tion may lead to new research into the neuro-muscular control of aerial maneuvers in animals (*3*, *4*) and will aid efforts to engineer controllers and actuators that effect wing movement in biometic flying robots (*10*). Passive stability during flapping may thus be analogous to a process in terrestrial locomotion in which neural input and passive dynamics interact to augment stability (*11*).

A major goal of functional morphology and comparative biomechanics is to understand how animal design relates to movement, ecology, and behavior. Thus, it is also important that Hedrick *et al.* show that animals with wings that are large relative to their body size decrease yaw velocity more quickly than animals with proportionally small wings.

Hypotheses about maneuverability and eco-morphology in birds and bats have been dominated by the assumptions of fixed-wing, gliding aerodynamics (*12*). It has been recognized for some time that flapping must be integrated with such models (*3*), and the model of Hedrick *et al.* is a vital step in this direction.

Yaw during hovering and slow flight is just one type of maneuver; an almost limitless array of combinations of yaw, pitch, roll, and flight velocity are available to flying animals. Now that technology has developed to the point where detailed measurements of flapping maneuvers have become feasible (*1–8*), a world of comparative research is opening in which the flapping counter-torque model can be used to test the functional significance of flapping motions in maneuvering dynamics.

References
1. L. Lehmann, M. Dickinson, *J. Exp. Biol.* **204**, 627 (2001).
2. S. Fry, R. Sayaman, M. Dickinson, *Science* **300**, 495 (2003).
3. D. Warrick, M. Bundle, K. Dial, *Integr. Comp. Biol.* **42**, 141 (2002).
4. T. Hedrick, A. Biewener, *J. Exp. Biol.* **210**, 1897 (2007).
5. J. Iriarte-Diaz, S. Swartz, *J. Exp. Biol.* **211**, 3478 (2008).
6. T. L. Hedrick, B. Cheng, X. Deng, *Science* **324**, 252 (2009).
7. B. Tobalske *et al.*, *J. Exp. Biol.* **210**, 2368 (2007).
8. D. Riskin *et al.*, *J. Theor. Biol.* **254**, 604 (2008).
9. S. Vogel, *Life in Moving Fluids: The Physical Biology of Flow* (Princeton Univ. Press, Princeton, NJ, ed. 2, 1994).
10. J. Zufferey. *Bio-Inspired Flying Robots: Experimental Synthesis of Autonomous Indoor Flyers* (EFPL Press, Lausanne, 2008).
11. R. Full *et al.*, *Integr. Comp. Biol.* **42**, 149 (2002).
12. U. Norberg, J. Rayner, *Philos. Trans. R. Soc. London B Biol. Sci.* **316**, 335 (1987).

10.1126/science.1172839

GENOMICS

Green Evolution, Green Revolution

The genomes of two species of green algae provide clues to how green plants evolved.

John M. Archibald

The trees and plants that color our continents are more closely related to aquatic microorganisms—unicellular algae, in particular—than they are to the animals and fungi with which they cohabit. The smallest of these algae, called picophytoplankton, are individually miniscule (less than 2 μm in diameter) but collectively massive in ecological and evolutionary importance. On page 268 of this issue, Worden *et al.* (*1*) present the genome sequences of two such microbes, which belong to the green algal lineage *Micromonas*. Their analyses provide crucial insights into the plasticity of the eukaryotic genome over short evolutionary time scales and also shed light on the genetic "toolkit" that may have been present in the ancestors of today's land plants and green algae.

We are in the midst of a revolution in our exploration of the hidden microbial majority on Earth. Even the tiniest of cells can now be probed, poked, and sorted, and, with a bit of effort, subjected to DNA sequence analysis (*2*). In the case of photosynthetic eukaryotes, two microalgal genome sequences were available in 2004 (the diatom *Thalassiosira* and the red alga *Cyanidioschyzon*); by early 2009, almost a dozen
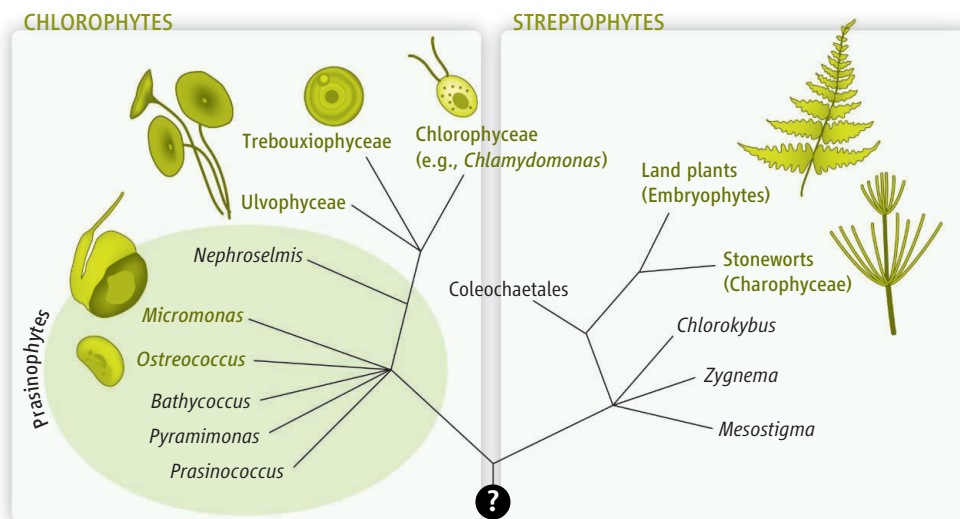
had been sequenced (*3*). Several of these sequences are derived from organisms within the green lineage, such as the model lab alga *Chlamydomonas* (*4*), providing valuable reference points for comparison to the genomes of land plants like *Arabidopsis* (*5*).

