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## Programmed Cell Death

Jean Claude Ameisen's Perspective "The origin of programmed cell death [PCD]" (31 May, p. 1278) discusses possible evolutionary roots of cell suicide. In addition to the cited examples, sporulation in *Bacillus* is worth mentioning. In the final stage of sporulation, the spore matures and is released from the mother cell, which produces the coat proteins and then lysis, completing its terminal differentiation program. This is controlled by the $\sigma^K$ sporulation factor, which is functional only in the mother cell. The coding sequence in *B. subtilis* is separated into two truncated genes that are brought together in-frame by a site-specific recombination event 3 hours after onset of sporulation. This leads to excision of a 48-kilobar element in between the two portions of the $\sigma^K$ gene. Recent sequence analysis of this nonessential DNA indicates a possibility that the element is a cryptic remnant of an ancestral temperate phage (*1*). Microcycles, a reformation of spores just after germination when vegetative multiplication is disadvantageous because of suddenly changed conditions, were observed in sporulating microorganisms [reviewed in (*2*)]. Such reformation shows that PCD in microorganisms is precisely controlled to the advantage of the spore and that elaborate mechanisms preventing accidental activation of the pathways are in place.

Factors similar in function to those produced by eukaryotes controlling cell survival and development have also been found in prokaryotes (*3*). Some signals trigger cascades of preprogrammed events only at a certain growth stage, in the so-called preparatory phase (*2*). Depending on the signal, the consequence of intercellular communication may lead to the production of secondary metabolites, expression of virulence factors, or differentiation during which the fate of some cells is predetermined as fatal. Thus, we can perceive PCD as one of the wide repertoire of programs available in a genome.

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The figure in Ameisen's Perspective (p. 1279) suggests that multicellular plants diverged from multicellular animals 0.7 billion years ago. Surely this is a mistake. Virtually all sources derive the multicellular plants from green algae, which date back at least 1.5 billion years. Is Ameisen suggesting that the multicellular animals derive from green algae?

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*Response*: In adverse environmental conditions, *B. subtilis* undergoes asymmetrical cell division, the mother cell becoming terminally differentiated and undergoing PCD, while helping the other cell become a nonproliferating long-lived spore (the equivalent of a germ cell) (*1*).

*Bacillus subtilis* provides an example of how a major theoretical conundrum concerning the evolution in unicellular organisms can be solved: In order not to be counterselected, a cell suicide program has to be regulated in such a way that the death of some individuals in a unicellular colony will benefit (or at least will not impede) the survival of other individuals. As I proposed, the coupling of PCD regulation to that of cell differentiation and of intercellular communication represents one such possible mechanism. An important feature of the genetic regulation of sporulation and PCD in *B. subtilis* is asymmetrical cell division, which allows a complex intercellular regulation of the expression and activation of four transcription factors, $\sigma^E$ to $\sigma^K$. This crisscross regulation ensures that the $\sigma^K$ sporulation factor, which leads to spore differentiation and to mother cell death, is expressed only in the mother cell and only at a late stage of the forespore differentiation in order to prevent premature mother cell death (*1*). Such temporally and spatially regulated gene expression provides an example of how the coupling of PCD to intercellular communication can ensure a selective advantage to some cells of a colony at the expense of the sacrifice of others, thus avoiding the death of the whole colony in adverse environmental conditions. Although sporulation occurs only in some bacteria (such as myxobacteria and streptomyces), a usual and less extreme form of cell differentiation in response to adverse environmental conditions is the somewhat similar stationary phase (*2*). In *Escherichia coli*, for example, the stationary phase (*2*) and PCD (*3*) are two possible (and likely concomittent) responses to nutrient limitation; it is tempting to speculate that intercellular communications similar to those operating in *B. subtilis* allow the reciprocal fine tuning of these responses. The existence and nature of such a social control of cell survival and cell death in *E. coli* and other bacteria remain to be investigated.

Fulton addresses the divergence time of multicellular plants. Recent phylogenic analyses suggest that plants, fungi, and animals, as well as dinoflagellates, chromophytes, and ciliates, diverged rapidly around 1 billion years ago (*4*). Estimates of plant, animal, and fungi branching have led to contradictory results, suggesting either that plants and animals diverged more recently than fungi (*5*) or that animals and fungi diverged more recently than plants (*6*). One of the most recently published exhaustive phylogenic analyses suggests that animals, fungi, and plants last shared a common ancestor about 1 billion years ago and that animals and fungi are more recently related than animals and plants (R. F. Doolittle *et al.*, Articles, 26 Jan. 1996, p. 470). Accordingly, the branching of plants before fungi and animals in the phylogenic tree at a point of around 1 billion years ago should have been shown more accurately. The main aim of presenting the tree was, however, to illustrate the fact that various forms of PCD have been identified in divergent kingdoms of organisms, suggesting either that PCD is an evolutionarily conserved feature of ancient origin or that PCD evolved independently several times.

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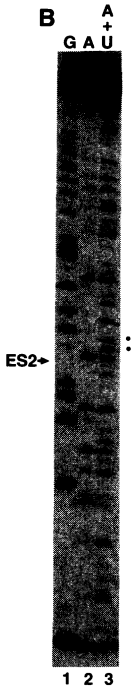
## Corrections and Clarifications

The two markers on the right side of the electrophoresis gel shown in figure 3B (p. 1190) of the Research Article "RNA editing: A mechanism for gRNA-specified uridylate insertion into precursor mRNA" by M. L. Kable *et al.* (30 Aug., p. 1189) were placed incorrectly during publication. The correct figure appears at right.



In the response by D. S. McKay *et al.* (p. 1640) to letters titled "Past life on Mars?" (20 Sept., p. 1639), the microscope technology mentioned should have read, "field emission gun scanning electron microscope."

In the editorial "New online tools for scholars: 2" by Floyd E. Bloom (20 Sept., p. 1637), in the next-to-last paragraph, the fourth line should have read, "online materials will be available each Thursday around 5 p.m. Eastern Time. . . ."

The title of the report "Interaction of U2AF$^{65}$ RS region with pre-mRNA branch point and promotion of base pairing with U2 snRNA" by J. Valcárcel *et al.* (20 Sept., p. 1706) was printed incorrectly on page 1706. It was correct in the table of contents.

In the issue of 9 August, the photograph in the table of contents (p. 712) and in the Research News article "Genes vs. teams: Weighing group tactics in evolution" (p. 739) should have been credited to the Honeybee Science Research Center, Tamagawa University, Tokyo.

### Letters to the Editor

Letters may be submitted by e-mail (at science_letters@aaas.org), fax (202-789-4669), or regular mail (*Science*, 1200 New York Avenue, NW, Washington, DC 20005, USA). Letters are not routinely acknowledged. Full addresses, signatures, and daytime phone numbers should be included. Letters should be brief (300 words or less) and may be edited for reasons of clarity or space. They may appear in print and/or on the World Wide Web. Letter writers are not consulted before publication.