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Double-Stranded, Site-Directed Mutagenesis Kit

- 70-90% mutagenesis efficiency
- No M13 or single-stranded rescue
- EndA⁻ XLmutS strain improves reproducibility of mutagenesis
- Works with any plasmid with a unique nonessential restriction site

The Chameleon¹³ Double-Stranded, Site-Directed Mutagenesis Kit can be used with a single mutagenic primer to generate point mutations, insertions and deletions, and with three mutagenic primers at once to generate triple mutations. This kit is a complete system that includes XLmutS and XL1-Blue competent cells. • Catalog #200509 • Catalog #200508 (for Neo^r vectors)

LXSIIC^{im}

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- Avoids use of mutagens and carcinogens
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Epicurian Coli XL1-Red Competent Cells are suitable for generating random mutations within a gene that has no selectable or screenable phenotype. Overnight growth in the XL1-Red mutator strain results in ~1 base change per 2000 nucleotides. • Catalog #200129

+ Purchase of this product is accompanied by a license to use it in the polymerase chain reaction (PCR) process in conjunction with an authorized thermal cycler. This product is sold under licensing ar Molecular Systems, Inc., F. Hoffmann-La Roche Ltd. and The Perkin Elmer Corporation. * Patent pending

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Mismatch Detect[™] Kit

Non-Rauro SSCP Alternative

- High mutation detection efficiency
- Rapid turnaround time
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- No radioisotopes or silver staining required
- No organic extraction, precipitation, centrifugation or blotting steps
- No secondary detection steps required
- No specialized equipment or reagents required

The new Mismatch DetectTM Point Mutation Screening Kit provides a simple, rapid method for detecting dispersed point mutations. Research efforts at Ambion have resulted in a substantially improved RNase cleavage-based assay in a non-radioisotopic format. Using the Non-Isotopic RNase Cleavage Assay (NIRCATM), target regions of 500–1000 bp can be screened in a single step using an efficient, one-day procedure, including data analysis.

In the NIRCA[™] method, the substrates for RNase digestion are RNA/RNA duplexes made by hybridizing complementary wild type and experimental transcripts. The transcripts are produced by *in vitro* transcription of PCR^{*} products containing opposable T7 and SP6 phage promoters. (PCR primers which contain the SP6 and T7 promoters are used to generate such PCR products.) Wild type and test transcripts are hybridized to form double-stranded RNA targets which are treated with RNase. The cleavage products are then separated on agarose gels containing ethidium bromide and assessed under UV light. Experimental samples are scored as positive for mutations if they contain cleavage products not seen in the wild type control.

The NIRCATM method has a comparable sensitivity to SSCP, but the method allows larger fragments to be analyzed, results are available immediately because no autoradiography or secondary detection steps are needed, and the electrophoresis step is complete in less that an hour with the convenience of agarose gels. Also, the size of the cleavage products provides an indication of the location of the mutation.

Also available are p53 Screening Modules which, when used with the Mismatch Detect[™] Kit, allow the human p53 tumor suppressor gene to be screened for point mutations using either cDNA or genomic DNA strategies. The modules contain a complete set of primers and control DNAs.



*The Polymerase Chain Reaction (PCR) is covered by patents owned by Hoffman-La Roche. Use of the PCR process requires a license which may be obtained by purchase and use of authorized reagents or by otherwise negotiating a license.

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CHINE RATIONAL





1



362 Autoimmune attack may cause rare epilepsy



436 A snag in the zipper

NEWS & COMMENT		PERSPECTIV
A Molecular Approach to Cancer Risk	356	Pas de Deux or N
Report Advocates "Value-Added" Ph.D.	358	L. H. Philipson
Nuclear Waste: Academy Fends Off Charges of Bias	358	Adaptive Mutation in the Garden?
In the U.S., Engineers Oust Old Regime	359	
NASA, Academy to Re-Examine EOS	360	The Silica Balan
Germans Buy Nature's Publisher	360	A Reestimate P. Tréguer, D. N
NASA Panel Would Drop Ames Lab	361	J. DeMaster, A.
AAAS Colloquium: Partisan Politics	361	RESEARCH
RESEARCH NEWS		Mercury-199 NM Site in MerR and L. M. Utschig, J
Antibodies Linked to Rare Epilepsy	362	
U.S. Climate Tilts Toward the Greenhouse	363	Continent-Ocear
Anthropologists Overturn Old Ideas About New Developments	364	in the Mantle Ba A. M. Forte, A.
Dwarfs and Dim Galaxies Mark Limits of Knowledge	366	Selectivity of En Bivalve Extinctio D. Jablonski and
Researchers Find Molecules That Muzzle Killer Cells	367	Seismic Images of Beneath the East
New Hope Against Blindness AIDS Drug: Experiencing Local Delays	368 369	17°05′ and 17°3 J. C. Mutter, S Buhl, R. S. De A. J. Harding
DI	EPAR	MENTS
THIS WEEK IN SCIENCE	345	RANDOM SAMPI

