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Genetically engineered foods: still a controversial problem

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Commentary on

Pellegrino, E, Bedini, S, Nuti, M & Ercoli, L, 2018, "Impact of genetically engineered maize on agronomic, environmental and toxicological traits: a meta-analysis of 21 years of field data", *Sci Rep.*, vol. 8(1), p. 3113-3120

1. Matter of concern

The argument about genetically engineered (GE) cultures is still very hot. The topics under debate are the safety for humans and animals fed with transgenic food, reduction of herbicides and pesticides, environmental effects, yields, profit for farmers. A recent meta-analysis by Pellegrino et al., (Pellegrino et al., 2018), tried to give some updated answers. The authors examined GE corn with single or stacked traits, such as herbicide tolerance and insect resistance. The second one is expressed in the so called Bt (Bacillus thuringiensis) maize producing a toxin against certain pests (Lepidoptera larvae). Pellegrino et al. claim that these transgenic cultures show a better performance than the conventional ones for a lesser amount of mycotoxins and increased yield, and that they have the same substantial equivalence of composition with non-GE crops. In addition, they state that non-target organisms are not killed by the toxins secreted by GE maize. These conclusions were spread by the media, with too optimistic and in some way deceptive articles. For instance, Dana Dovey reported on Newsweek (February 22, 2018) that "the new study analyzed approximately 6,000 peer-reviewed studies published between 1996 and 2016 to draw its conclusion. Ultimately, results showed that GMO corn increased crop yield by up to 25 percent and also had health benefits as it decreased the amount of food contaminants".

Moreover, we may mention the article published by the Italian newspaper Il Sole 24 Ore (February 15, 2018), where GE corn is defined as "more productive and risk free" and for this reason "promoted" by the authors of the meta-analysis. These claims are misleading since they report in partisan way the results found by the researchers. However, a careful analysis raises some doubts also about certain statements by Pellegrino et al., since there are a number of weakness and flaws in their study. I will try to highlight the most controversial points.

2. Biased studies

First, the authors have drawn the results working on 76 studies only (the most part was carried out in USA), after the examination and selection of 6,006 (from 1996

to 2016) peer-reviewed publications. They state to have applied "rigorous criteria for study selection, such as the inclusion in the dataset of field observations comparing GE maize with its true non-GE isoline or near isoline, throughout its overall cultivation period". Nothing else. At the end, the 1,26% of all the studies was taken in consideration. It is a very low number (obviously, not mentioned by the media!) to obtain "reliable" conclusions from the analysis of several parameters monitored throughout a twenty years period. And the same article often contains several different parameters.

Furthermore, about 1/3 of the data reported in the meta-analysis comes from studies where at least one of the authors declared to have a conflict of interest (COI).

With reference to this topic, a recent research (Guillemaud, Lombaert & Bourguet, 2016) has analyzed a large set of articles (n = 672) focusing on the efficacy or durability of GE Bt crops and the ties existing between the researchers, involved in these studies, and the companies selling transgenic seeds. It was demonstrated that connections between researchers and the biotech industry are quite frequent, with 40% of the scientific papers considered having a COI. Of note, the existence of a COI was associated with a 50% higher frequency of results favorable to the interests of the GE crop companies, in comparison to the scientific papers with absence of COI.

Therefore, the presence of COI in scientific research may present a risk that the study outcome may be improperly influenced by commercial interests. This is a more and more common condition, determined by the high financial stakes involved in the development of transgenic cultures and the increasing weight of private funding in research.

Various hypothesis could be identified that may explain the observed association between study outcome and presence of COI: contractual agreements of researchers with companies, restrictions in data publication imposed by industry funders, industry bias aimed at obtaining friendly studies and researchers accommodating toward the interests of their industrial sponsors (Diels, Cunha, Manaia, Sabugosa-Madeira, Silva, 2011). Coming back to the meta-analysis, the evidence of possible influences exerted by transgenic companies show that the results displayed by Pellegrino et al. might be biased at their origin. Ultimately, there is a serious lack of reliable studies on GE cultures, i.e. independent from the huge economic interests of the biotech sector. This problem might be overcome only by strongly increasing public research.

3. Yields increase?

The meta-analysis has found that GE Bt corn hybrids increased yield by 10.1%, calculated on the average grain yield of the GE isolines in comparison the yield of the conventional control cultures. The authors state that global losses of maize production due to pests are estimated at 31.2%, while the yield gain provided by insect pest management by means of chemical insecticides is estimated about 18%. For this last information, they quote the reference 25 (Oerke 2006), that looks to be wrong, since the study regards herbicides, not "insect pest management". However, some critical observations have to be made. Firstly, researchers know that Cry toxins are a family of crystal-forming proteins produced by Bt, and many of them think that the natural and GE Cry insecticidal proteins are the same. This is no true. Natural Cry proteins are not identical to the proteins to which humans or other nontarget organisms are exposed by the production and consumption of GE food and feed. We have to keep in consideration that they have different properties, and for this reason the reliability of risk assessment needs a careful control for each new genetically engineered event (Bizzarri, 2012; Lantham, 2017). But, nothing of that is done. Secondly, if the aim is to compare the yield of GE maize vs the conventional one, non-transgenic isoline or near isoline are not the right control, since they are often low yielding cultivars. Such comparison should be carried out with conventional corn providing a satisfying production, treated according to good agricultural practices that can minimize the plague of pathogenic insects and the consequent loss of harvest.

