Why Scientists are Worried about the GMO Potato and Apple

When Brazilian research scientists fed tiny pieces of RNA to young honey bees, they expected little to happen—certainly nothing earth-shaking. The RNA used is not naturally found in bees. It was taken from jellyfish, chosen because it was *supposed* to have an insignificant impact. The RNA didn't cooperate.

After mixing just a single meal of RNA into the natural diet of the worker bee larvae, as the bees grew older, scientists discovered that a staggering 1461 genes showed significant changes compared to controls.[1] In other words, about 10% of all the bees' genes, including those vital to health, were either turned up in volume, or more often than not, turned down.[2] The authors of the study concluded that such a massive change "undoubtedly" triggered changes in the bees' development, physiology, and behavior.

Perhaps the scientists from the United States Department of Agriculture (USDA) missed this 2013 study when they recently approved potatoes and apples genetically engineered not to brown. "Arctic" apple slices (nicknamed the "Botox apple") can supposedly sit on the shelf for 15-18 days without discoloring to reveal their age. Sliced up "Innate" potatoes will similarly not show any darkening day after day until they eventually dry up.

To accomplish this effect, scientists at Okanagan Specialty Fruits and J. R. Simplot introduced genetically engineered genes that make their apples and potatoes produce double stranded RNA (dsRNA) to shut off the browning genes. dsRNA is the same type of RNA that was fed to bees.

The question that serious scientists are asking is: If we (or bees, or birds, or deer) consume the dsRNA in the apple or potato, can it influence how our genes work? Will these genetically modified organisms (GMOs), eaten as apple pies, french fries, or whatever, change *our* development, physiology, and behavior?

One of those serious scientists is Dr. Jack Heinemann, a professor of genetics and molecular biology, and director of the Centre for Integrated Research in Biosafety at the University of Canterbury in New Zealand. For more than a decade, he has been warning the agencies that approve GMOs about the need to test new dsRNAs for safety.

RNA as Gene Controller

RNA is the way-station molecule between genes (made of DNA) and the proteins that they specify. Years ago, scientists were sure that the influence went only in one direction: DNA would pass on a code to RNA, which would then design proteins on that basis. Now it is understood that types of RNA such as dsRNA exert a significant influence in the opposite direction. "These small dsRNA molecules control genes," says Heinemann. "They turn them on or turn them off."[3]

Genetic engineering can introduce new dsRNAs into our food. This can be done intentionally, as in the case of the apple and potato, or totally by accident. In either case, these may be "new patterns that we've never seen before," says Heinemann. "We can be exposed to these and potentially have genes regulated by those dsRNA molecules."

Author: Jeffrey M. Smith April 8, 2015

"We have to be able to assess, *before we use these foods*," asserts Heinemann, "whether they can have an adverse effect on people or on other organisms in the environment." When he expressed his concerns to the governments' GMO regulators in Australia and New Zealand, they dismissed them.

Government Safety Assurances are a Sham

RNA, according to the regulators, is too unstable. It would be destroyed long before it could enter the blood supply. And even if it were to get into the blood, they claim it wouldn't have any effect whatsoever.

While it's true that most RNA are not stable, Heinemann points out that "surprisingly, the form of RNA called dsRNA is very *very* stable. . . . And it's now been shown that they can be taken up after digestion of the food into our blood supply." More importantly, in a groundbreaking study conducted in China in 2012,[4] dsRNA fed to mice "transferred to the liver and down-regulated an important liver enzyme."

This study provided early evidence that the excuses used by the regulators were just that, and not backed by science. So when Heinemann read the governments' evaluation of a GMO wheat variety that used dsRNA to alter its starch production, he was alarmed to find that all the new published research about dsRNA was totally ignored.

"When we looked at the regulator's risk assessment, we found that they never considered the potential adverse effect of the intended dsRNA either on people—and this was an approval to test it on people—or on unintended targets in the environment." They simply *assumed* "that RNA cannot be toxic."