1

	PERSPECTIVES
56	Pas de Deux or More: The Sulfonylurea 7372 Receptor and K ⁺ Channels
58	L. H. Philipson and D. F. Steiner
58	Adaptive Mutation: Who's Really Z 373 in the Garden?
59	
50	The Silica Balance in the World Ocean: 375
50	A Reestimate P. Tréguer, D. M. Nelson, A. J. Van Bennekom, D.
61	J. DeMaster, A. Leynaert, B. Quéguiner
51	RESEARCH ARTICLE
	Mercury-199 NMR of the Metal Receptor 380 Site in MerR and Its Protein-DNA Complex L. M. Utschig, J. W. Bryson, T. V. O'Halloran
52	REPORTS
53 54	Continent-Ocean Chemical Heterogeneity 386 in the Mantle Based on Seismic Tomography
66	Selectivity of End-Cretaceous Marine 389 Bivalve Extinctions D. Jablonski and D. M. Raup
67 68 69	Seismic Images of Active Magma Systems 391 Beneath the East Pacific Rise Between 17°05' and 17°35'S J. C. Mutter, S. M. Carbotte, W. Su, L. Xu, P. Buhl, R. S. Detrick, G. M. Kent, J. A. Orcutt, A. J. Harding
ARTI	MENTS
45	RANDOM SAMPLES 371
47	BOOK REVIEWS 449 Microtubules, reviewed by P. Wadsworth • Other Books of Interset • Vignatus • Backs Province
49 55	PRODUCTS & MATERIALS 456
45 47 49 55	RANDOM SAMPLES37BOOK REVIEWS44Microtubules, reviewed by P. Wadsworth • Oth Books of Interest • Vignettes • Books ReceivedPRODUCTS & MATERIALS45

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COVER

Space-filling model of the molecular-based magnetic material Cs_Mn"[V"(CN)_], which orders ferrimagnetically at 125 kelvin in an external field of 25 gauss. The atoms are described by their van der Waals radii; manganese(II) centers are pink, vanadium(II) centers are red, carbon centers are gray, and nitrogen centers

are blue-green. The cesium cations, which occupy the interiors of every cube, have been omitted. See page 397. [Image: K. Llewellyn, Beckman Institute Visualization Laboratory, and M. Rosenblatt and D. White, University of Illinois at Urbana-Champaign]

