Ntziachristos et al. respond:

The physics of photon propagation[1] in tissues unequivocally supports the notion that planar imaging is surface weighted because signal intensity from deep-seated tumors drops exponentially as a function of depth. Therefore, planar imaging will preferentially detect and localize superficial fluorochrome activity. Indeed, Hoffman and his colleagues[2] had to use invasive skin flap windows in previous work to improve on tumor visualization in the lung using planar imaging. Similarly, changes in tumor vascular volume fraction because of angiogenesis alter the internal optical properties of the lesion and nonlinearly modulate the intensity reported, which can obscure quantification. The spectral images presented in our Perspective were provided by Cambridge Research & Instrumentation (CRI), which originally obtained their dual-color mouse tumor model from AntiCancer, the company for which Hoffman is Chairman of the Board. Therefore, our comments regarding the weak fluorescence of this mouse and subsequent spectral analysis reflect back to AntiCancer, which originally provided the mouse images for analysis to CRI.

1. Ishimaru, A. *Wave Propagation and Scattering in Random Media,* vol. 1 (Academic Press, New York, 1978).
2. Yamamoto, N. *et al. Clin. Exp. Metastasis* **20**, 181–185 (2003).

Bt toxin not guilty by association

To the editor:

In a Perspective in the September issue (*Nat. Biotechnol.* **22**, 1105–1109, 2004), Heinemann and Traavik suggested that horizontal gene transfer from *Bt* crops (transgenic plants expressing a *cry* gene from *Bacillus thuringiensis*) may pose a food safety or other environmental hazard because "it is noteworthy that *B. thuringiensis* has "a significant history of mammalian pathogenicity" and is thus not irrelevant to food safety or other environmental issues." The reference is to a review from us, but misconstrues our original intent because the original text in our review actually runs: "*Bt* does *not* have a significant history of mammalian pathogenicity..."[1] [emphasis added].

In the April issue, the authors make a correction indicating that they wrongly cited our reference but persist in their opinion by now referring to the close relationship between *B. thuringiensis*, *Bacillus cereus* and *Bacillus anthracis*, of which strains of the latter two do have significant pathogenicity. In their corrigendum[2], to support their allegation that plants containing a *cry* gene may constitute a hazard, they state: "Members of this group are so closely related that they may be considered members of the same species, often differing only by the presence or absence of certain plasmids". Thus, they damn *B. thuringiensis*, and the use of its genes, by association with *B. cereus*, or worse, with *B. anthracis*, the causal agent of anthrax.

The authors are correct in noting that *B. thuringiensis*, *B. cereus* and *B. anthracis* are closely related; they are also correct in noting that the main differences are often due to the presence or absence of certain plasmids[3]. What they fail to note is that in this group of bacteria, as in many others, host specificity is largely determined by plasmid-encoded factors. Thus, the distinctive feature of *B. thuringiensis* is the production of insecticidal crystal proteins, and it is only the genes encoding these proteins (which are mostly plasmid-borne) that are expressed in transgenic plants. Moreover, these genes are derived from strains of *B. thuringiensis* that have been used as safe and environment-friendly sprayable pesticides for decades, including by many organic farmers.

Furthermore, the focus of Heinemann and Traavik's original Perspective is on transgenic plants expressing *Bt* toxin proteins from the bacterium, not on the bacterium itself. Clearly, the safety of a single gene product does not inherently reflect that of the complex organism from which it originates. We are not suggesting that safety issues should not be considered, but to date there have been many years of safe *Bt* toxin use. The overwhelming evidence is that *B. thuringiensis*, and transgenic crops expressing *cry* genes, are not a threat to mammalian species. The authors of this paper are using a poor interpretation of good science to imply a potentially serious risk.

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1. de Maagd, R.A., Bravo, A. & Crickmore, N. *Trends Genet.* **17**, 193–199 (2001).
2. Heinemann, J.A. & Traavik, T. *Nat. Biotechnol.* **23**, 488 (2005).
3. Rasko, D.A., Altherr, M.R., Han, C.S. & Ravel, J. *FEMS Microbiol. Rev.* **29**, 303–329 (2005).