a Curie-Weiss term from the very weakly antiferromagnetically coupled Fe^{3+} ions. Below T_c, the susceptibility increases with increasing field until it reaches a critical field, which is consistent with a London penetration depth. The Meissner effect is complete at 0.5 mT. The electron paramagnetic resonance spectra show one Dysonian in shape resonance due to the conduction electrons of the BEDT-TTF chains and one Lorentzian in shape resonance due to the Fe^{3+} ions. Electronic band structure calculations based on crystal data obtained at 300 K confirm a metallic behavior with both electron and hole pockets in the Fermi surface (which are, more probably, tubes resulting from the two-dimensional character of the crystal structure). In conclusion, this phase truly is the first molecule-based paramagnetic superconductor.

The paper by Kurmoo *et al.* also illustrates how small chemical modifications may result in drastic changes in the physical properties of molecular electron-transfer salts. The derived (BEDT-TTF)$_4$[YFe(C_2O_4)$_3$]C_6H_5CN salts obtained by substituting Y = K or NH_4 or H_2O are semiconductors. This may be related to differences in the structures, which consist of layers of (BEDT-TTF)$_2^{2+}$ dimers separated by isolated neutral (BEDT-TTF)^0 molecules for the K or NH_4 derivatives, whereas in the H_2O derivative, chains of equivalent (BEDT-TTF)$^{+3/4}$ are observed (hence, the so-called β″-structure). By contrast, the underlying hexagonal network of Fe and Y is similar in the three compounds. Striking also is the observation of alternate [Fe(C_2O_4)$_3$]$^-$ anion layers that are exclusively composed either of Δ or Λ enantiomers, even though the three compounds were prepared from racemic [Fe(C_2O_4)$_3$]$_3^-$ starting salts.

If the behavior of β-(BEDT-TTF)$_4$[(H_2O)Fe(C_2O_4)$_3$]·C_6H_5CN is a result of BCS singlet-state superconductivity, then the Fe^{3+} ions cannot be directly immersed in the gas of electrons condensed in pairs; instead, they must be shielded from the superconducting BEDT-TTF layers. A similar situation is encountered in the two-dimensional high-T_c copper oxides, in which the presence of magnetic impurities suppresses superconductivity when located in the Cu-O planes but not when located outside of these planes. Another explanation may be found in the possible existence of triplet-state superconductivity, which has been suggested to be more appropriate for describing the behavior of molecular superconductors and less sensitive to magnetic perturbation (*9*). Be that as it may, the finding of Kurmoo *et al.* is a major breakthrough in the field and opens up brilliant prospects for the interplay of conductivity and magnetism in molecular solids.

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The Origin of Programmed Cell Death

Jean Claude Ameisen

Cells from multicellular organisms self-destruct when they are no longer needed or have become damaged. They do this by activating genetically controlled cell suicide machinery that leads to programmed cell death (PCD). To survive, all cells from multicellular animals depend on the constant repression of this suicide program by signals from other cells (*1*). It has been assumed that such an altruistic form of cell survival regulation arose with multicellularity and would have been counterselected in unicellular organisms (*1*). Recent findings indicate, however, that a similar process of socially advantageous regulation of cell survival also operates in single-celled eukaryotes.

PCD has now been described in four unicellular organisms (*2–5*) that emerged between 2 and 1 billion years ago and belong to three diverging branches of the eukaryote phylogenic tree (see the figure): the kinetoplastid parasites *Trypanosoma cruzi* (*2*) and *Trypanosoma brucei rhodensiense* (*3*), among the first mitochondrial eukaryotes; the free-living slime mold *Dictyostelium discoideum* (*4*); and the free-living ciliate *Tetrahymena thermophila* (*5*). Unicellular eukaryote PCD is similar (*4*)—or identical (*2*, *3*)—to apoptosis, the usual PCD phenotype in cells from multicellular animals (*1*). Its features include cytoplasmic blebbing and vacuolization, chromatin condensation, and DNA fragmentation. Environmental stress (such as starving) and extracellular signals that activate the cyclic AMP pathway (which induce differentiation to a reversible G_0/G_1-arrested stage) also induce PCD in cells that remain undifferentiated and cycling (*2*, *4*). In low-density cultures of dividing protists, PCD is induced "by default" if cell differentiation is not triggered, unless certain environmental conditions are provided (*2*, *5*). Finally, in the kinetoplastid parasites, PCD is also regulated by signals from their multicellular host (*2*, *3*). So, like multicellular organisms, survival of unicellular eukaryotes depends on the prevention of self-destruction by extracellular signals.