Green photosynthetic eukaryotes are divided into two branches, chlorophytes and streptophytes (see the figure). The streptophyte branch is composed of land plants and their closest relatives, such as stoneworts (*6*) and the aquatic unicell *Mesostigma* (*7*, *8*). Molecular data [for example, (*9*)] show that

the prasinophytes are the earliest offshoots of the chlorophyte branch; in the eyes of many, these organisms represent our best guess as to what the ancestor of green eukaryotic life looked like (*10*). It has long been hoped that a solid understanding of prasinophyte biology would open a window on the chlorophyte-streptophyte common ancestor.

The first prasinophyte genomes to be sequenced were from a pair of *Ostreococcus* species (*11*, *12*), the reining champions of eukaryotic cellular miniaturization (*13*). *Ostreococcus* genomes, too, are tiny: Just ~13

The Canadian Institute for Advanced Research, Program in Integrated Microbial Biodiversity, Department of Biochemistry and Molecular Biology, Dalhousie University, Halifax, Nova Scotia B3H 1X5, Canada. E-mail: john.archibald@dal.ca

Green revolution. This evolutionary tree depicts a consensus view of the green tree of life, based on (*10*) and with consideration of new data, for example, from (*8*). By sequencing the genomes of two prasinophytes, Worden *et al.* (*1*) expand our knowledge of the genes present in the ancestors of land plants and green algae.

million base pairs in size and with ~8000 genes, they are clearly the product of reductive evolution (*14*). In the case of *Micromonas*, Worden *et al.* now show that bigger is better. The authors sequenced the genomes of strains CCMP1545 and RCC299, isolated from temperate and tropical oceans, respectively (*1*). Although modest by eukaryotic standards, the *Micromonas* genomes are less streamlined than those of *Ostreococcus*. Both are ~20 million base pairs in size and possess ~10,000 genes. Comparison of the *Micromonas* genomes to one another, to those of *Ostreococcus* (*11*, *12*), and to other algae, plants, and nonphotosynthetic eukaryotes provides fascinating insights into how green plants evolved.

Of particular note among the 1384 genes shared by both *Micromonas* strains but absent in *Ostreococcus* is an impressive suite of transcription factor genes, the origins of some of which can now reasonably be moved to the common ancestor of chlorophytes and streptophytes. Compared with *Ostreococcus*, *Micromonas* has a richer set of nutrient transporter gene families (most of which are also found in land plants); *Micromonas* also contains a more complex suite of genes potentially involved in combating reactive oxygen species and heavy metals. *Micromonas* thus appears to be the more flexible of the two in terms of environmental "adaptability," which could explain its broader global distribution (*1*). Both *Micromonas* and *Ostreococcus* are clearly sexual: A slew of conserved meiosis-specific genes exist in all four genomes, and the presence of hydroxyproline-rich

glycoprotein genes suggests—by analogy to *Chlamydomonas*—the existence of a (yet to be observed) sex-related, thick-walled stage of their life cycle (*1*). The prasinophytes are thus a lot more complex than previously believed.

The two *Micromonas* strains analyzed by Worden *et al.* are morphologically indistinguishable from one another and were previously assumed to be members of the same genus and species (their 18*S* rRNA sequences are ~97% identical), yet CCMP1545 and RCC299 share only 90% of their genes. Phylogenomic analysis reveals that many genes that occur in one *Micromonas* genome, but not the other, are very similar to those found in organisms as evolutionarily distant as animals, fungi, and bacteria (*1*). One interpretation is that such genes are the product of horizontal gene transfer, through which an organism incorporates genetic material from an unrelated or distantly related species; this process is gaining increasing acceptance as a real force in eukaryotic genome evolution (*15*).

