

processes within living organisms that appear to us as purposeful unidirectional motion.

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# Oogamy: Inventing the Sexes

The male–female dichotomy has evolved independently in nearly all lineages of multicellular organisms. Why this should be the case is still uncertain, but recent studies of mating-type genes in green algae open a promising new way to explore molecular-genetic aspects of the evolution of dichotomous sexes.

David L. Kirk

We probably all feel that, as private individuals, we have an intimate knowledge of sex, but biologists who study sex have long felt compelled to admit the extent of their ignorance. This is well illustrated by three quotes from knowledgeable pundits spanning more than a century: “we do not even in the least know why new beings should be produced by the union of two sexual elements, instead of by...parthenogenesis” [1]; “sex has always been an embarrassment to population biologists” [2]; and “empirically, we really know very little about sex” [3]. Two questions in particular have puzzled evolutionary biologists for many generations [1–9]. First, given that sexually reproducing organisms pass on only half as many genes to each of their offspring as organisms that reproduce parthenogenetically, why is parthenogenesis so rare, and sexual reproduction so common among eukaryotes? And

second, as eukaryotic sex was almost certainly initially isogametic — involving fusion of morphologically similar gametes — what selective advantage accounts for the fact that there have been so many independent evolutionary inventions of oogamy, in which tiny, motile male gametes fuse with large, immotile female gametes? (The many groups in which oogamy has evolved independently include animals, fungi, red algae, brown algae and several different kinds of green algae, including the ancestors of the land plants and the algal group that will be discussed below.)

A number of answers have been proposed for each of those questions, but the point has not yet been reached where either question has been answered to the satisfaction of all of those who worry about such things [8–10]. However, a study by Nozaki *et al.* [11], reported in this issue of *Current Biology*, opens a highly promising new route for elucidating the molecular nature — if not the

ultimate cause — of the evolutionary pathway from isogamy to oogamy in a group of closely related, recently evolved organisms known as the volvocine green algae.

It has been said of the volvocine algae that “Few groups...hold such a fascination for evolutionary biologists... It is almost as if [they] were designed to exemplify the process of evolution” [12]. Members of this group range in size and complexity from *Chlamydomonas*, a biflagellate unicell, to *Volvox*, a spherical multicellular organism with a division of labor between thousands of small, terminally differentiated, biflagellate somatic cells, and a few large, non-motile reproductive cells. Between those phylogenetic extremes lies an assortment of colonial genera that have traditionally been included in the family Volvocaceae, such as *Gonium*, *Pandorina* and *Eudorina*, which contain 8, 16 or 32 identical biflagellate, *Chlamydomonas*-like cells, plus *Pleodorina*, which never has more than 128 cells, but exhibits a germ–soma division of labor resembling that of *Volvox*. Nozaki *et al.* [11] studied a newly discovered species of *Pleodorina* called *P. starrii* [13]. A simplified version of a molecular phylogeny of the volvocine algae, including *P. starrii*, that was based on comparative sequencing of five

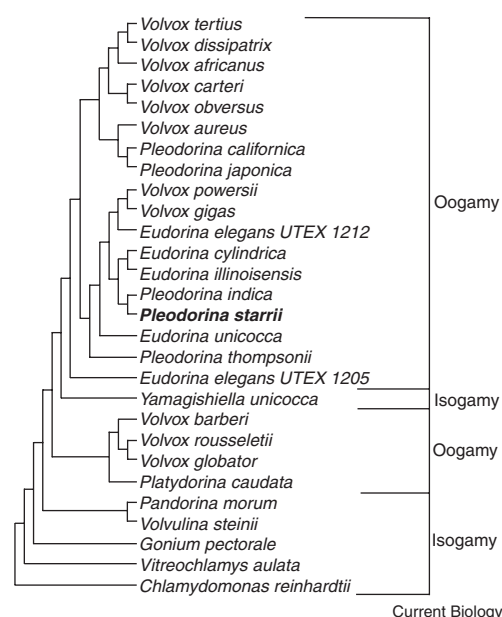
chloroplast genes [13,14], is shown in Figure 1.

A considerable amount of effort has gone into exploring the cellular and molecular changes that underly the evolution of multicellularity and cellular differentiation in this group of algae [15]. But new work of Nozaki *et al.* [11] opens the way for an entirely new kind of study: a molecular-genetic analysis of the evolution of oogamy. In the unicellular alga *C. reinhardtii*, sexual reproduction is isogamous; that is, it involves fusion of gametes that are of two different mating types — mating-type plus (MT+) and mating-type minus (MT−) — but are similar in size and motility. Several of the smaller colonial volvocine algae are similarly isogamous. But other volvocaceans, and particularly the larger ones, are oogamous (Figure 1): in these species, small, motile sperm produced by males find and fuse with large, non-motile eggs produced by females (Figure 2). Indeed, it has been shown that in these volvocaceans there is a statistically significant increase in the ratio of egg volume to sperm volume with increasing adult size [2,10,12], just as the dominant model for the evolution of gamete dimorphism [5] predicts.

Ferris and Goodenough [16] laid the groundwork for the work of Nozaki *et al.* [11] by cloning the *MID* (minus-dominance) gene of *C. reinhardtii*, and showing that it encodes a putative transcriptional regulator that is both necessary and sufficient to cause *C. reinhardtii* cells to differentiate and mate as MT− cells. Nozaki *et al.* [11] used primers based on the *C. reinhardtii* *MID* gene sequence to amplify and clone the *MID* ortholog of an oogamous species, *P. starrii*, and have demonstrated that this '*PleMID*' gene is present only in the male strain, is expressed in males only after spermatogenesis has been induced by starvation, and encodes a protein that eventually becomes localized abundantly in the nuclei of mature sperm. From these observations, Nozaki *et al.* [11] infer that *P. starrii* males are descendents of the dominant (MT−) strain of their isogamous

Figure 1. Isogamy and oogamy.

