Viral recombination

To the editor:

In Russ Hoyle's commentary concerning virus resistant transgenic plants in the July issue of *Bio/Technology* (**12**:662-663), our recent paper[1] was incorrectly summarized and consequently his extrapolations may have been misleading. Our experiments were initiated to determine if RNA transcripts containing viral RNA are available within transgenic cells for recombination with a replicating RNA virus. Mr. Hoyle incorrectly states that these experiments were conducted in cowpeas that had been transformed to resist cowpea chlorotic mottle virus (CCMV). In reality, the experiments were conducted in susceptible *Nicotiana benthamiana* plants expressing a small segment of the CCMV genome. These transgenic plants were inoculated with a CCMV deletion mutant capable of replication but incapable of systemic movement. The deleted portion of the viral genome was available in the transgenic plant's transcript. Thus, RNA recombination between the replicating virus and the plant's transcript could restore the deletion and regenerate a viable systemically infecting virus. Although Mr. Hoyle states that no viable viruses were recovered, all four recombinant viruses were viable and capable of systemically infecting both *N. benthamiana* and the natural host, cowpeas. Sequence analysis of the recombinant viruses revealed point mutations that identified the involvement of the transgenic RNA in the recombination event. Further analysis indicated that each recombinant was a distinct variant of wild type CCMV.

Mr. Hoyle further states that our work was "virtually the same experiment" as was reported by De Jong and Ahlquist in 1992.[2] The Ahlquist paper reports the construction of a viable hybrid virus in which the Sunn-hemp mosaic virus movement protein gene was substituted for the CCMV movement protein gene. This hybrid was not a result of RNA recombination within a transgenic cell and reference to this paper appears inappropriate.

Although previous results made our RNA recombination results predictable, our experiments have clearly demonstrated that RNA recombination involving transgenic RNA can provide viable viruses. We have published these results so that decisions concerning the release of virus resistant transgenic plants can be based on reliable data.

References

1. Greene, A.E. and Allison, R.F. 1994. Recombination between viral RNA and transgenic plant transcripts. *Science* **263**:1423-1425.
2. De Jong, W. and Ahlquist, P. 1992. A hybrid plant RNA virus made by transferring the noncapsid movement protein from a rod-shaped to an icosahedral virus is competent for systemic infection. *Proc. Natl. Acad. Sci. USA* **89**:6808-6812.

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Mr. Hoyle replies:

We owe Professor Allison an apology: The July column in question incorrectly stated that the Michigan State experiment involved cowpea plants rather than tobacco plants. However, the commentary never disputed that viral recombination had occurred, nor that researchers had recovered viable viruses. We did point out that no "new" or unexpected viruses had been generated that created novel risks, environmental or otherwise. The point was that Allison's experiment did not demonstrate any new risks that would even begin to justify new regulatory schemes, reassessments, or moratoria on the development of transgenic plants, as some have claimed.

Success rates and valuation

To the editor:

The article "Biopharmaceutical R&D Success Rates and Development Times" (*Bio/Technology* **12**:674-677, July) contained some interesting information on the measurement and prediction of success of drug development programs. The author calculated "success rate" factors for different stages of drug development through to market. It will be interesting to monitor how this type of information is combined with other business information to assess the valuation of biotech companies.

The concept of creating data which can be used as a tool to predict the potential success of a biotech company's core development projects comes at a particularly apt time, when the changes in the Listing Rules of the London Stock Exchange have sped the way for a series of initial public offerings to take place. However, the poor performace of biotech stocks, both in the U.S. and the U.K., has highlighted the power of general market conditions to influence prices. Something is only worth what you are willing to pay for it!

The Ernst & Young First Annual Report on the European Biotechnology Industry, "A New Industry Emerges," highlighted the contrast between the knowledge and experience of investors and analysts in the U.S., and the understanding of the biotech industry in the U.K. It is clear that further yardsticks to aid evaluation of biotech companies and to assess their long-term potential need to be developed.

In the search for performance indicators to replace the traditional measures such as price-earnings ratio and profitability, there could be a place for a "success rate" factor. However, such factors need to be applied, and the results interpreted with extreme care, as much as more subjective considerations need to be taken into account. This is especially true of privately held investments, or publicly held investments that are traded at low volumes—traditionally, privately held stocks are more subjectively evaluated than publicly traded stocks. Also, the impact of changes in the regulatory environment under the new European Medicines Evaluation Agency will cloud the picture for a considerable time. As the article points out, the use of general data for a therapeutic product group could also lead to the