In addition to regurgitating the same outdated arguments of dsRNA instability and lack of influence, they added three more.

According Heinemann, the regulators claimed, that dsRNA "would never accumulate to levels that would have a biological effect." But he points out, "There are *zero* experiments testing how much dietary dsRNA is necessary for a biological effect." It was a baseless argument.

Then, using rather strained logic, they flatly claimed, according to Heinemann, "because RNA is everywhere, it must be safe. It is our background baseline of safety." While Heinemann acknowledges that "The chemical properties of RNA molecules are generally the same," it's not their chemical composition—the nucleic acids—that is critical. "They miss the most important thing about nucleic acids," he says. "The activity of nucleic acids is the *specific sequence* of nucleotides along the backbone of the molecule." And it's that specific sequence that determines if and how the dsRNA influences gene expression. So some dsRNA will be safe and some will not.

The point becomes obvious when you realize that GMO companies like Monsanto are hoping to get approval for crops they engineered with dsRNA to kill insects. "Every RNA molecule eaten by insects does not kill them," says Heinemann. "But certain dsRNA molecules do, because of the order of their nucleotides."

In their final argument, the regulators contradict themselves by acknowledging that the order of the dsRNA may be important. But the dsRNA used in the GMO wheat, they contend, must be safe. Why? Because the dsRNA sequence comes from wheat itself. And since humans are so far away from wheat in

the biological order of things, there couldn't possibly be a sequence match between wheat RNA and human DNA.

Finding Hundreds of Sequence Matches in the Human Genome

Not only does this betray a certain arrogance, from a mathematical perspective it's preposterous. The active portions of the dsRNA are typically very small—between 7 and 21 nucleotides in length. And there are just 4 types of nucleotides that make up the code. So what is the probability that a sequence of just 7-21 nucleotides will match up with a corresponding section of the human DNA, which stretches *3 billion* nucleotides in length? We don't have to guess. Using the sequence of dsRNA that was likely produced in the GMO wheat, Heinemann and his team used "bioinformatics" to confirm not just one match, but hundreds of them.[5]

Heinemann is quick to point out that just because there's a sequence match does not mean that any particular dsRNA will have an effect on gene regulation. It's a *potential* threat, but one that has to be taken very seriously.

Feeding Studies Required

In order to evaluate the real risk, you can't rely on computer models alone. Heinemann insists there must be at least feeding studies using those organisms that will be exposed to the dsRNA if the GMO is released outdoors or commercialized.

The bee study demonstrates why. While computer analysis identified several sequence matches, only by actually feeding the jelly fish derived dsRNA to the bees were scientists able to confirm which of those matches resulted in "misregulated" genes. In addition to these "direct" effects, many of the changes in the 1461 genes were, according to the authors, attributed to "*indirect* downstream secondary effects" of the dsRNA. That is, the genes that were altered directly due to the matched sequences produced altered amounts of RNA or proteins. These altered amounts in turn influenced the activity of yet more genes, which in turn, affected yet more.

To make things even more complicated, the single dsRNA meal affected hundreds of genes when the bees were quite small, but they influenced a whole different set of genes when the bees were older—with little overlap. Because different genes activate at different stages of development and in different types of cells, feeding studies must be conducted at different ages and evaluate different tissues and organs.

USDA and EPA Cautions About Unpredicted Side Effects

In 2013, Heinemann and colleagues published a full protocol for assessing the risk of dsRNAs in a highly respected risk assessment journal *Environment International*.[6] Not long after, USDA scientists published a similar analysis[7] and cited Heinemann's work. In early 2014, the US Environmental Protection Agency (EPA) also published a white paper[8] that verified Heinemann's concerns about risk assessment, as did a subsequent analysis by the EPA's Science Advisory Panel.[9]

The USDA scientists' paper, for example, called for "sequencing genomes for species" that will be exposed to the dsRNA to "understand those that may be affected." All the papers acknowledged the need for comprehensive testing conducted under a variety of conditions. And they admitted that the current

assessment protocols for evaluating the impact of GMOs or chemical pesticides are not sufficient to evaluate all the risks associated with dsRNA. The EPA paper stated, for example: "The knowledge gaps make it difficult to predict with any certainty whether unintended effects will occur in non-target species as a result of exposure to dsRNA."

