National Academy forum challenges anti-GMO claim that DNA in food 'invades' bloodstream

"Science knows it doesn't know everything. Otherwise, it'd stop."

Dara O'Briain's quip during a science comedy performance from a few years back succinctly summarized one of my favorite aspects of science. We're always making more of it. It never runs out. Unlike dogma–which Francis Crick amusingly misused to describe his hypothesis once—it's not fixed in place and time in some historical tome. Science keeps moving, keeping the valuable bits, discarding the unreliable bits, testing things, improving strategies and learning more about how we all exist in this universe.

If you aren't participating in some field of science, though, it can be hard to keep up with the rapid pace of the research. Some of the data is also difficult to understand as an outsider. Relying on the news media is uneven—they may write catchy headlines touting single studies with dramatic claims—but typically they don't return to follow up in a few years to see how those claims played out. This has been deemed " single study syndrome". As a result, bad story piles on bad story, often tracing to an original poorly reported news account. Some responsible journalists are trying to draw attention to the problems of this type of reporting. But it continues to happen almost every day.

An illustrative example of the kind of single-study drama in genomics can be traced to a 2012 piece by Ari LeVaux in *The Atlantic*: "The Very Real Danger of Genetically Modified Foods". This article claimed that micro-RNA (miRNA) from normal rice was somehow damaging gene expression in mice. The actual researchers who performed this preliminary work had claimed that the small, fragile nucleotide molecules from rice were somehow capable surviving numerous barriers of digestion and absorption to ultimately turn down gene expression in mouse livers, possibly impacting their cholesterol levels (Zhang et al, *Cell Research*, 2012).

The piece was filled with errors, capably described and deconstructed by scientist and science journalist Emily Willingham, and other experts in the field were very wary of the claims of the process of how the process worked. LeVaux was forced to back away from the irresponsible statements such as:

> The Chinese RNA study threatens to blast a major hole in Monsanto's claim. It means that DNA can code for microRNA, which can, in fact, be hazardous.

Although the original research had nothing to do with genetic modification, LeVaux's misleading interpretation of it took on a life of its own. It was widely adopted as dogma among folks who seek reasons to trash-talk biotechnology.

Some of the wildest and most irresponsible claims emanated from the same "green" and "progressive" web sites that regularly challenged the safety of vaccines. A typical example: "GM Wheat May Damage Human Genetics Permanently," announced GreenMedInfo, a scientifically-thin but popular website

frequented by alternative medicine advocates.

No study, no matter how well executed it appears to be, should stand alone. Research gains credibility or is discarded based on its ability to be reproduced. But it takes time to plan, fund and perform subsequent experiments, publish them and examine their context among other work in the field. Science journalists are rarely patient enough or able to publish follow up pieces on research findings that say—*well, that didn't seem to work out*.

LeVaux never did, but at least there were some attempts to follow up, to examine the science and unscare people who might have been unnerved by the earlier claims amplified by the *Atlantic* fiasco. Virginia Hughes, writing at *National Geographic*, reviewed subsequent research indicating that sequence contamination likely explained why the original findings were not reliable.

> And sometimes the data didn't make sense — they found miR-168, for example, in animals that had never eaten food containing miR-168, suggesting that it could have been the result of a contamination….

Willingham also followed up with more details on the failures to replicate the initial claims, which also appear to include mistaken identity of the sequences.

> They found, through a critical application of a new technique for identifying the RNA, that the alleged plant RNA was more likely to be native animal RNA, not RNAs ingested in the diet.

The GLP's Jon Entine also addressed the claims and the complicity of some mainstream organizations, such as Consumers Union, whose GMO policy is guided by Michael Hansen, and the Union of Concerned Scientists, where Doug Gurian-Sherman directed research before decamping to the anti-GMO Center for Food Safety. to circulate them.

> Don't hold your breath for rollbacks of their disgraceful journalism and public comments by LeVeaux … Gurian-Sherman, Hansen and others whose statements have ranged from credulous to intellectually dishonest to fraudulent manipulation and misrepresentation of results. Expect chief GMO demonizer Jeffrey Smith—who is a charlatan—to continue to hype this unproven danger in his "analysis" of the "dangers" of GMOs. They are single study syndrome sycophants.

But these takedowns and few others didn't have the reach and impact of the initial publication's megaphone. As a result, these claims still show up on anti-GMO websites and are sometimes repeated in the mainstream press.

The study lived on in other ways. Some researchers really hoped that the original researchers had happened upon a mechanism that would allow delivery of therapeutic miRNA to cells, so work continued, even resulting in the filing of patents and companies hoping to capitalize on this research, if it should hold

