

Editor-in-Chief: Floyd E. Bloom
Editor: Ellis Rubinstein
Managing Editor: Monica M. Bradford
Deputy Editors: Philip H. Abelson (*Engineering and Applied Sciences*); John I. Brauman (*Physical Sciences*); Thomas R. Cech (*Biological Sciences*)

Editorial

Assistant Managing Editor: Dawn McCoy; **Senior Editors:** Eleanore Butz, Gilbert J. Chin, R. Brooks Hanson, Pamela J. Hines, Barbara Jasny, Katrina L. Kelner, Paula A. Kiberstis, Linda J. Miller, L. Bryan Ray, Phillip D. Szurmi, David F. Voss; **Associate Editors:** Beverly A. Purnell, Linda R. Rowan; **Contributing Editors:** Richard Peters, Robert Sikorski; **Letters:** Christine Gilbert, *Editor*; Steven S. Lapham, *Associate Editor*; Charlene King, *Assistant*; **Book Reviews:** Katherine Livingston, *Editor*; Jeffrey Hearn, *Editorial Assistant*; **Editing:** Cara Tate, *Supervisor*; Erik G. Morris, *Senior Copy Editor*; Jeffrey E. Cook, Harry Jach, Etta Kavanagh, Joshua Marcy, Christine M. Pearce; **Copy Desk:** Ellen E. Murphy, *Supervisor*; Joi S. Granger, Abigail Hollister, Janet Miller Rife, Beverly Shields; Jessica Moshell, *Assistant*; **Editorial Support:** Carolyn Kyle, *Editorial Assistant*; Candace Gallery, Josh Lipicky, Diane Long, Patricia M. Moore, Anita Wynn, *Manuscript Assistants*; **Administrative Support:** Sylvia Kihara, Brent Gendleman; **Computer Specialist:** Roman Frillarte

News

News Editor: Colin Norman; **Features Editor:** Tim Appenzeller; **Deputy News Editors:** Elizabeth Culotta (contributing editor), Jean Marx, Jeffrey Mervis, Richard Stone; **News & Comment/Research News Writers:** David Ehrenstein (intern), Constance Holden, Jocelyn Kaiser, Richard A. Kerr, Andrew Lawler, Elliot Marshall, Elizabeth Pennisi, Robert F. Service, Gretchen Vogel; **Bureaus:** Berkeley, CA: Marcia Barinaga (contributing correspondent); San Diego, CA: Jon Cohen; Chicago, IL: James Glanz (contributing correspondent); Boston, MA: Wade Roush; **Copy Editors:** Linda B. Felaco, Anna K. Brinkmann; **Contributing Correspondents:** Barry A. Cipra, Ann Gibbons, Charles C. Mann, Anne Simon Moffat, Virginia Morell, Gary Taubes, Ingrid Wickelgren; **Administrative Support:** Scherraine Mack, Fannie Groom

Production & Art

Production: James Landry, *Director*; Wendy K. Shank, *Manager*; Elizabeth A. Harman, *Assistant Manager*; Daniel T. Helgerman, Vicki J. Jorgensen, Cynthia M. Penny, Kameaka Williams, *Associates*; **Art:** Amy Decker Henry, *Design Director*; C. Faber Smith, *Art Director*; Elizabeth Carroll, *Associate Art Director*; Katharine Sutliff, *Scientific Illustrator*; Holly Bishop, Preston Morrighan, Darcel Pugh, *Graphics Associates*; Patricia M. Riehn, *Graphics Assistant*; Leslie Blizard, *Photo Researcher*; **Technology Manager:** Christopher J. Feldmeier

Science International: Europe Office

Editorial: Richard B. Gallagher, *Office Head and Senior Editor*; Stella M. Hurtley, Julia Uppenbrink, *Associate Editors*; Belinda Holden, *Editorial Associate*; **News:** Daniel Clery, *Editor*; Nigel Williams, *Correspondent*; Michael Balter (*Paris*), Patricia Kahn (*Heidelberg*), *Contributing Correspondents*; **UK Editor, Science's Next Wave:** John MacFarlane; **Administrative Support:** Janet Mumford, Elizabeth Elderred-Martos; **Asia Office:** Japan News Bureau: Dennis Normile (contributing correspondent); China Representative: Hao Xin

