the market of GMOs as or in products under Directive 2001/18/EC. EPEC report to DG SANCO. Available from: http://ec.europa.eu/food/food/biotechnology/evaluation/docs/gmo_cultivation_report_en.pdf.

European Commission. (2013). Proposal for a regulation of the European Parliament and the Council on protective measures against pests of plants. COM 267 final. Available from: http://eur-lex.europa.eu/procedure/EN/202627.

European Commission. (2014). Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions. Available from: http://ec.europa.eu/research/innovation-union/pdf/state-of-the-union/2013/research-and-innovation-as-sources-of-renewed-growth-com-2014-339-final.pdf.

FAO. (2012). The state of food and agriculture: investing in agriculture for a better future. Available from: http://www.fao.org/docrep/017/i3028e/i3028e00.htm.

Fisher MC, Henk DA, Briggs CJ, et al. (2012). Emerging fungal threats to animal, plant and ecosystem health. Nature, 484, 186–94.

Grassini P, Eskridge KM, Cassman KG. (2013). Distinguishing between yield advances and yield plateaus in historical crop production trends. Nat Commun, 4. Article number: 2918. DOI: 10.1038/ncomms3918.

Katzek J. (2014). At the end of the day everything boils down to politics: the evolving of German policy toward GMO crops and the existing stagnation. GM Crops Food, 5, 178–82.

Krezhova D. (Ed) (2011). Recent trends for enhancing the diversity and quality of soybean products. Publisher: InTech.

Kuntz M. (2012). Destruction of public and governmental experiments of GMO in Europe. GM Crops Food, 3, 1–7.

Kuntz M. (2014). The GMO case in France: politics, lawlessness and postmodernism. GM Crops Food, 5, 163–9.

Leyser O. (2014). Moving beyond the GM debate. PLoS Biol, 12, 6, e1001887.

Marshall A. (2014). Drought-tolerant varieties begin global march. Nat Biotechnol, 32, 308.

McCouch S, Baute GJ, Bradeen J, et al. (2013). Agriculture: feeding the future. Nature, 499, 23–4.

Parker C. (2009). Observations on the current status of *Orobanche* and *Striga* problems worldwide. Pest Manag Sci, 65, 453–9.

Pyšek P, Richardson DM. (2010). Invasive species, environmental change and management, and health. Ann Rev Environ Resour, 35, 25–55.

Ray DK, Mueller ND, West PC, Foley JA. (2013). Yield trends are insufficient to double global crop production by 2050. PLoS ONE, 8, 6, e66428.

Sabalza M, Miralpeix B, Twyman RM, et al. (2011). EU legitimizes GM crop exclusion zones. Nat Biotechnol, 29, 315–7.

Schouten H. (2014). Reply to The slippery slope of cisgenesis. Nat Biotechnol, 32, 728.

Smyth SJ, Phillips PWB. (2014). Risk, regulation and biotechnology: the case of GM crops. GM Crops Food, 5, 170–7.

Tester M, Langridge P. (2010). Breeding technologies to increase crop production in a changing world. Science, 327, 818–22.

Wager R, McHughen A. (2010). Zero sense in European approach to GM. EMBO Rep, 11, 258–62.

Wang Y, Cheng X, Shan Q, et al. (2014). Simultaneous editing of three homoeoalleles in hexaploid bread wheat confers heritable resistance to powdery mildew. Nat Biotechnol, 32, 947–51.

Wheeler T, von Braun J. (2013). Climate change impacts on global food security. Science, 341, 508–13.

Zhang J, Khan SA, Heckel DG, Bock R. (2015). Full crop protection from an insect pest by expression of long double-stranded RNAs in plastids. Science, 347, 991–4.

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