However, the control cultures normally used in studies with GE plants are not managed under these conditions. In fact, excellent results can be achieved with good agricultural practices (Pazzi, Lerner, Colombo & Monastra, 2006) to prevent fungal attack (correct agronomic practices with crop rotation and so on, suitable varieties, reaping time, correct drying, adequate hygiene and sanitary conditions during transportation, storage, silage and processing, analytic controls of in-coming raw materials, etc.), applied through sustainable agricultural methods. Furthermore, talking about "progress in agriculture" the possibility to take advantage from naturally resistant cultivars of maize, and from biological control against pests is completely disregarded. With reference to the last point, a very recent research has evaluated the in field performances of two atoxigenic strains of A. flavus endemic to Italy

in artificially inoculated maize ears and in naturally contaminated maize. This approach is representative of a strategy based on the use of beneficial biocontrol organisms, very useful in the context of ecological agriculture (Magdoff F. 2007). Co-inoculation of atoxigenic strains with aflatoxin producers resulted in highly significant reductions in aflatoxin concentrations (>90%) in both years only with atoxigenic strain A2085. The average percent reduction in aflatoxin B1 concentration in naturally contaminated maize fields was 92.3% (Mauro, Garcia-Cela, Pietri, Cotty, Battilani & Battilani, 2018).

This study has obtained an excellent result in fighting aflatoxins without GE corn. In conclusion, a correct comparison between transgenic and conventional cultures should be made by using the best controls.

4. Herbicide decrease, GE maize composition, TOs and NTOs organisms

The very low number of the available data has prevented the authors from assessing the extent of insecticide and herbicide decrease used in GM crops compared to non-transgenic ones. This is an additional serious flaw of this study.

The results on the so-called "substantial equivalence" have indicated that the composition of GE maize grain did not differ from that of the isolines for protein, lipid, and fiber content. However, these analyzes are unsatisfactory for humans because they do not take in consideration many data necessary for the evaluation of our safety (for example, the impact on the immune system).

This kind of information, at best, is suitable for animal feed made with GE corn.

The authors state that target organisms (TOs) were killed by Bt maize, whereas non-target organisms (NTOs) were not affected. In this regard it is interesting to read the comments made to the meta-analysis by the entomologist Stefano Maini (Bologna University, Italy). He wrote in clear and convincing way:

> It seems that this report and relative meta-analysis is just "a half-analysis" because the authors did not take into account several issues! First, the main target of GE maize, Ostrinia nubilalis (ECB), has not been considered in the meta-analysis and the study was limited to Diabrotica spp. (WCR), which was included as target pest of GE maize several years later. Although, the authors stated at page 7 that "... only the data on Diabrotica ssp. abundance were sufficient to perform a reliable meta-analysis", this seems to me a very important shortcoming. In fact, all their conclusions should be limited to the papers dealing with WCR and those published more recently since GE maize hybrids resistant to WCR have been introduced much later on than 21 years ago (ref. title)! In addition, WCR damage is not really linked to mycotoxins and there are evidences that the presence of ECB does not increase the level of mycotoxins in non-GE fields. Second, only Braconidae parasitoids have been included in the meta-analysis even though these are rare parasitoids on ECB. In my opinion, the analysis should have included other ECB parasitoids such as Tachinidae, Ichneumonidae and egg parasitoids (Trichogrammatidae). The flaws of this paper convince me that authors do not know maize entomofauna at all. In Europe, GE maize growing seems not a very 'sustainable' agriculture because GE maize reduces biodiversity (due to the potential few GE maize hybrids available for farmers) and for the possible increase of the glyphosate use. In addition, I want to underline that WCR and ECB can be reduced by classical biological control or crop rotation and not only with GE maize cultivation[1].

In addition, although not directly connected with the meta-analysis we have discussed, some papers that evaluated the GE food safety should be carefully consulted (Wilson, 2006; Finamore, 2008; de Vendômois, 2009; Bizzarri, 2012; Gab-Alla, 2012; El-Shamei, 2012; Kiliçgün, 2013; Séralini, 2014; Abdo, 2014; Zdziarski, 2014; Ibrahim, 2016)

5. The concern still remains

In conclusion, this kind of studies raise a more general question. Why traditional plants were left and replaced by few cultures, poor in agrobiodiversity, that are very weak in some geographical and ecological contexts? It is necessary to remind that a deep dietary shift has been achieved in Africa during the second half of last century. In 1948, few African people obtained their carbohydrate calories from corn. Calories came from starch from cassava, sorghum and millet, which are much less prone to aflatoxin contamination, but after this change these plants markedly declined (Pitt, 2017). Clearly there were no economic interests to support agronomic research for improving the yields of these traditional crops. The profound shift, occurred in Africa, from a more diverse food system prior to the 1960s to one where corn and nuts supply most calories is impressive. At the end, the western agricultural model and its technocratic paradigm were imposed, spreading a very harmful pervasive standardization.

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[1] Comments reported in the web page of the article.

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