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29 MARCH 1996
VOL. 271 • PAGES 1777-1952

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Diversity
During
Adversity

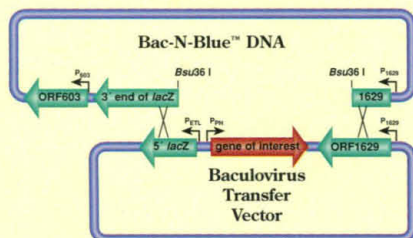
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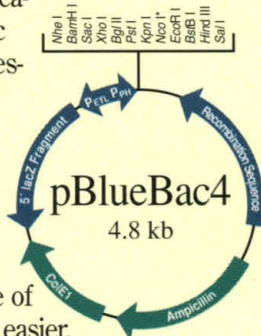
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1. Davis, T.R. *et al.* (1993) *In Vitro Cell. Dev. Biol.* **29A**: 388-390.

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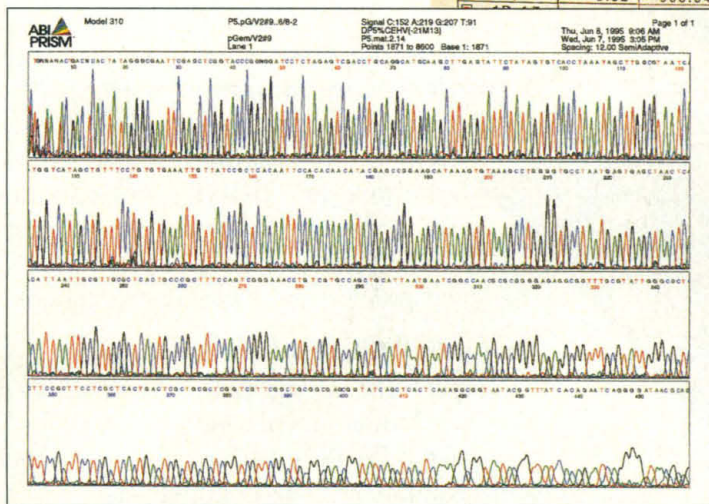
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References

1. Fodde, R., and Loosekoot, M., *Human Mutation*, 3, 83, (1994).
2. Fischer, S.G. and Lerman, L.S., *Proc. Natl. Acad. Sci., U.S.A.*, 80, 1579 (1983).
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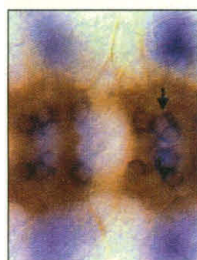
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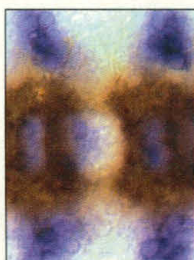
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1810 & 1848
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COVER

Optical micrograph (crossed polarizers) showing parallel dark rods of FeTiO_3 (up to 20 micrometers long) that precipitated from solution in the mineral olivine during tectonic transport of a piece of mantle to a location high in the Swiss Alps. These rods formed under high pressure at depths greater than 300 ki-

lometers, indicating profound subduction of continental rocks after the collision of Africa and Europe and their return to the surface carrying this piece of mantle. See page 1841 and News story on page 1811. [Image: L. Dobrzhinetskaya, H. W. Green II, and S. Wang]



RESEARCH ARTICLE

Interaction Between Wingless and Notch Signaling Pathways Mediated by Dishevelled

1826

J. D. Axelrod, K. Matsuno, S. Artavanis-Tsakonas, N. Perrimon

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Isolation, Structure, and Electronic Calculations of the Heterofullerene Salt $\text{K}_6\text{C}_{59}\text{N}$

1833

K. Prassides, M. Keshavarz-K., J. C. Hummelen, W. Andreoni, P. Giannozzi, E. Beer, C. Bellavia, L. Cristofolini, R. González, A. Lappas, Y. Murata, M. Malecki, V. Srdanov, F. Wudl

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L. Dobrzhinetskaya, H. W. Green II, S. Wang

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Identification of D-Peptide Ligands Through Mirror-Image Phage Display

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Altered Sensory Processing in the Somatosensory Cortex of the Mouse Mutant Barreless

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A Neural Tetraspanin, Encoded by *late bloomer*, That Facilitates Synapse Formation

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W. E. Skaggs and B. L. McNaughton

