An inconvenient version of events

To the editor:

I am writing as coordinator of the "GMOs [genetically modified organisms] in Agriculture" project in response to the editorial in the December issue[1], in which the Italian National Research Institute for Food and Nutrition (INRAN; Rome) is accused of failing to publish data that indicated the superiority of genetically modified (GM) maize.

The fumonisin results to which you refer were not in fact part of the INRAN project. In 2005, we commissioned Tommaso Maggiore to grow both a GM and a conventional crop of maize. He was given responsibility only for growing the maize and for collecting data, as is clear from INRAN's agreement with him. He was not asked to test for the presence of mycotoxins, such as fumonisins; that part of the work was specifically assigned to the team directed by Marina Miraglia of the Istituto Superiore di Sanità (Rome), a recognized expert in the field.

Maggiore decided to conduct his own research on the maize. He did not, however, inform us of this. He claims he sent Gianni Pastore of INRAN a letter by e-mail on February 23, 2006, with a file containing his data on fumonisins, but we have carried out a careful check and have no record of such a letter. Both the INRAN server and Pastore's computer do, however, show that on February 27, 2006, a report was received from Maggiore. In the accompanying letter, he apologizes for the delay in submitting his report, and he also writes that it does not contain the data on fumonisins, which he had not yet analyzed.

Not only do we have no record of the letter dated February 23, but it is hard to understand why, if he had sent a report including the fumonisin results to INRAN on that date, he would have followed it four days later with a second letter that makes no reference to the earlier one, informing us that he had not yet carried out the analysis. We have also checked our records from February 27, 2006, to the present and there is no trace of a second report from Maggiore, so this cannot be merely a matter of confusion about dates.

We look forward to hearing from Maggiore and his supporters an explanation of how this letter has suddenly appeared and why it contradicts what was said in the letter we do have.

Although INRAN was informed on February 27 that Maggiore intended to analyze fumonisins, it is only recently that we were informed of the results, and then only indirectly. At the conference on Research in GMOs in Agriculture in Rome on March 7, 2006, Pastore presented all the data in Maggiore's report, naturally with proper acknowledgement to Maggiore. In particular, he included the observation that the yields of GM maize had been higher than those of conventional maize. That was what had been found, and that was what he presented. The positive results for GM organisms were shown, not concealed. Pastore could not describe the results on fumonisins obtained by Maggiore because they had not been sent to INRAN.

There is certainly no question of suppression. If Maggiore had wanted to publish his results in a scientific journal, he could have asked for authorization to do that, but he did not. Instead, the directorate of Salute, Agricoltura, Ricerca (SAGRI; http://www.salmone.org/chi-e-sagri) organized a press conference on November 13, 2007, to publicize his work, and it came to our knowledge only at that time.

In your editorial, you express your disappointment that the Italian media did not consider it a major news story, though you acknowledge that it was covered by *La Stampa* and others. I have to say that I was very surprised to read this. Over the past few years, we have frequently been told that it is a breach of scientific ethics to disseminate results that have not been peer reviewed. Yet when SAGRI and Maggiore do this, your only criticism is of the media for not giving the event even greater coverage than it received.

Furthermore, I would like to draw your attention to an aspect of our research. In the trial, the conventional corn was not treated to protect it against the pyralid moth, whose larvae promote the fungus that yields fumonisins. That was appropriate in a scientific experiment designed to compare GM and conventional maize, but it means the results are not representative of commercial maize grown in Italy. Even if Maggiore's value of 6,000 p.p.b. is correct (and we see no reason to prefer it to the figure of 2,450 p.p.b. obtained by Miraglia, an official expert in the field) there is no crisis and no need to rush.

In your editorial, you accuse INRAN of deliberately suppressing results because they were positive for GM crops; this is completely untrue and an unwarranted slur on the reputation of INRAN and its researchers.

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1. Anonymous. *Nat. Biotechnol.* **25**, 1330 (2007).

***Nature Biotechnology* responds:**

Our editorial did not accuse INRAN "of deliberately suppressing results because they were positive for GM crops." Indeed, we never made any assertion that all of the data from the trial had been suppressed: we said that in the original meeting intended to discuss this matter in a public forum on March 7, 2006, "the full field trial data were never shown."

It is clear the data from Tommaso Maggiore on fumonisin levels, however, were not discussed in any of the presentations at that public forum. Giovanni Monastra insists this is because INRAN had no such data from Maggiore, who had conducted the yield studies. He also insists that his colleague, Gianni Pastore, who presented

yield results at the public forum in March 2006, could not have described the results on fumonisin levels from Maggiore because they simply had not been sent to INRAN. Maggiore continues to insist otherwise, however.