 Spontaneous Magnetization at 230 K W. R. Entley and G. S. Girolami Orientational and Magnetic Ordering 400 of Buckyballs in TDAE-C₆₀ D. Mihailovic, D. Arcon, P. Venturini, R. Blinc, A. Omerzu, P. Cevc Superantigen-Dependent, 403 Cell-Mediated Cytotoxicity Inhibited by MHC Class I Receptors on T Lymphocytes J. H. Phillips, J. E. Gumperz, P. Parham, L. L. Lanier 	Mutations in the Sulfonylurea426Receptor Gene in Familial PersistentHyperinsulinemic Hypoglycemia of InfancyHyperinsulinemic Hypoglycemia of InfancyP. M. Thomas, G. J. Cote, N. Wohllk, B. Haddad,P. M. Thomas, G. J. Cote, N. Wohllk, B. Haddad,P. M. Mathew, W. Rabl, L. Aguilar-Bryan, R. F.Gagel, J. BryanInduction of Apoptosis in Uninfected429Lymphocytes by HIV-1 Tat ProteinC. J. Li, D. J. Friedman, C. Wang, V. Metelev,A. B. PardeeFGF Binding and FGF Receptor432
Superantigen-Dependent, du 403 Cell-Mediated Cytotoxicity Inhibited by MHC Class I Receptors on T Lymphocytes J. H. Phillips, J. E. Gumperz, P. Parham, L. L. Lanier	Induction of Apoptosis in Uninfected429Lymphocytes by HIV-1 Tat ProteinC. J. Li, D. J. Friedman, C. Wang, V. Metelev,A. B. PardeeFGF Binding and FGF Receptor432
Lanier	FGF Binding and FGF Recentor 432
Cloning of Immunoglobulin- Superfamily Members Associated with HLA-C and HLA-B Recognition by Human Natural Killer Cells M. Colonna and J. Samaridis405The Role of Igβ in Precursor B Cell Transition and Allelic Exclusion408	Activation by Synthetic Heparan-Derived Di- and Trisaccharides D. M. Ornitz, A. B. Herr, M. Nilsson, J. Westman, CM. Svahn, G. Waksman Measurement of Interhelical Electrostatic Interactions in the GCN4 Leucine Zipper K. J. Lumb and P. S. Kim
 F. Papavasiliou, Z. Misulovin, H. Suh, M. C. Nussenzweig FAP-1: A Protein Tyrosine Phosphatase 411 That Associates with Fas T. Sato, S. Irie, S. Kitada, J. C. Reed 	Nicotinic Receptor Binding Site Probed 439 with Unnatural Amino Acid Incorporation in Intact Cells M. W. Nowak, P. C. Kearney, J. R. Sampson, M. E. Saks, C. G. Labarca, S. K. Silverman, W. Zhong, I. Thorson, I. N. Abelson, N. Davidson et al.
Initiation of Protein Synthesis by the Eukaryotic Translational Apparatus on Circular RNAs Cy. Chen and P. Sarnow415Adaptive Mutation in Escherichia coli:✓Alaptive Mutation in Escherichia coli:✓	TECHNICAL COMMENTS Patterns of Human Growth 442 C. Heinrichs, P. J. Munson, D. R. Counts, G. B. Cutler Jr., J. Baron; M. Lampl, N. Cameron, J. D. Veldhuis, M. L. Johnson Veldhuis, M. L. Johnson
A Role for Conjugation J. P. Radicella, P. U. Park, M. S. Fox Evidence That F Plasmid Transfer Replication Underlies Apparent Adaptive Mutation T. Galitski and J. R. Roth	Variability Among Human Umbilical 447 Vein Endothelial Cultures C. A. Watson, L. Camera-Benson, R. Palmer- Crocker, J. S. Pober; A. E. Koch, P. J. Polverini, S. L. Kunkel, L. A. Harlow, L. A. DiPietro, V. M. Elner, S. G. Elner, R. M. Strieter

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386

Continental versus

oceanic mantle

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THIS WEEK IN SCIENCE

edited by DAVID LINDLEY

Silicic cycling

Silicon passes through the world's oceans in a geologicalbiological cycle. Reviewing global sinks and sources, Tréguer et al. (p. 375) find that almost 200 million tons of silicon enter the oceans each year, mainly as silicic acid weathered from rocks and carried by rivers. Dissolved silica is taken up by diatoms, silicoflagellates, and radiolarians, and a few percent of their skeletal material eventually ends up as sediment on the seafloor, whence it returns to the geological half of the cycle.

Trace element

The abundant isotope mercury-199 can be used in nuclear magnetic resonance, but it had been thought that its linewidths would be too broad to provide useful spectra of metal recognition sites in proteins. Utschig et al. (p. 380) show, however, that one- and two-dimensional ¹⁹⁹Hg spectra can resolve structural aspects of mercury coordination in its main receptor, the MerR protein, in both its uncomplexed and DNA-bound forms. Mercury substitution would allow other metalloproteins, such as zinc finger transcription factors and iron and copper enzymes, to be studied by this method.