An RNA Polymerase II Elongation Factor Encoded by the Human *ELL* Gene

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A. Shilatifard, W. S. Lane, K. W. Jackson, R. C. Conaway, J. W. Conaway

Failure of the Cystic Fibrosis Transmembrane Conductance Regulator to Conduct ATP

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M. M. Reddy, P. M. Quinton, C. Haws, J. J. Wine, R. Grygorczyk, J. A. Tabcharani, J. W. Hanrahan, K. L. Gunderson, R. R. Kopito

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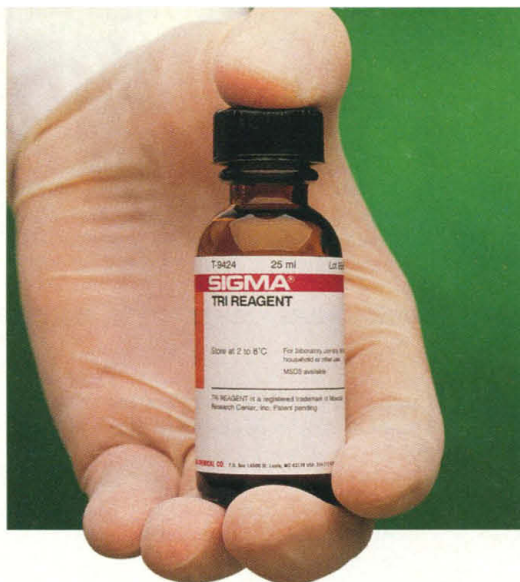
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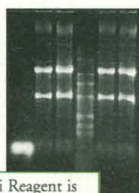
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Out of the depths (I)

More and more rocks exposed at the Earth's surface are now recognized as coming from deep in the mantle. These include xenoliths, which are small rocks carried upward by magmas that may come from depths of 400 kilometers or more, and larger rock packages, typically exposed by tectonic processes in continental collision zones and containing high-pressure minerals such as diamond. Dobrzhinetskaya *et al.* (p. 1841; see the news story by Kerr, p. 1811) show that the Alpe Arami peridotite, a large rock massif in the Alps, may have come from depths of 300 kilometers or more. Olivine in the rocks contains inclusions of a new phase of FeTiO_3 (see the cover) that indicate original exsolution of the perovskite phase at high pressures.

■

Out of the depths (II)

The rates and methods by which silicic magmas ascend through the crust have been uncertain. Brandon *et al.* (p. 1845) studied the dissolution of epidote, a mineral that is stable at high pressures in magmas but dissolves at shallow depths, to evaluate magma emplacement and cooling rates. Preservation of epidote in some dikes and intrusions implies that the parent magmas were emplaced and crystallized within 1000 years or so. Such rates are too fast for ascent of these magmas in diapirs.

■

No old greenhouse?

The latest Cretaceous climate has often been considered to be a warm greenhouse climate. Certainly high-latitude regions were warmer than comparable regions today, but there is evidence that the tropical oceans

Inhibited by cross talk

Multiple signal transduction pathways are often required during development to determine cell fates. How these signaling pathways are integrated, however, is frequently unclear. Axelrod *et al.* (p. 1826; see the Perspective by Blair, p. 1821) examined the interaction between the Notch and Wingless signaling pathways during pattern formation in the developing *Drosophila* wing. During the induction of bristles on the wing margin, *dishevelled*, a gene known to function in the Wingless pathway, acts to inhibit signaling by Notch. Experiments in vitro suggest that this interaction is direct because Dishevelled interacts physically with the carboxyl terminus of Notch. This interaction provides a molecular mechanism for the inhibitory cross talk observed between the pathways.

were cooler than one would expect. D'Hondt and Arthur (p. 1838) analyzed oxygen isotopes from planktonic foraminifera in Late Cretaceous sediments from a wide range of latitudes and found that the tropical oceans were cool. There was also a small latitudinal sea surface temperature gradient, indicative of enhanced poleward heat transport but not of a greenhouse-controlled climate.

■

What makes a queen

The differentiation of queen and worker castes in honeybee colonies is regulated by differential pheromone production. Plettner *et al.* (p. 1851; see the Perspective by Robinson, p. 1824) used deuterated enzyme substrates to work out the biosynthetic pathways for these pheromones. Various isomeric compounds that perform different functions in different castes are related, and slight changes in the functioning enzymes produce the caste-specific blends.