The two *Micromonas* genomes also have unexpectedly different gene and genome structures. For example, CCMP1545 genes have on average more and larger spliceosomal introns than those of RCC299, many of which contain novel intronic repeats dubbed "introner elements." These elements make up 9% of the CCMP1545 genome but are absent from RCC299 (*1*). Understanding the importance of these strain-specific differences in gene and

genome structure and content will go a long way toward understanding the differences in their biology and ecology.

It is exciting to think that some of the smallest eukaryotes on our planet can provide key insights into the early history of multicellular green plants. Worden *et al.* have made a substantial contribution to this story, laying the foundation for further comparative genomic analyses on a much broader diversity of plants and algae. Dozens of lineages up and down the green line are ripe for genome sequencing, and if the past few years are any indication, we will have answers sooner rather than later.

References
1. A. Z. Worden et al., *Science* **324**, 268 (2009).
2. D. Vaulot, W. Eikrem, M. Viprey, H. Moreau, *FEMS Microbiol. Rev.* **32**, 795 (2008).
3. M. S. Parker, T. Mock, E. V. Armbrust, *Ann. Rev. Genet.* **42**, 619 (2008).
4. S. S. Merchant et al., *Science* **318**, 245 (2007).
5. The *Arabidopsis* Genome Initiative, *Nature* **408**, 796 (2000).
6. K. G. Karol, R. M. McCourt, M. T. Cimino, C. F. Delwiche, *Science* **294**, 2351 (2001).
7. B. Marin, M. Melkonian, *Protist* **150**, 399 (1999).
8. N. Rodríguez-Ezpeleta et al., *Mol. Biol. Evol.* **24**, 723 (2007).
9. L. Guillou et al., *Protist* **155**, 193 (2004).
10. L. A. Lewis, R. M. McCourt, *Am. J. Bot.* **91**, 1535 (2004).
11. E. Derelle et al., *Proc. Natl. Acad. Sci. U.S.A.* **103**, 11647 (2006).
12. B. Palenik et al., *Proc. Natl. Acad. Sci. U.S.A.* **104**, 7705 (2007).
13. C. Courties, A. Vaquer, M. Trousselier, J. Lautier, *Nature* **370**, 255 (1994).
14. P. J. Keeling, *Trends Genet.* **23**, 151 (2007).
15. P. J. Keeling, J. D. Palmer, *Nat. Rev. Genet.* **9**, 605 (2008).

CANCER

Puzzling Patterns of Predisposition

Patrick J. Pollard and Peter J. Ratcliffe

Mutations in a gene that encodes a metabolic enzyme have been linked to certain brain tumors, but is the gene a tumor suppressor or an oncogene?

Following Theodor Boveri's seminal observation of abnormal chromosomal constitution in malignant tumors, successive advances in genetic analysis have shed new light on the cause of cancer. The latest of these, high-throughput DNA sequencing, is now providing an unprejudiced picture of cancer-associated mutations across the genome. The most intriguing are mutations in genes of known biological function but with previously unsuspected links to cancer. Thus, the recent

Henry Wellcome Building for Molecular Physiology, University of Oxford, Oxford OX3 7BN, UK. E-mail: pjr@well.ox.ac.uk

identification of mutations in a specific isoform of the enzyme isocitrate dehydrogenase (IDH1) in glioblastoma multiforme (a malignant human brain tumor) has generated widespread interest (*1*). On page 261 of this issue, Zhao *et al.* (*2*) propose a mechanism through which this enzyme promotes oncogenesis.

Heterozygous IDH1 mutations have been identified in up to 80% of certain types of glioblastoma multiforme (*1*, *3–5*). Remarkably, the mutations are confined to a single residue, Arg[132]. Although the majority are Arg[132] → His substitutions, five other exchanges (to Ser, Cys, Gly, Val, and Leu) have been observed. Although heterozygous

mutation at a single site might suggest dominant gain of function, six dissimilar substitutions would be surprising for such a mechanism. This has engendered a lively debate as to whether *IDH1* is an atypical tumor suppressor gene (in which a mutation causes loss of function) or an oncogene (in which a mutation causes gain of function) (*6*).

IDH1 is one of three isocitrate dehydrogenases that catalyze the oxidative decarboxylation of isocitrate to α-ketoglutarate (α-KG). IDH1 and IDH2 require nicotinamide adenine dinucleotide phosphate (NADP) as co-substrate, whereas IDH3 requires nicotinamide adenine dinucleotide (NAD). IDH2 and IDH3