

Maize MON 87427

Organisation: The European GMO-free Citizens

Country: The Netherlands

Type: Others...

a. Assessment:

Molecular characterisation

see Others

Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)

see Others

b. Food Safety Assessment:

Toxicology

see Others

Allergenicity

see Others

Nutritional assessment

see Others

Others

Discovery of Key Molecular Pathways of C1 Metabolism and Formaldehyde Detoxification in Maize through a Systematic Bioinformatics Literature Review

Download Download as PDF (Size:1187KB) ePub, PP. 571-585 DOI: 10.4236/as.2015.65056
903 Downloads 1.425 Views Citations Author(s) Leave a comment P. Deonikar¹, S. Kothandaram¹, M. Mohan¹, Cori Kollin², Phoebe Konecky², Rachael Olovyanniko², Zachary Zamore², Brian Carey², V. A. S. Ayyadurai^{1*} Affiliation(s)

¹International Center for Integrative Systems, Cambridge, MA, USA. ²Livingston High School, Livingston, NJ, USA. ABSTRACT

Computational systems biology approaches provide insights to understand complex molecular phenomena in living systems. Such understanding demands the need to systematically interrogate and review existing literature to refine and distil key molecular pathways. This paper explores a methodological process to identify key molecular pathways from systematic bioinformatics literature review. This process is used to identify molecular pathways for a ubiquitous molecular process in all plant biological systems: C1 metabolism and formaldehyde detoxification, specific to maize. The C1 metabolism is essential for all organisms to provide one-carbon units for methylation and other types of modifications, as well as for nucleic acid, amino acid, and other biomolecule syntheses. Formaldehyde is a toxic one-carbon molecule which is produced endogenously and found in the environment, and whose detoxification is an important part of C1 metabolism. This systematic review involves a five-part process: 1) framing of the research question; 2) literature collection based on a parallel search strategy; 3) relevant study selection based on search refinement; 4) molecular pathway identification; and 5) integration of key molecular pathway mechanisms to yield a well-defined set molecular systems associated with a particular biochemical function. Findings from this systematic review produced three main molecular systems: a) methionine biosynthesis; b) the methylation cycle; and c) formaldehyde detoxification. Specific insights from the resulting molecular pathways indicate that normal C1 metabolism involves the transfer of a carbon group from serine through a folate-mediated pathway to methionine, and eventually the methylation of a biomolecule. In photosynthetic tissues, C1 metabolism often proceeds in reverse towards serine biosynthesis and formate oxidation. C1 metabolism, in maize, appears to be present in the developing embryo and endosperm indicating that these cells are vulnerable to perturbations in formaldehyde detoxification. These insights demonstrate the value of a systematic bioinformatics literature review process from a broad spectrum of domain literature to specific and relevant molecular pathways. **KEYWORDS**

Systematic Review, Bioinformatics, Molecular Pathway, C1 Metabolism, Formaldehyde, Detoxification, Maize, Methionine Biosynthesis, Methylation Cycle, Folate-Mediated Pathways Cite this paper

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3. Environmental risk assessment

see Others

4. Conclusions and recommendations

Do not approve. More research needed.

5. Others

see above 1rst others

6. Labelling proposal

Not to label, not to be approved.

Organisation: La Nature

Country: France

Type: Individual

a. Assessment:

5. Others

I am against the spread of GM plants and seeds which can damage what nature created. Artificialisation of land for financial purposes could lead to a future disaster: Therefore I say no to GMOs for my children and no to Monsanto who would sell its children to make money.

Organisation: Testbiotech

Country: Germany

Type: Non Profit Organisation

a. Assessment:

Molecular characterisation

The process of genetic engineering involves several deletions and insertions in the maize plants. In order to assess whether the sequences encoding the newly expressed proteins or any other open reading frames (ORFs) present within the insert and spanning the junction sites raise any safety issue, the proteins that might emerge from these DNA sequences were assumed as raising no safety issues.

However, the molecular characterisation of the plants did not take into account the emergence of new double stranded miRNA that might be transmitted as a biologically active substance at the consumption level to humans or animals. miRNA might be transmitted to the consumer and there is dispute over whether it might interact with gene regulation in mammalian cells (see, for example, Zhang et al., 2011; Lukasik & Zielenkiewicz, 2014). The emergence of new versions, combinations and concentrations of miRNA was neither assessed in the single plants nor in the stacked event. Uncertainties related to the emergence of these molecules were not addressed.

According to EU Member States experts, analyses show that CP4 EPSPS protein level in forage derived from glyphosate-treated plants almost doubled in comparison with the one obtained from untreated plants. Instead of asking the applicant for explanations for this surprising effect, EFSA simply concluded that only grain is subject to importation and left

aside the data from forage which are very relevant for the overall risk assessment of the plants.

Lukasik, A., & Zielenkiewicz, P. (2014) In Silico Identification of Plant miRNAs in Mammalian Breast Milk Exosomes – A Small Step Forward? PLoS ONE 9(6): e99963.