■

Magnetic transfer

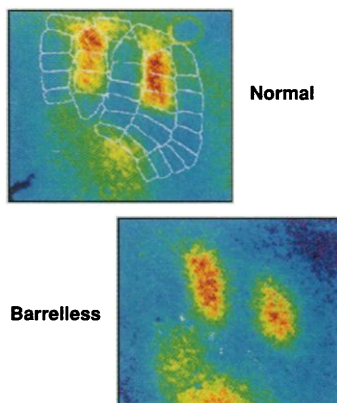
Higher contrast can be obtained in magnetic resonance imaging (MRI) if the nuclei being studied have a greater fraction of

spins aligned "up" versus "down." Recently, optical pumping methods have been used to align spins in the noble gases, such as ^3He and ^{129}Xe . Navon *et al.* (p. 1848; see the news story by Service, p. 1810) now show that when spin-polarized ^{129}Xe is introduced into solution, it can efficiently transfer magnetization to solvent protons through the nuclear Overhauser effect. This effect may find use in conventional MRI and in protein and surface nuclear magnetic resonance.

■

Not quite connected

Nose whiskers are an important part of the mouse sensory sys-



tem. Each whisker projects through the thalamus into barrel structures in the cortex,

which respond primarily to their "center" whisker but can also integrate signals from neighboring barrels. Welker *et al.* (p. 1864) have identified a naturally occurring mutant in which the barreloid structures of the thalamus are altered and individual cortical barrels are absent. Although sensory processing still occurs and overall input topology is preserved, spatial and temporal discrimination between individual whisker responses is reduced.

■

Nerve and muscle

Formation of the neuromuscular junction occurs when the growth cone of a developing neuron contacts its muscle target and forms a synapse. Kopczyński *et al.* (p. 1867; see the news story by Roush, p. 1807) identified a gene (*late bloomer*, or *lbl*) in *Drosophila* that encodes a member of the tetraspanin family of cell surface proteins. In embryos with mutant *lbl* genes, synapse formation is delayed and other neurons form abnormal connections to the muscle cell targets.

■

Linking cell growth and elongation factors

One form of myeloid leukemia in humans is associated with a chromosomal translocation that has a breakpoint in the *ELL* gene, but the function of *ELL* has been unknown. Shilatifard *et al.* (p. 1873) found that *ELL* encodes a transcriptional elongation factor that increases the catalytic rate of RNA polymerase II transcription by suppressing the transient pausing of polymerase. Recently, the product of the von Hippel-Lindau tumor suppressor gene was also found to be an elongation factor.

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As a result of these Apple innovations, ordinary people can sit down at all kinds of PCs and actually get some work done. Of course, if they sit down at a Macintosh, they can build 3-D graphics. Use virtual reality in very real ways. Videoconference across continents. Collaborate with colleagues on the far side of the corporate campus. Build interactive sites on the World Wide Web. And more. That's the Mac advantage.



More than a few of the things that seem standard on a personal computer today were pioneered by Apple.

People do know the difference.

Today, 56 million people do their work the Macintosh way. Some in school. Some at home. And, when you look at the numbers from recent studies, quite a few in business. We command a 47% share of the U.S. commercial publishing market. And 76.2% of the color pre-press market. And though our dominance in graphics-related businesses may not

shock you, consider this: we have a 50% share of the chemical, pharmaceutical, biotechnology, scientific and engineering computing markets.

And then, there's the fact that Macintosh brand loyalty is the highest of any PC in the world: 90% of Macintosh customers buy a Mac the next time around. Which leads people like Andrew Laham, MIS Director at the law firm Fleming, Hovenkamp & Grayson, to say, *"There would be a major crisis if we had to do without Macs. In fact, there would be an open revolt."* Indeed, if the mail we've received lately is any indication, more than a few CFOs out there would revolt, too, if their companies didn't use Macintosh computers.

"NASA saved \$800,000 a year on maintenance alone when we replaced their legacy system with a Macintosh system," says Steve Monteith, a member of the Research Triangle Institute TechTracS Team.

And if you replace a Windows system with a Mac? According to a recent study by the Gartner Group, technical support costs for Macintosh tend to be 25% lower than support costs for Windows.** Even *PC World* magazine ranked Apple as one of the best for reliability and service among all makers of personal computers.

See the future. Turn on a Mac.