Political Science Posing as Science

Knowing that USDA and EPA scientists and advisors warned about unpredictable unintended effects that could escape detection by current risk assessments, one might think that the approval of the apple and the potato should have at least waited until those assessments were thoroughly updated. But that would require those in charge of the USDA to make decisions based on science. Even a cursory review of the history of US GMO regulations demonstrates just the opposite.

In the 1990s, for example, FDA scientists repeatedly warned their superiors about inherent dangers of genetically engineering crops for human consumption. They wrote of possible toxins, allergens, new diseases, and nutritional problems that would be hard to detect in the gene-spliced foods. But the person in charge of GMO policy at the agency was Michael Taylor, a political appointee, not a scientist. In fact, he was the former attorney for Monsanto. The policy he oversaw falsely claimed that the agency was not aware of information showing that GMOs were significantly different, and therefore no safety testing would be required. Companies like Monsanto, who told us that DDT, Agent Orange, and PCBs were safe, would determine on their own if their GMOs were safe.

As a result of Taylor's policy, companies don't even have to inform the FDA before putting a GMO onto the market. While many *do* participate in the FDA's "voluntary consultation," it is pure theater. At the end of this meaningless exercise, the FDA issues a letter that simply reminds the GMO producer that it's *their* job to determine if their GMO is safe. In the case of Monsanto's Roundup Ready herbicide-tolerant soybeans, for example, the FDA letter to the company stated:

> "… it is our understanding that, based on the safety and nutritional assessment *you* have conducted, *you* have concluded that the new soybean variety is not materially different in composition, safety, or any other relevant parameter from soybean varieties currently on the market and that it does not raise issues that would require premarket review or approval." [emphasis added]

Note that these official FDA letters *never* state that the agency approves the GMO or deems it safe. In the case of the new potato, for example, that determination is entirely in the hands of its maker, J. R. Simplot.

In an interview with Simplot's Vice President of Plant Sciences, Haven Baker, he assures us that their potato is just fine. How does he know? He says the USDA's outdoor "field trials demonstrate that their Innate™ potatoes were found to pose no health or environmental risks, [and] create no harm to other species." The USDA did not, however, conduct *any* sequence matching analyses or feeding trials; and there's no evidence that J. R. Simplot did either.

But to make sure we're completely put at ease, Baker adds, "The FDA's parallel review of Innate™ potatoes, which is also underway, will ensure that they are safe for consumption."

Simplot also claims, without releasing their data, that the Innate potato will have lowered amounts of a possible carcinogen that's activated during frying. But even though Simplot supplies McDonalds with roughly half of all its french fries, the fast-food chain stated that they have no plans to use genetically modified potatoes.

The question is, will you?

The Innate potato and Artic apple may be available for consumption as early as 2016. To ask food companies to reject the use of these GMOs, please sign the petition here.

Additional Resources

Judy Carman, Jack Heinemann, and Sarah Agapito-Tenfen, New paper on dsRNA risks - briefing for non-specialists, 21 March 2013 http://www.gmwatch.org/index.php/news/rss/14698-new-paper-on-dsrna-risks-briefing-for-non-specialists

Recent papers providing more evidence that dietary dsRNA survives in humans/mammals and may alter gene expression:

Mlotshwa, S., Pruss, G. J., MacArthur, J. L., Endres, M. W., Davis, C., Hofseth, L. J., Pena, M. M. & Vance, V. A novel chemopreventive strategy based on therapeutic microRNAs produced in plants. *Cell Res*, doi:10.1038/cr.2015.25 (2015). http://www.nature.com/cr/journal/vaop/ncurrent/full/cr201525a.html

