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Research raises concerns over functionality, cancer causing impact of GMOs

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Scientist Dr Shiva Ayyadurai's recent research has raised alarming questions on the functionality of Genetically Modified Organisms (GMOs) and their impact on plant behaviour as carcinogens.

The MIT (Massachusetts Institute of Technology)-based Indian origin scientist's research has shown that GMOs have bad impact on molecular system of plant which results in excessive accumulation of formaldehyde - classified by the US Environmental Protection Agency (EPA) as a probable human carcinogen under conditions of unusually high or prolonged exposure.

Dr Ayyadurai's new study published in the peer-reviewed Journal of Agricultural Sciences, 2015, applies modern computational systems' biology methods to reveal genetically-modified soy creates significant disruption in basic cellular functions leading to a sharp increase in levels of formaldehyde, a known carcinogen. In the GMO, formaldehyde dramatically accumulates and glutathione, an antioxidant, is depleted. The study is the first systems biology analysis of its kind.

According to the research paper by Dr Ayyadurai and Prabhakar Deonikar, published in the journal, the safety assessment of GMOs is a contentious topic. Proponents of GMOs assert that GMOs are safe since the FDA's policy of substantial equivalence considers GMOs "equivalent" to their non-GMO counterparts, and argue that GM is simply an extension of a "natural" process of plant breeding, a form of "genetic modification," though done over longer time scales.

Meanwhile, anti-GMO activists counter that GMOs were unsafe since substantial equivalence was unscientific and outdated and it originated in the 1970s to assess safety of medical devices, which were not comparable to the complexity of biological systems, and contend that targeted GM was not plant breeding.

Dr Ayyadurai, who was in Delhi recently to propagate his research analysis, says, "The heart of the debate appears to be on the methodology used to determine criteria for substantial equivalence. Systems biology, which aims to understand complexity of the whole organism, as a system, rather than just studying its parts in a reductionist manner, may provide a framework to determine appropriate criteria, as it recognises that GM, small or large, may affect emergent properties of the whole system."

He explains, "Herein, a promising computational systems biology method couples known perturbations on five biomolecules caused by the CP4 EPSPS GM of Glycine max L. (soybean), with an integrative model of C1 metabolism and oxidative stress (two molecular systems critical to plant function). The results predict significant accumulation of formaldehyde and concomitant depletion of glutathione in the GMO, suggesting how a "small" and single GM creates "large" and systemic perturbations to molecular systems equilibria."

Dr Ayyadurai adds, "The results from this study suggest a substantial difference in the molecular systems of non-GMO and GMO versions of soybean, as observed in the temporal dynamics of two biomarkers, formaldehyde and glutathione, which predict metabolic disruptions in C1 metabolism."

In non-GMO plants, formaldehyde, a known toxin, remains at near zero levels, as it is naturally cleared through a process of formaldehyde detoxification, a molecular system resident in all plants, bacteria and fungi. Concomitantly, glutathione, a known anti-oxidising agent, in non-GMO plants, is naturally replenished and remains at non-zero steady state levels, to support such system detoxification of formaldehyde. However, in the GMO case of soybean, or RRS, there is a significant accumulation of formaldehyde and a concomitant depletion of glutathione, suggesting how a "small" and single GM can create "large" and systemic perturbations to molecular systems equilibria.

He adds that the results of this research were particularly relevant, as the United States White House on July 2, 2015, had ordered a review of rules for GM crops.

"The computational systems biology approach, herein, and the resultant predictions, may inform regulatory agencies in their efforts for "Improving Transparency and Ensuring Continued Safety in Biotechnology," to adopt a systems biology approach using a combination of *in silico*, computational methods used herein, and subsequent targeted experimental *in vitro* and *in vivo* designs, to develop a

systems understanding of “equivalence” using biomarkers, such as formaldehyde and glutathione, which predict metabolic disruptions, as criteria for modernising the safety assessment of GMOs, while fostering a much-needed transparent, collaborative and scientific discourse,” states Dr Ayyadurai.

Regulatory agencies, currently reviewing rules for GMO safety, may wish to adopt a systems biology approach using a combination of *in silico*, computational methods used herein, and subsequent targeted experimental *in vitro* and *in vivo* designs, to develop a systems understanding of “equivalence” using biomarkers, such as formaldehyde and glutathione, which predict metabolic disruptions, towards modernising the safety assessment of GMOs, according to the synopsis of the research paper.