As they say, you can't simply rest on your laurels. So what's next? Let's start with Copland, our upcoming operating system.† Copland won't just change the look of the Macintosh desktop; it will incorporate an entirely new technology called OpenDoc* that will change the way you think about computers. (Sound like hype? Check out *InfoWorld*—they named OpenDoc the winner of the 1995 Landmark Technology Award.)

And then there are the 53 new software patents we were awarded in 1995, patents on everything from wireless communication, power management and manufacturing systems to data encoding, data compression and encryption. That's more than enough innovation to bring another generation, or three, of intelligent business tools to market.

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*The Power Macintosh® 6100/66 DOS Compatible runs the Mac OS and Windows 3.1.† To receive a copy of the Gartner Group study "Technical Support Costs in Dual-Platform Computing Environments," call 1 800 232-9335. † Don't look for a product named Copland at your local reseller. It's only a code name for our soon-to-be-released operating system. Substantiation for claims made in this ad on file with Apple Computer, Inc. ©1996 Apple Computer, Inc. All rights reserved. Apple, the Apple logo, Macintosh, OpenDoc and Power Macintosh are registered trademarks of Apple Computer, Inc. Mac is a trademark of Apple Computer, Inc. PowerPC is a trademark of International Business Machines Corporation, used under license therefrom. All Macintosh computers are designed to be accessible to individuals with disability. To learn more (U.S. only), call 800-600-7808 or TTY 800-755-0601.

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1. *Standard & Poor's Insurance Rating Analysis*, 1995; Lipper Analytical Services, Inc., *Lipper-Directors' Analytical Data*, 1995 (Quarterly).

2. Source: Morningstar, *Variable Annuities/Life* 1/30/96. 3. Of the 2,575 variable annuity funds tracked by Morningstar, the average fund had annual expenses of 1.27% plus an insurance expense of 1.24%. Source: Morningstar, Inc., for periods ending January 31, 1996. 4. *Standard & Poor's Insurance Rating Analysis*, 1995.

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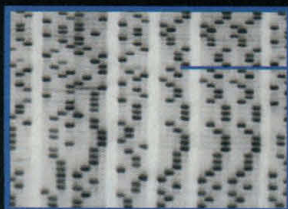
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Transgenic Models of Metabolic Disease

C. Ronald Kahn, Joslin Diabetes Center
E.M. Rubin, University of California

Intracellular Membrane Trafficking

Jennifer Lippincott-Schwartz, National Institute of Child Health and Human Development

Ion Transport and Disease***

William Harris, Children's Hospital, Boston
Mark T. Keating, University of Utah

Health Outcomes Research

Allan S. Detsky, University of Toronto

Regulation of Apoptosis: Cellular, Molecular and Genetic Factors

John D. Mountz, University of Alabama at Birmingham

Translational Research in Dermatology*

Juoni Uitto, Thomas Jefferson Medical College

Delivering Information to Clinicians in the Era of National Networking***

Edward H. Shortliffe, Stanford University School of Medicine
David Lipman, National Library of Medicine

Developmental Biology: Organogenesis***

Jeffrey A. Whitsett, Children's Hospital Medical Center, Cincinnati
Jeffrey I. Gordon, Washington University School of Medicine

The New Biology of Obesity

Jeffrey S. Flier, Harvard Medical School

Emerging Infections***

Ruth Berkelman, National Center for Infectious Diseases
Monica M. Farley, Emory University School of Medicine

Training in Subspecialty Medicine: Current Status and Public Policy

Eric G. Neilson, University of Pennsylvania
Robert J. Mayer, Harvard Medical School

Abstract Presentations

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James B. Dale, University of Tennessee School of Medicine

Cardiovascular

Christine Seidman, Harvard Medical School

Hematology

Dorothea Zucker-Franklin, New York University

Oncology

George Bosi, Memorial Sloan Kettering Cancer Center

Clinical Epidemiology/Health Care Research**

Pamela G. Williams-Russo, Cornell University Medical Center

Pulmonary/Critical Care

Jeffrey M. Drazen, Harvard Medical School

Gastroenterology/Hepatology/Nutrition

Tadataka Yamada, University of Michigan School of Medicine

Immunology/Allergy/Rheumatology

William J. Koopman, University of Alabama at Birmingham

Gerontology/Aging

Mark A. Suptano, University of Michigan School of Medicine

Endocrinology/Metabolism

Leslie DeGroot, University of Chicago Medical Center

Renal/Hypertension

Barry M. Brenner, Harvard Medical School

Inflammation

William M. Nauseef, University of Iowa

Regulation of Gene Expression

Herbert H. Samuels, New York University

Physiology

J. Chris Gillin, University of California, San Diego

Cytokines/Growth Factors

Derek LeRoith, National Institute of Diabetes and Digestive and Kidney Diseases

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Bibliography Software for Networks