Why has evolution favored such a system of cell destruction? PCD allows constant selection for the fittest cell in the colony, optimal adaptation of cell numbers to the environment, and tight regulation of the cell cycle and cell differentiation. PCD may be particularly useful when cells are interacting: in the trypanosomes, PCD may regulate the communication between unicellular and multicellular organisms that allow the establishment of a stable host-parasite relation (*2*, *3*); and in the slime mold, PCD allows the induction of dead stalk cells that participate in the formation of a multicellular aggregated body (*4*).

How and when did unicellular organisms select for genes allowing cell suicide? Primitive forms of PCD occur in prokaryotes when plasmid or viral genomes compete with bacterial genomes in a bacterial colony; when bacteria from different species compete; and upon terminal differentiation of *Myxobacteria* and *Streptomyces*, which allows the transient formation of multicellular aggregated bodies (*6*). These findings suggest a multistep scenario for the emergence of death genes during evolution: in prokaryotes, (i) selection for killer genes encoding toxins used for offense in evolutionary arms races between different species, and concomitant selection for genes encoding toxin antidotes for defensive purposes; and (ii) selection for the induction of such genes in adverse environmental conditions to allow control of death and survival in cells sharing the same genome, providing a selective advantage to the

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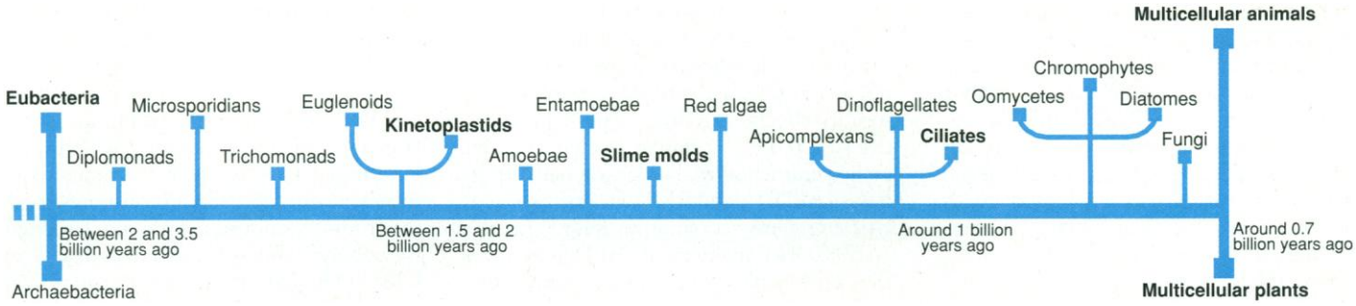

Programmed cell death and evolution. Various forms of PCD have been identified (in bold) in several branches of the phylogenic tree. No data on PCD are available for members from other branches. The tree and estimated divergence times are adapted from (*11*).

best-adapted offspring by preventing flawed offspring from competing for resources. The hypothesis that the eukaryote cell is a symbiont that arose from fusion of different bacteria species suggests that PCD may have evolved from a resolution of conflict between heterogeneous genomes within a cell, a process similar to step (i), that subsequently led to enforced cooperation.