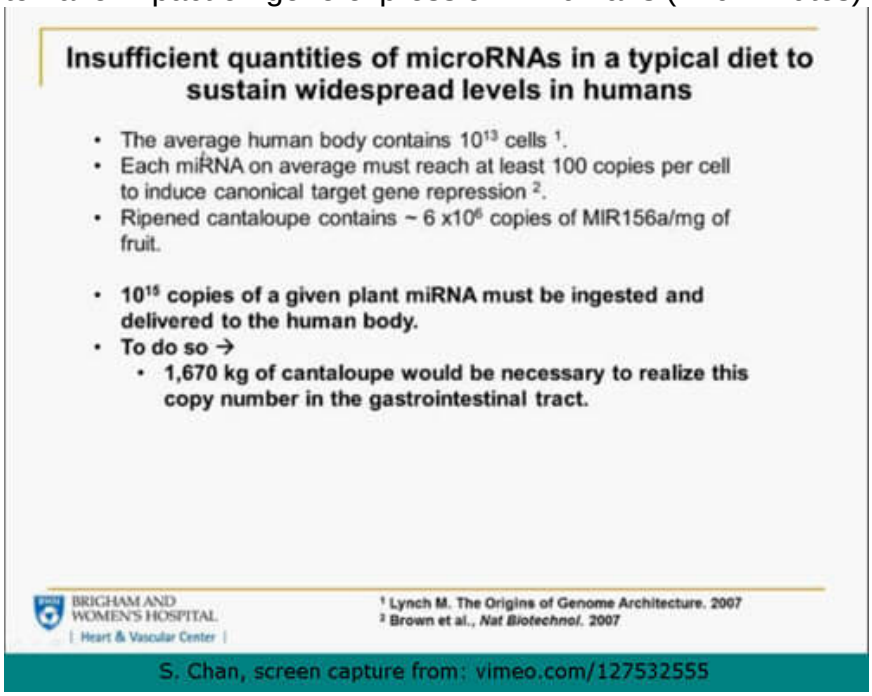
up. However, patents and companies' basic research are not peer-reviewed and do not constitute evidence.

A recent scientific review of the work in this field noted that conflicting results, low levels of detection and non-physiological levels of miRNAs required for impacts suggest that "gastrointestinal uptake of dietary plant miRNA is not occurring in healthy consumers". However, this story—that humans should not be concerned about absorbing foreign DNA from ingested food—did not exactly make its way into the headlines.

Another researcher recently told much the same story to the National Academy of Sciences panel investigating genetically-engineered crops with expectations of issuing a summary statement on GMO safety sometime next year. Stephen Chan, MD/PhD, Assistant Professor of Medicine, Harvard Medical School, is very interested in non-coding RNAs in his cardiovascular research and had been enthusiastic about the possibility of the delivery of miRNA to humans. Chan, like other researchers, became hopeful that diet-delivered sequences could have positive impact on humans.

In his talk Chan provided helpful context about the field of miRNAs and their possible functions, and the early claims about cross-species effects. He went on to note, though, that in the years after the original splashy study, "additional studies reveal systematic discrepancies" with the claims. His own lab was among those unable to replicate the initial research group. His research team looked at bees, mice and humans to locate any transfer of miRNAs across species. Levels of miRNAs that could have impact on gene expression simply weren't found. ("Ineffective delivery of diet-derived microRNAs to recipient animal organisms") This also did not grab headlines in the media, let alone at *The Atlantic*, which had run the original, now clearly discredited, story.

On one particularly effective slide, Chan summarized how much dietary miRNA would need to be present to have impact on gene expression in humans (~26 minutes).



Chan noted that you would have to eat over 1600 kilograms of cantaloupe to get the necessary 10^{15} copies of plant miRNA into the digestive tract. And that doesn't even account for the fact that few miRNA would survive the harsh gastrointestinal environment to make it into the body's tissues. It's just not realistic.

"We're not even in the realm of possibility of seeing the number of copies of miRNA, at least in the normal diet, in order to see this type of effect," he said. Chan then pointed to other studies that suggest contamination of samples may explain some of the other instances of previously-described presence of plant sequences in other organisms.

In typical cautious scientific language, Chan concluded that the claims in the original work were driven largely by a single lab's results, whose data has not been replicated in other labs. The miniscule miRNA levels detectable show that the original study's findings were neither a "robust nor widespread" occurrence, and were more than likely the result of contamination artifacts. In one of the most telling statements, during the question period, he said that his lab has abandoned this work because it seems…well, fruitless, it sounded to me. Although he acknowledged there may be some special situations and other ways to deliver extraordinary amounts of miRNA, and that it's fine for others to pursue investigations of such situations, this mechanism of dramatically affecting mammalian biology by ingesting miRNA from plants was unlikely.

And so, science moves on. But you won't hear this 'corrected science' from anti-GMO activists and it's unlikely to be reported in the media. In fact, some people continue to push the unsound early claims

without telling you about the unsuccessful subsequent efforts to replicate them. For example, activist Jeffrey Smith peddled more iterations of the claims well after they were proven wrong:

> And it's now been shown that they can be taken up after digestion of the food into our blood supply," he said. More importantly in a groundbreaking study conducted in China in 2012, dsRNA fed to mice "transferred to the liver and down-regulated an important liver enzyme".

Don't let them play their shell game on you—where they point to one nugget, and wave their hands frantically to distract you from the real science. In the meantime, responsible scientists will continue to do the hard work, usually without fanfare or headlines. It's hard to keep current in science, but it is crucial to making the best decisions to have the all the information. I applaud the National Academy of Science's efforts to seek out the best and most current thinking on these issues. And I look forward to their synthesis of the evidence in their report and recommendations.

Mary Mangan, Ph.D., received her education in microbiology, immunology, plant cell biology, and mammalian cell, developmental, and molecular biology. She co-founded OpenHelix, a company providing training on open source software associated with the burgeoning genomics arena, over a decade ago. All comments here are her own, and do not represent her company or any other company. You can contact Mary via twitter: @mem_somerville