Reference Manager for Windows Version 7 is now available in a Network Edition. The new edition allows any number of licensed user accounts to simultaneously access a database in the bibliographic management program. Multiple users can retrieve references and prepare bibliographies from the same database and each user can maintain individual preferences in separate settings files. Only one user at a time can edit a database. Other new features include the ability to print indexed bibliographies grouped by authors, key words, periodicals, or publication dates, and the ability to create a new reference based on all or part of an existing reference. **Research Information Systems. Circle 145.**

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membrane. Single or assortment packs of pre-cut membrane are available. In addition, mesh or tubular feed spacers can be loaded in the cell body with membrane and permeate carrier to simulate the flow characteristics of a wide variety of commercially available spiral-wound membrane elements. **Osmonics. Circle 146.**

Literature

Integrated Separation Systems 1996 Catalog features an expanded line of protein electrophoresis and molecular biology products. New types of precast polyacrylamide gels in single and gradient percentages are now available to suit a variety of protein and nucleic acid separations. **Integrated Separation Systems. Circle 147.**

Spectrum 2000 FT-IR Spectrometer is a brochure on a modular system that is the next step in Fourier transform infrared (FT-IR) spectroscopy performance and usability. Advances include new optical and sampling features; control enhancements; and faster ways to generate, display, and interpret spectra. **Perkin-Elmer. Circle 148.**

The World of Immunological Excellence: 1996/7 Product Guide is a catalog detailing monoclonal antibodies to human, rat, and mouse antigens; cytokines and growth factors; cytoskeletal, extracellular, and other cell components; hormones; antibodies for flow cytometry; reagents for immunochemistry, sera, and blood products; and more. **Harlan Bioproducts for Science and Serotec. Circle 149.**

Selecting the Right Shaker for Your Laboratory is a 16-page booklet covering topics ranging from design features that minimize vibrations to the need for shielded wiring, electronic enclosures, and catch basins to protect against corrosive spills. **New Brunswick Scientific. Circle 150.**

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Wong, X. et al. Matrix metalloproteinase inhibitor BB-94 inhibits human colon tumor growth and spread in a patient like ortho-topic model in nude mice. *Cancer Res.* 54, 4726-28 1994.
Hofmann, R. Orthotopic is orthotopic: why orthotopic transplant metastatic models are different from all other models? *J. Cellul. Biochem.* 56, 1-4, 1994.

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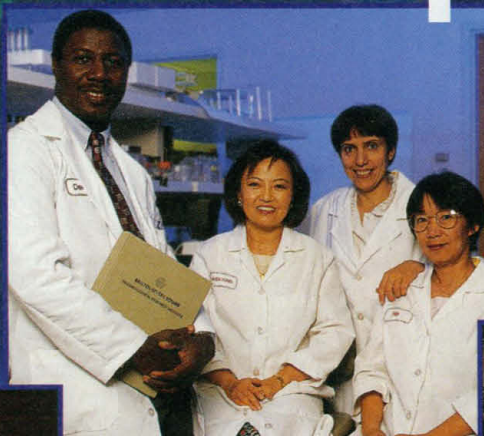
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RESEARCH INVESTIGATOR. Lead a group of 10 individuals responsible for the production of recombinant proteins at up to 2-10 grams per batch to be released to discovery scientists for animal studies; production of cell culture supernatant and fermentation cell paste to release to process design scientists for purification development; operation of bank of small scale cell culture reactors, small cell fermentators and of bank of BIOCAD units as specified by process design scientists to support design studies. Minimum M.S. in Chemical Engineering, Biochemical Engineering or Biotechnology with 5 yrs. or greater experience in biopharmaceutical manufacturing setting and at least 2 yrs. of leading a mid-sized technical staff. Expertise in cell culture reactor operation, both at bench scale and at scales up to 100L; expertise in fermentation operation. Ref. #38.

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