Although such an evolutionary scenario is plausible, an alternative model would remove the need for a multistep process in the emergence of cell suicide machinery. In multicellular animals, some gene families function solely as inducers (the Ced-3/ICE/CPP32 cysteine proteases) or inhibitors (CED-9/Bcl-2/Bcl-XL) of PCD (*1*). However, most genes that control the cell cycle and cell differentiation—including proto-oncogenes, tumor suppressor genes (*1*), cyclins, and cyclin-dependent kinases (*7*, *8*,)—also participate in the control of PCD, and mitotic catastrophes resulting from uncoordinated activation of cyclins in mammalian cells and in yeast mutants have a phenotype similar or identical to apoptosis (*8*). In bacteria, the autolysins that participate in cell division can also induce self-destruction. If effectors of the cell cycle machinery can also be effectors of the self-destruction of the cell in which they operate, then the requirement for coupling cell survival to the prevention of self-destruction is as old as the origin of the cell (*10*).

The evolution of PCD would share similarities with the evolution of genetic diversity. The inability of a cell to avoid random genetic mutation has led to the selection of both DNA proofreading and repair mechanisms and the amplification of DNA diversity by genetic reassortment. The view that an intrinsic inability to avoid random self-destruction is an "original sin" of the cell, an inherent consequence of progression through the cell cycle, implies that selective pressures regulate the cell cycle machinery so that cell suicide is repressed. Such a scenario provides a simple mechanism for the selection of upstream inducers of PCD that allow enhanced fitness of the colony through the rapid dismisal of an individual once a mistake has been made during the cell cycle.

Is the origin of social control of cell survival coextensive with the origin of the cell, or have there been several parallel evolutionary attempts toward PCD? Do unicellular eukaryotes share effectors and regulators of cell suicide with multicellular animals? Are mutations that uncouple the cell suicide machinery from extracellular signals counterselected in unicellular colonies, as in multicellular animals (*1*, *7*)? The identification of the genes that regulate cell suicide in other unicellular organisms should help to address these questions.

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10. The conserved Ced-3/ICE/CPP32 cysteine protease gene families that are considered as downstream executioners of apoptosis in multicellular animals may in fact be upstream regulators of cell suicide or may act in conjunction with regulators of the cell cycle (or both). This is consistent with findings indicating that (i) the Bcl-2 survival gene product prevents apoptosis downstream of ICE activation [M. Enari, A. Hase, S. Nagata, *EMBO J.* **14**, 5201 (1995)]; and (ii) granzyme B, which directly activates CPP32 [A. J. Darmon, D. W. Nicholson, R. C. Bleakley, *Nature* **377**, 446 (1995)], also requires cdc2 cyclin-dependent kinase activation in order to induce apoptosis (*8*).
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Infertility Treatment: A Nuclear Restorer Gene in Maize

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The best seed corn is a true hybrid, the parents being of different and carefully selected lines. But controlling the parentage of corn requires the intervention of humans, because individual corn plants self-fertilize, serving as both the male and female parent. Historically, corn breeders had to remove the tassel from corn plants by hand to prevent self-fertilization, a tedious process at best. So the discovery that some corn plants natually have no pollen was welcomed, and these strains were adopted for use in hybridization.

But these convenient plants had a cost. Between 1969 and 1970, an epidemic of southern corn leaf blight (*1*) struck a strain of sterile U.S. maize that accounted for 85% of the U.S. hybrid maize grown for commercial seed production—the Texas male-sterile cytoplasm [cmsT (cytoplasmic male sterility–T)] system. The subsequent intense interest in the biology of cytoplasmic male sterility (CMS) and its modulators is continued in this issue of *Science*, in which Cui *et al.* (*2*) report the identity of a gene–*Rf2*, one of the restorers of fertility genes—that can inhibit CMS. *Rf2* turns out to be an aldehyde dehydrogenase.

Cytoplasmic male sterility is a maternally inherited trait that suppresses the production of viable pollen and causes sterility in male, but not female, plants (*3*). The sterility effects of CMS, mediated by mito-

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