Zhang, L., Hou, D., Chen, X., Li, D., Zhu, L., Zhang, Y., Li, J., Bian, Z., Liang, X., Cai, X., Yin, Y., Wang, C., Zhang, T., Zhu, D., Zhang, D., Xu, J., Chen, Qu., Ba, Y., Liu, J., Wang, Q., Chen, J., Wang, J., Wang, M., Zhang, Q., Zhang, J., Zen, K., Zhang, C.Y. (2011) Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA. Cell Research, 22(1): 107-126.

Comparative analysis (for compositional analysis and agronomic traits and GM phenotype)

The data presented by Monsanto only contains data from one year while the plants were grown under 'normal' agricultural conditions.

Under these conditions, analysis of agronomic traits showed that there are several statistically significant differences in comparison to the isogenic line. However EFSA considered these differences as being biologically not relevant. Some of the data were based on methodologies that were considered as not appropriate (such as pollen and seed characteristics), however EFSA did not request further data.

Also for compositional analysis, several significant differences were shown between maize MON 87427 and its conventional counterpart. Those plants sprayed with glyphosate showed a much higher number of significant differences.

In summary, there are indications that unintended effects derive from the process of genetic engineering. Further, environmental interactions might play a role in triggering these significant differences. It is possible that some of the relevant changes in plant composition and plant characteristics may only be observed under specific environmental conditions. Thus, the observed differences should have triggered a request from EFSA for more studies, for example, to grow the plants under defined environmental extreme stress conditions. Such conditions can also reveal genetic potential for instability in the expression of the newly introduced DNA (see, for example, Trtikova et al., 2015).

Trtikova, M., Wikmark, O.G., Zemp, N., Widmer, A., Hilbeck, A. (2015) Transgene Expression and Bt Protein Content in Transgenic Bt Maize (MON810) under Optimal and Stressful Environmental Conditions. PloS one, 10(4): e0123011.
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0123011>

b. Food Safety Assessment: Toxicology

A subchronic 90 days feeding study was performed with rats. The study showed several significant differences which were considered incidental by EFSA, for example: „Higher mean body weights and body weight gains, both statistically significant at most of the time

points, were noted throughout the treatment period in females of the GM diet group compared with the control group. The difference in terminal body weight was approximately 8 %.“
„Males given the GM maize showed a significantly lower mean serum cholesterol level and a significantly higher mean chloride level in comparison to the male control group. In females fed the GM maize mean serum alanine aminotransferase activity was significantly higher, while urea nitrogen was significantly lower in comparison to the female control group.“
„Significant differences in some organ weights were noted between females fed the GM diet and those given the control diet: higher brain weight (absolute only), lower ovary/oviducts and thymus weight (both relative to body weight only), and lower thyroid/parathyroid weights (absolute only).“

Further, according to the EFSA opinion, diets were formulated in accordance with the specifications of the Purina Mills Inc. Certified Rodent LabDiet® 5002. However, recent research has shown that the same diets might be contaminated with transgenic material (Mesnage et al., 2015). In the study by Mesnage et al., the Purina 5002 diet was contaminated with around 12.8% GM soy and 35.6% GM maize and was not labelled. Such contaminations can mask any health effect of the genetically engineered plants. Based on the data presented from this feeding study, safety of Maize MON87427 can not be concluded.

The plants are usually treated with glyphosate and will contain pesticide residues. However, EFSA did not assess possible health effects of the residues and there is no data concerning the amount of glyphosate residues within MON 87427 plants. This is especially concerning in the light of a recent report by the International Agency for Research on Cancer. According to the IARC, a body of the World Health Organisation (WHO), glyphosate was shown to be “probably carcinogenic to humans” (Guyton et al., 2015). Further, a Testbiotech report (Bauer-Panskus, 2014) concluded that there are many open questions regarding the risk assessment of glyphosate, on issues such as subchronic toxicity, long-term toxicity, genotoxicity, endocrine effects and ecotoxicology.

Bauer-Panskus, A. (2014) Testbiotech comment on the German Renewal Assessment Report (RAR) on the active ingredient glyphosate. <http://www.testbiotech.org/en/node/1094>

Guyton, K.Z., Loomis, D., Grosse, Y., El Ghissassi, F., Benbrahim-Tallaa, L., Guha, N., ... & Straif, K. (2015) Carcinogenicity of tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate. *The Lancet, Oncology*, 16(5): 490-491.

Mesnage, R., Defarge, N., Rocque, L.-M., Spiroux de Vendômois, J., Séralini, G.-E. (2015) Laboratory Rodent Diets Contain Toxic Levels of Environmental Contaminants: Implications for Regulatory Tests. *PLoS ONE* 10(7): e0128429.
<http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0128429>

Others

As a legal dossier compiled by Professor Ludwig Kraemer (Kraemer, 2012) shows, EU regulations require the monitoring of effects on health at the stage of consumption in case of uncertainties. Thus for example monitoring of health effects, taking into account residues from spraying with herbicides must be required. Epidemiological parameters that are suitable to detect relevant health effects have to be defined.

3. Environmental risk assessment

Any spillage from the kernels has to be monitored closely.

4. Conclusions and recommendations

In the light of the substantial lack of data and major gaps in the risk assessment, no market authorisation can be given.
