Immune System Response in Mice Fed a Diet of MON 810 Maize

**Background**

A report by Finamore et al. was released in the Journal of Agricultural and Food Chemistry titled, “*Intestinal and Peripheral Immune Response to MON810 Maize Ingestion in Weaning and Old Mice*”. The authors’ stated in their conclusion:

*“… the results obtained indicate that the consumption of MON810 maize used in the present study induced alterations in intestinal and peripheral immune response of weaning and old mice. Although the significance of these data remains to be clarified to establish whether these alterations reflect significant immune dysfunctions, these results suggest the importance of considering the gut and peripheral immune response to the whole GM crop, as well as the age, in the GMO safety evaluation.”*

The following response is intended to address potential questions about the study findings in the broader context of existing published research studies and the weight of evidence approach in addressing the safety of MON 810 as well as for GM crops generally.

**Additional Resources**

Report abstract available at: <http://pubs.acs.org/doi/abs/10.1021/jf802059w>

**Key Points**

* **The authors found a shift in a number of measures which reflect the number of immune cell types and in the immune system chemicals used for inter-cellular communications. The authors concede (see quotation above) that the meaning of these findings is not clear. The changes noted by the authors have not been directly linked to the biotech trait. The authors state that there may be variables other than the presence of Cry1Ab which may account for these findings, for example varying mycotoxin levels.**
	+ The changes reported are not associated with any known health effects, either in the animals or humans.
	+ The immune system normally responds to a wide variety of stimuli. There is no evidence that the observed effects represent any kind of abnormal response.
	+ Changes in the immune system, even if present, do not necessarily translate into lack of safety. Many foods and food components, which are routinely consumed, are known to modulate the immune system, e.g., fish oil, omega-3 and omega-6 fats etc.).
* **The test system used by the authors cannot yet be relied on. It has not previously been used to assess food safety and the system has not been validated for this use.**
	+ There were differences in mycotoxin levels in the control and GM corn which may account for some or all of the observed findings. Further, the authors concede that there may be differences other than the presence of Cry1Ab which may account for these findings.
	+ The normal ranges for the parameters measured are unknown; consequently it isn’t possible to assess whether the results observed with the traditional laboratory mouse diet (which is an artificial diet mix) represent typical or expected values for mice.
	+ There were no reference diets to enable a comparison to changes that would vary in response to other dietary changes, including other materials that are widely regarded as safe for consumption. For example- how do the results with MON 810 compare to mushrooms, beef, chili peppers, etc.
* **There are a large number of studies available that validate the safety of GM products. Numerous studies from different laboratories have been conducted on biotech crops that show no adverse affect on animal health.**
* **MON 810 has a history of safe use since its introduction in 1996. This product has been thoroughly tested and has been consumed by humans and animals for over a decade. MON 810 dossiers have been thoroughly reviewed by hundreds of independent scientists on behalf of regulatory authorities around the world and have been approved by a number of countries. Regulatory authorities in more than 20 countries have concluded that MON 810 is as safe as conventional corn.**

**Looking Deeper**

* **The authors looked at a variety of parameters in young and old mice fed a 1) standard mouse diet with conventional corn, 2) a MON 810 “parental control” diet with conventional corn or 3) GM corn (MON 810).**
	+ Many of the cellular response parameters were unchanged.
	+ Among parameters which did change, the direction and magnitude of the change was often variable in the different age groups.
* **The effects presented in this report are not biologically relevant.**
	+ The small changes in the number of white blood cell (lymphocyte) subtypes and cytokine levels(signaling molecules used in cell communication) are not unexpected.
	+ The observed changes are not associated with any known health effects. The authors did not measure any high level physiological responses (other than body weight) that would have linked the observed cellular changes to biologically relevant health effects.
	+ There is no direct evidence that the small differences observed indicate any potential to cause allergies or other immunotoxic effects, either in animals or humans. In fact, the authors conclude, based on testing immune response to Cry1Ab, that it has “low immunogenicity”.
* **The authors’ claim that Cry1Ab caused the reported changes is unsupported.**
	+ The authors acknowledge that protein profiles, unrelated to the Cry1Ab protein expression, differ among corn varieties, and are a potential source of the observed effects.
	+ Differences in mycotoxin (fungal toxin) levels in the control and GM corn may also play a role in explaining the observed effects, as noted by the authors.
* **The authors’ conclusions regarding the effect of animal age on the lymphocyte and cytokine profiles are not supported in their analysis.**
	+ There were no statistical comparisons made between animal age groups.
	+ Changes observed were inconsistent in direction and magnitude in mice of different ages and exposure durations, i.e.- no particular pattern was apparent in these findings.
	+ Given that the significance of the findings “remains to be clarified” as noted by the authors, claims of an age effect are certainly premature. The information provided does not establish any specific or meaningful effect of the MON 810 corn relative to controls. If any of the effects are meaningful, more information is needed to understand what those effects are, how they may change with age, and whether the effects are typical and normal.
	+ Any inference with regard to age in mice and a correlation with age effects in humans or other animals based on the work in Finamore et al should be taken with caution because there is no established negative health effect.
* **The authors’ suggestion that MON810 contains “antigens” or that Cry1Ab is antigenic is unfounded.**
	+ There are no measurements of antibodies in this work, and thus no test has been performed that could possibly measure allergenicity.
	+ The authors themselves indicate that their results with pure Cry1Ab protein indicate “low immunogenicity”.
	+ The stimulation index for white cells challenged with Cry1Ab was actually *lower* in MON810 fed mice, indicating a lower probability of an immunologically relevant response due specifically to the Cry1Ab protein in MON 810.
* **Any suggestion that this animal-based bioassay system should be used routinely for food safety assessment is very premature. In order to use such a system:**
	+ Normal ranges for all parameters need to be established using established positive and negative controls.
	+ Findings need to be correlated with some type of meaningful hazard, risk or health effect.
	+ Effects of foods in general on the immune parameters measured must be established so that we can compare the safety of a novel (GM or otherwise) food to conventional varieties as well as to other food types.