paring apples and oranges," as Fowlkes would have us believe.

Finally, one would wonder why Fowlkes did not comment on the use of somatostatin, an IGF-1 inhibitor, in cancer patients.

IGF-1 has had, to date, a shaky track record in clinical trials, as Cephalon's ALS trials, and others, have shown. In the future, use of IGF-1 with the protein that naturally binds to it, BP-3, or given locally, as GeneMedicine is planning to do in an upcoming trial with the drug for neuromuscular regeneration, may show us that the drug can be used safely and effectively. However, research to date has not demonstrated such use is possible.

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Chloroplast-transgenic plants: Panacea-No! Gene Containment-Yes!

To the editor:

It is unfortunate that Stewart and Prakash have missed the point of maternal inheritance of foreign genes in MOST crops, when they are engineered via the chloroplast genome. Such false and irresponsible statements, solely based on speculation and cursory knowledge or understanding of published literature (or lack of credible track record in this area of research) creates panic among the public and sets the clock back on evolving new concepts and technologies.

One of the most thoroughly studied systems for the maternal inheritance of herbicide resistance genes is the mutant chloroplast *psbA* gene conferring resistance to triazine[1,2]. Several backcross generations using pollen from susceptible plants had no effect on the maternal transmission of herbicide resistance[3]. Most importantly, crossing resistant weed plants with closely related crop species did not alter their maternal inheritance[4-6]. This may be because of the prokaryotic nature of chloroplast genes which may have to acquire eukaryotic features (such as promoters, terminators, preferred codons, etc.) in order to function effectively in the nucleus. Frustratingly low levels of expression of *Bacillus thuringiensis* insecticidal proteins from native genes in plants genetically engineered via the nuclear genome should serve as a good example to understand this.

Based on a number of these studies, several authors reported in the early eighties that maternal inheritance of triazine resistance prevents spread via pollen. A few years later Darmency and coworkers reported that there may be an occasional but negligible (about 0.2–2%) paternal transmittance of plastid DNA. However, these plants lost their resistance trait in F5 and showed low levels of atrazine tolerance; these results were interpreted as the regular loss, in each generation, of a cytoplasmic factor (other than the chloroplast) encoding atrazine resistance[2]. Screening of over 200 angiosperms for biparental inheritance of the plastid DNA turned out to be negative[7]. There was also another report of haploid plants derived from anther culture showing low levels of atrazine resistance, but then it was explained that the vegetative cell had plastids (from which these plants were derived) but not the generative cell where plastids are destroyed[8]. In cases where atrazine resistance was suspected to be paternally inherited, Levings and coworkers demonstrated that the *psbA* gene was present in the mitochondrial genome and that the *psbA* transcript was present only in mitochondria of atrazine resistant plants[9,10]. Further studies on the transfer of atrazine resistance trait revealed an extra chloroplastic mechanism[11]; this resulted in the discovery of other modes of action of atrazine that are nuclear encoded, including Cyt P450 and GST[12]. These reports helped to understand instances where strict maternal inheritance of atrazine resistance was not observed. Aforementioned examples could be used to understand plants that are genetically engineered via the chloroplast genome.

Keeler et al.[13] focus on the role of gene flow to weedy wild relatives as a potential problem because "that is a far greater concern than any other mode of escape of transgenes." They point out that, with only rare exceptions, all crops have wild relatives somewhere in the world and therefore, escape of transgenes is a strong possibility somewhere. Authors further point out that "transgenes can only reach weed populations if carried to weeds on viable pollen; if the crop produces no pollen or viable pollen, there will be no gene flow." Also, authors have summarized valuable data on the distribution of weedy wild relatives of 60 important US crop plants and potential hybridization between crops and wild relatives, and warn against genetic engineering of several crops via the nuclear genome, including rice, oats, sorghum, canola, sunflower, lettuce, artichoke, radish, etc. Chloroplast transformation could be an effective solution for these crops.

With Murphy's law in action, there are always exceptions to most theories, laws, or observations, and maternal inheritance of chloroplast genomes is certainly not an exception. This should not diminish the value or importance of this technology. Authors of both articles[14,15] clearly acknowledge this fact by cautiously pointing out that "the prevalent pattern of plastid inheritance found in the majority of angiosperms is uniparental maternal" and that "chloroplast genomes are maternally inherited for most of the crops." It is known that in pines (gymnosperms) plastids are transmitted in a biparental mode. Paternal transmission of pollen in tobacco has been reported, but with provisos. In "Transmission of paternal chloroplasts in *Nicotiana*," the authors mention that there is occasional (0.07–2.5%) paternal transmission in a species typically exhibiting strict maternal inheritance. In the letter by Stewart and Prakash, it has been pointed out that in *Brassica napus* transgene escape via chloroplast genome is a serious problem; unfortunately, they are totally ignorant of the fact that in rapeseed, paternal mitochondrial DNA is transferred to the egg but not the chloroplast DNA[16]. None of the articles referred to by Stewart and Prakash report a transgene present in the chloroplast genome. It is illogical to extrapolate studies from the nuclear genome to that of the chloroplast genome. Regarding the issue of having overstated the biosafety of chloroplast engineering, we can only assume that it is an artifact of the critics' minds. The importance of ecologically sound regulation is paramount. To somehow suggest that we are proponents for undermining it provides for comic relief, and once again underlines the unbridgeable hiatus between what we wrote and the viewpoint of our critics. Responsible scientists should refrain from creating panic among the public but rather address concerns through further studies and a thorough analysis of published literature.

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