ScienceNOW: www.sciencenow.org

Editor: Erik Stokstad

Science's Next Wave: www.nextwave.org

Managing Editor: Wendy Yee; **Associate Editor:** Nicole Ruediger; **Canada Editor:** Charles Boulakia

Richard S. Nicholson
Publisher

Beth Rosner
Associate Publisher

Michael Spinella
Membership/Circulation Director

EDITORIAL

The Evolution of Genomics

This year's Genome Issue goes one step beyond the genome project. In its broadest sense, the issue is concerned with taking the sequence information that is the output of the project to the next level—making it useful in studies ranging from understanding the function associated with the sequence to making the transition from gene discovery to the clinic. Two review articles as well as a special fold-out chart are concerned with analyzing the data and using structural and functional criteria to elaborate a universal system in which genes and proteins can be described and classified in a logical and efficient way.

These complex and exciting challenges are a consequence of progress made in ascertaining the full genomic sequences of model organisms, as well as advances in sequencing the human genome. Although only 2 percent of our genetic material has been sequenced so far, more than 50 percent of the human gene complement is likely to be represented in collections of expressed sequence tags. It is believed that some improvement of the technology might still allow the genome project to meet its 2005 deadline [see Rowen *et al.* (p. 605) for a discussion of the state of the art].

A full description of our genome will not be sufficient to understand its functional organization, neither for individual units nor at a more integrated level. Hence, novel technologies and conceptual tools must be designed that promote a systematic approach to gene function: a transition from "structural genomics" to "functional genomics," as discussed by Hieter (p. 601). Functional genomics will no doubt increase the number of cases in which genes can be associated with particular phenotypes, either normal or pathological. The question, as discussed by Holtzman *et al.* (p. 602), becomes how to successfully make the transition from genomics to clinical practice in a way that fulfills scientific criteria and respects ethical as well as social concerns.

However, whether or not they are linked to genetic diseases, it is imperative that newly isolated gene products be classified so that the future exhaustive list of our genes can be based on rational criteria and thus reflect some internal properties of our genome. Two articles in this issue address this key question (Henikoff *et al.*, p. 609, and Tatusov *et al.*, p. 631) and discuss the bases for the elaboration of a system of classification.

The past 15 years have revealed that genes can be organized as families, as defined by a discrete number of functional protein building blocks. It has become equally clear that animals tend to have the same complement of genes, although copy number may vary as the result of large-scale genome duplications. Although these links among proteins should facilitate their classification, Henikoff *et al.* emphasize that local duplication, rearrangement of protein-coding segments and combinations of modules, as well as unequal expansion of some subfamilies at the expense of others, have made this challenge much more complex than anticipated. These evolutionary relationships between genes may nevertheless be used as a driving principle in a system of classification. Tatusov *et al.* report that comparison between seven complete genomes led to the definition of more than 700 rows of orthologous groups, that is, groups of genes that show orthologous relationships based on the presence of an ancient conserved protein domain.

However, the combination of various protein motifs in the course of evolution did not follow any particular organizing principle, and new chimeric proteins (containing more than one motif) of all kinds are being reported. The challenge may well be to build up a logical classification system to account for a fundamentally illogical process. This precise issue was addressed in these columns 20 years ago by Jacob in his seminal paper "Evolution and tinkering."* Jacob suggested that recycling of preexisting material, rather than the design of new players, was a source of molecular and regulatory innovations. By sequencing genomes, we can now contemplate the result of evolutionary tinkering and realize how important it has been in producing genetic novelties. Most importantly, the mere description of our genetic material may turn out to be decisive in our understanding of evolutionary mechanisms. The combination of protein motifs may have allowed genes to become highly pleiotropic, which in turn may have introduced important constraints on their future potential variations.

Structural genomics is under way, functional genomics is coming; let us embark for "evolutionary genomics," as it is surely on the horizon.

Denis Duboule

The author is in the Department of Zoology, University of Geneva, Switzerland.

*F. Jacob, *Science* **196**, 1161 (1977)