Baier, S. R., Nguyen, C., Xie, F., Wood, J. R. & Zempleni, J. MicroRNAs are absorbed in biologically meaningful amounts from nutritionally relevant doses of cow milk and affect gene expression in peripheral blood mononuclear cells, HEK-293 kidney cell cultures, and mouse livers. *J. Nutr.* **144**, 1495-1500, doi:10.3945/jn.114.196436 (2014). http://www.ralf-kollinger.de/wp/wp-content/uploads/2014/02/Milch-micro-RNAs-Are-Absorbed-in-Biologically-Meaningful-Amounts-from...-.pdf

> "We conclude that miRNAs in milk are bioactive food compounds that regulate human genes."

Lukaski, A. & Zielenkiewicz, P. In silico identification of plant miRNAs in mammalian breast milk exosomes - a small step forward? *PLoS ONE* **9**, e99963 (2014). open access http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0099963

---

[1] F.M.F. Nunes, et al, Non-Target Effects of Green Fluorescent Protein (GFP)-Derived Double-Stranded RNA (dsRNA-GFP) Used in Honey Bee RNA Interference (RNAi) Assays, *Insects* **2013**, *4*(1), 90-103; http://www.mdpi.com/2075-4450/4/1/90

[2] Because of the limitations of the equipment used, this may be an underestimate of the number of genes affected.

[3] Quotes taken from authors interview with Dr. Jack Heinemann, conducted in person in China, July 2013.

[4] Zhang, L., Hou, D., Chen, X., Li, D., Zhu, L., Zhang, Y., Li, J., Bian, Z., Liang, X., Cai, X., Yin, Y., Wang, C. H., Zhang, T., Zhu, D., Zhang, D., Xu, J., Chen, Q., Ba, Y., Liu, J.-J., Wang, Q., Chen, J.,

Wang, J., Wang, M., Zhang, Q., Zhang, J., Zen, K. & Zhang, C.-Y. Exogenous plant MIR168a specifically targets mammalian LDLRAP1: evidence of cross-kingdom regulation by microRNA. *Cell Res* **22**, 107-126 (2012).

[5] Jack Heinemann, Evaluation of risks from creation of novel RNA molecules in genetically engineered wheat plants and recommendations for risk assessment, An Expert Opinion by Jack Heinemann, August 28, 2012. Centre for Integrated Research in Biosafety at the University of Canterbury in New Zealand. http://www.thenutritionalhealingcenter.com/wp-content/uploads/2012/10/Wheat-Heinemann-Expert-Scientific-Opinion.pdf. Update on submission: March 21, 2013 http://safefoodfoundation.org/wp-content/uploads/2013/03/opinion-on-possible-dsrna-mediated-adverse-effects_update-1.pdf

[6] Heinemann, J. A., Agapito-Tenfen, S. Z. & Carman, J. A. A comparative evaluation of the regulation of GM crops or products containing dsRNA and suggested improvements to risk assessments. *Environ Int* **55**, 43-55, doi:10.1016/j.envint.2013.02.010 (2013). http://gmojudycarman.org/wp-content/uploads/2013/06/comparative-evaluation-of-the-regulation-of-GM-crops-or-products-containing-dsRNA-and-suggested-improvements-to-risk-assessments.pdf

[7] Lundgren, J. G. & Duan, J. J. RNAi-based insecticidal crops: potential effects on nontarget species. *Biosci.* **63**, 657-665 (2013). http://bioscience.oxfordjournals.org/content/63/8/657

[8] RNAi Technology as a Pesticide: Program Formulation for Human Health and Ecological Risk Assessment. (United States Environmental Protection Agency, 2014. http://www.thecre.com/premium/wp-content/uploads/2012/04/RNAi-White-Paper.pdf

[9] Environmental Protection Agency, Transmittal of Meeting Minutes of FIFRA Science Advisory Panel, January 28, 2014. https://www.epa.gov/sites/production/files/2015-06/documents/012814minutes.pdf