Even if the Maggiore data were somehow misplaced by INRAN or misdirected by Maggiore himself, the fumonisin data from Marina Miraglia (mentioned by Monastra) were certainly available to INRAN, at least a week before the public conference in March 2006. These data showed that the fumonisin level was approximately twice as high in the nontransgenic crop as in the transgenic crop, an interesting differential but one that was not made available to interested parties. Indeed, INRAN chose not to formally discuss these data until after the November 13, 2007, press conference organized by SAGRI and supporters of Maggiore, and only then to counter the larger differential shown by Maggiore.

It is particularly surprising that Monastra was aware neither of the political and public interest in the fumonisin data (whether from Miraglia or from Maggiore) nor of the need to share them more widely in the light of the debate going on in Italy at that time. For example, an Italian parliamentary interpellation presented on June 6, 2007, by 33 senators specifically asked the minister of agriculture to disclose the fumonisin data (http://www.senato.it/japp/bgt/showdoc/showText?tipodoc=Sindisp&leg=15&id=269372). A petition referring to the suppressed data signed by many scientific societies and researchers was circulated on July 4, 2007, and available on the website of Siga (Societa Italiana di Genetica Agraria; http://www.siga.unina.it/Appello_OGM.html). In addition, an article published in the major Italian financial newspaper (*Il Sole 24 Ore*) published on July 8, 2007, also requested that these data be made available. This was written many months before the SAGRI press conference, and Monastra must have known of the article's contents because he replied in the newspaper the following week.

We agree with Monastra that the best place for publication of scientific results is in a peer-reviewed journal. In this case, the data were too preliminary for peer-reviewed publication, but they were of interest to the public and political debate going on in Italy last year and thus should have been made available for those who were interested (this does not mean they should have been press released). The fact that they *had* to be press released by SAGRI is unfortunate—it would not have been necessary for SAGRI to do this if the data had simply been made publicly available.

Transendothelial movement and caveolae

To the editor:

The article by Philip Oh *et al.*[1] from last year's March issue obfuscates the literature in the field of caveolae research, including articles from the authors' own laboratory, and contains very few original observations. Studies from the George Palade, Maia Simionescu and Nicolae Simionescu laboratories have imaged transendothelial movement of caveolae *in vivo*. Notably, Simionescu and coworkers[2] used 'live cell' electron microscopy to characterize the transendothelial movement by caveolae of thyroxin bound to prealbumin (transthyretin). By 'live cell' electron microscopy, I mean that markers targeted to caveolae were injected and the markers' uptake by endothelial-cell caveolae and delivery to surrounding tissue cells were followed as a function of time. The work is convincingly quantified and carried out in lung. These investigators also showed that caveolae transport across endothelial cells is very fast (completed in ~5 min; see Fig. 5 in ref. 2), which is what Oh *et al.*[1] report. Not only do Oh *et al.* fail to show in Figure 2 of their article that their monoclonal antibody (mAb) traverses endothelial cells *in vivo*, they also do not cite the M. Simionescu study. In general, they place undue emphasis on literature claiming that caveolae are sessile (static) structures. Several reports (including refs. 2–4) clearly show that caveolae do internalize molecules, both in cultured cells and in tissues.

Perhaps a more serious problem is that Oh *et al.* used a glycosyl phosphatidylinositol (GPI)-anchored protein to monitor "pumping" by caveolae. Aminopeptidase P (APP) has two isoforms, one in the cytosol and the other GPI-anchored to the external surface of the plasma membrane[5]. I assume that Oh *et al.*'s mAb was against the latter, although the paper does not identify the isoform used to generate the mAb or acknowledge that there is a GPI-anchored isoform of APP. GPI-anchored proteins were functionally and structurally localized to caveolae by immunofluorescence and immunogold 17 years ago[6,7], but many have claimed that the localization to caveolae is an artifact of applying cross-linking antibodies. Indeed, Schnitzer and coworkers[8] have published detailed studies showing that with their methods caveolae do not contain GPI-anchored proteins. They have even proposed that GPI-anchored proteins are in different lipidic domains. So how can they use a mAb against a class of molecules they believe is not in caveolae to monitor transendothelial movement by caveolae? They fail to mention in the paper that their own data have ruled out a role for caveolae in transendothelial movement of GPI-anchored proteins. Moreover, they imply in the last sentence of the first paragraph that the probes used by the M. Simionescu laboratory were not specific for caveolae (citing only their own work as validation for this claim), but they provide no electron microscopy evidence that APP is a specific marker for caveolae. If Schnitzer and colleagues now believe (in the Oh *et al.* paper[1]) that GPI-anchored proteins are in caveolae, they need to demonstrate that APP is internalized by caveolae in the absence of cross-linking antibodies. If, on the other hand, they believe that cross-linking antibodies relocate APP to caveolae by cross-linking, then the "pumping" they are measuring must be an artifact and their mass spectroscopy identification of APP in caveolae incorrect.

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1. Oh, P., Borgström, P., Simonson, A. & Schnitzer, J. *Nat. Biotechnol.* **25**, 327–337 (2007).
2. Heltianu, C., Dobrila, L., Antohe, F. & Simionescu, M.