Bucking the trend

Seismic imaging by Mutter *et al.* (p. 391) of the East Pacific Rise, a fast-spreading ocean ridge, shows that the underlying magma chamber is broadest where it is shallowest, presumably indicative of a faster spreading rate where there is stronger upwelling. In one spot, however, where observations from a submersible have revealed active

Natural born inhibitors

Natural killer (NK) cells have some receptors that activate cytotoxic activity and others, which bind to major histocompatibility (MHC) class I molecules, that inhibit cytotoxicity. Colonna and Samaridis (p. 405) found four related complementary DNAs (cDNAs) in NK cells that encode transmembrane proteins of the immunoglobulin superfamily. Correlation between these proteins and the inhibition of NK cells by different class I molecules suggests that the cDNAs might encode the corresponding receptors. The potential importance of MHC-reactive inhibitory receptors is demonstrated by Phillips *et al.* (p. 403), who have identified, on TCR $\alpha\beta^+$ cytotoxic T cell clones, a receptor that inhibits cytotoxicity against targets cells coated with a superantigen. Again, the target cells must also carry certain MHC molecules. How these inhibitory signals are collated with the activating ones will become a major focus of research (see also news by Barinaga, p. 367).



volcanism, the linear inverse trend between depth and width fails to hold, suggesting that departures from the general trend are diagnostic of current magmatic activity.

Spinning and rolling

Organically doped fullerenes have interesting and potentially useful magnetic properties, and the rotational freedom of each buckyball leads to unusual orientational ordering effects. Mihailovic et al. (p. 400) have uncovered a connection between the two phenomena: spin-ordering in the low temperature phase of C_{60} doped with tetrakis(dimethylamino)ethylene seems to be directly linked to the orientational ordering, and the link perhaps constitutes the microscopic mechanism that causes spin glass behavior of the magnetic material.

Lactose tolerance

The neo-Darwinian premise that mutations occur spontaneously without regard to fitness has been seriously challenged by the phenomenon of adaptive or directed mutation. Two reports (Radicella et al., p. 418; Galitski and Roth, p. 421; see also Perspective by Shapiro, p. 373) examine an adaptive mutation that leads to reversion of a lactose-utilization deficiency in a strain of Escherichia coli when lactose is the only source of carbon. The RecA and RecBCD homologous recombination functions are known to be necessary for adaptive mutation, and both reports now show that functions associated with plasmid transfer are also involved. The results of Radicella et al. suggest that the act of transfer (conjugation) is necessary.

SUR feat

The molecular target of sulfonylureas, which release insulin from cells of the pancreas and are used to treat patients with non-insulin-dependent diabetes mellitus, has now been identified. Aguilar-Bryan *et al.* (p. 423) have cloned the sulfonylurea receptor (SUR) from hamster, and find that it belongs to a family of proteins that contain adenosine triphosphate (ATP)-binding cassettes. Thomas *et al.* (p. 426) provide evidence that mutations in the SUR cause inappropriate insulin secretion and hypoglycemia in a disease known as familial persistent hyperinsulinemic hypoglycemia. Philipson and Steiner discuss these findings in a Perspective (p. 372).

-

Tagged by Tat

Infection by human immunodeficiency virus is accompanied by a progressive depletion of CD4⁺ T cells, leading to deterioration of immune function. Loss of these T cells is thought to occur through apoptosis, or programmed cell death, but the precise role of the virus in this process is unknown. Cell culture studies by Li et al. (p. 429) show that the virally encoded Tat protein, known as a key regulator of viral gene expression, may be a molecular trigger for T cell apoptosis. Tat-induced apoptosis shares features with other forms of apoptosis, including an association with activation of cyclin-dependent kinases.

Bad connection

Some transcription factors bind to DNA as homo- or heterodimers by means of a dimerization region constructed of coiled helices. It has been thought, on the basis of crystal structures, that electrostatic interactions between side chains of opposite charge favor the formation of dimers, but Lumb and Kim (p. 436) demonstrate that these electrostatic interactions are neutral or actually unfavorable for proteins in solution.



Did she just say 'Big Bang'or 'Big Bird'?

For a provocative interpretation of the language of science, tune into **The Nobel Legacy** on PBS. I n the day-to-day world, most people don't seem to talk much about science – not to their children nor to each other. Our world is powerfully enriched by science and technology. Yet, much of the public is simply unaware of science's everyday relevance. This is why Baxter is underwriting *The Nobel Legacy*, a three-part PBS science series. Increasingly, the public is called upon to make important decisions about science, on issues ranging from healthcare delivery to supercollider funding. To make sound decisions, the public needs to be better informed and scientifically aware.

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