The two alternative patterns of gamete differentiation are mapped onto a simplified version of the most recent and extensive molecular phylogeny of the volvocine algae [13,14]. The indication is that either oogamy evolved in this lineage twice, or that a reversion from oogamy to isogamy occurred in *Yamagishiella*. (Note also that several of the taxa included in this study appear not to be monophyletic.)

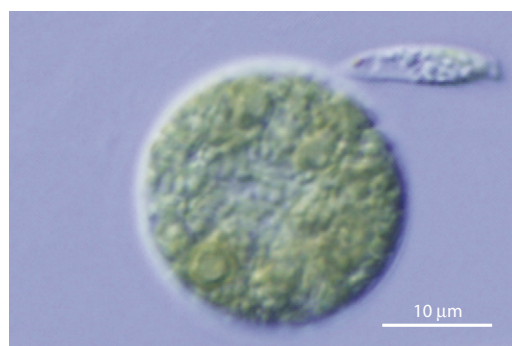


ancestor. This is the first time that a genetic connection has been established between one of the sexes of an oogamous species and one of the mating types of its isogamous ancestor. The story certainly will not end there, however, because the *MID* gene of *Gonium pectorale* has already been cloned, and efforts to clone the *MID* genes of other volvocaceans and study their action are now underway (H. Nozaki, personal communication).

This breakthrough provides an opportunity to address any number of extremely interesting questions, of which the following are but a sample. Can the connection between *MID* and maleness be generalized to other species of oogamous volvocaceans? In particular, does that connection exist in species on the *V. rousseletii* branch of the family tree (Figure 1), where it appears that oogamy may have arisen independently? Will

a *MID* transgene turn a female volvocacean into a male? (So far, *V. carteri* is the only species in which this question could be addressed, because that is the only oogamous species for which a nuclear transformation system has been developed.) Is the *MID* gene present in 'homothallic' *Volvox* species, which produce eggs and sperm within a single clone [17]? If so, does *MID* get selectively activated in sexual male cells and/or repressed in sexual female cells? It has been reported that, under certain circumstances, ultra-violet irradiation of a male strain of *V. carteri* causes a high-frequency, heritable gender reversal, producing 'she-males' [18]. What is the state of the *MID* locus in such she-males? *Pandorina morum* exists in nature as at least 20 reproductively isolated syngens, each of which consists of two mating types [19]. Is there greater variation at the *MID*

Figure 2. A sperm and an egg of *Pleodorina starrii* that are about to interact. (Photo by H. Nozaki.)



locus in *P. morum* than in other volvocacean species? Or is all the variation between syngens in the genes whose expression is regulated by *MID*? And, finally (at least for the moment), what are the genes that are under the control of the *MID* locus, and how different are they in isogamous and oogamous species?

It appears that the breakthrough reported by Nozaki *et al.* [11] will provide enough exciting new opportunities to keep them and many other investigators busy for some time to come!

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## Chemotaxis: Cofilin in the Driver's Seat

**A cell responds to a chemotactic signal by activating actin polymerization and forming a protrusion oriented towards the source. Recent work shows that the activity of cofilin, a protein that creates new barbed ends for actin filament elongation, amplifies and specifies the direction of the response in carcinoma cells.**

Sarah E. Hitchcock-DeGregori

Chemotaxis is the response of a cell to an extracellular diffusible or matrix-bound chemical signal that results in movement towards or away from the chemical, up or down a gradient. The signal molecule binds to a cell-surface receptor and the information is translated and amplified to stimulate local, directionally specific movement. While the signals and pathways for transmitting the information vary, in eukaryotes the actin cytoskeleton carries out the directional movement of the cell, via effects on actin polymerization and actin–myosin interactions.

Fundamental biological processes, including gastrulation,

migration of neurons during the establishment of the nervous system in development, immune responses, wound healing, and cancer cell migration during metastasis, depend on chemotaxis [1,2]. The mechanisms of chemotaxis have been intensively investigated in *Dictyostelium*, the social amoeba that responds to cyclic AMP when it becomes aggregation competent [3]. The other classic system for the study of chemotaxis is neutrophils, which respond to small peptides, such as fMLP produced by bacteria, and migrate to sites of infection where they phagocytose the bacteria [4]. Much has been learned about the pathways in *Dictyostelium* and neutrophils that lead to redistribution of signaling and

cytoskeletal proteins and activation of the actin cytoskeleton resulting in polarization and directional migration [1,2]. Following stimulation, the leading edge of the cell is driven forward by actin polymerization on new, fast-growing filament ends created by cofilin and nucleation of branches by the Arp2/3 complex, as well as elongation promoted by Ena/Vasp and formin families of proteins. The rear of the cell then follows via actin–myosin-mediated contraction.

A remaining question is, how are proteins in the signaling pathway that are abundant and widely distributed in an inherently non-polar cell activated to result in migration in a precise direction, up or down a chemical gradient? To address the question requires the ability to manipulate the molecules in the pathway and to monitor the results in space and in time. Progress has been made in metastatic breast carcinoma cells that undergo chemotaxis in response to epidermal growth factor (EGF), a model for cancer metastasis [5]. These cells are large and flat compared with