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THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

Patently obvious?

Patent applications filed by the National Institutes of Health (NIH) for thousands of partial complementary DNA sequences of unknown function have led to a broad discussion of whether this "interim policy" should be pursued; three articles this week explore this issue. Eisenberg (p. 903) presents an overview of the impact of NIH taking a lead role on patent protection rather than private industry and how this may affect product development. Adler (p. 908) discusses the advantages of filing the gene patent and puts this issue in the historical perspective of patent law. Kiley (p. 915) argues that these patent applications do not meet the original intention of the usefulness criterion and proposes a number of corrective legal measures.



Much like the halos around streetlamps on a foggy night, rings of scattered light occur around stars because of dust grains in the interstellar medium. Predehl et al. (p. 935) report measurements of interstellar dust halos at x-ray wavelengths taken with the Röentgen satellite. The bright x-ray source GX 5-1, positioned in the bulge of the Milky Way, was observed as the moon passed between it and the x-ray detectors. This lunar occultation revealed extended emission as GX 5-1 was blocked by the moon. From the details of the scattered radiation, the authors can deduce the dust grain characteristics of these halos.

Gamma rays and pulsars

More than a decade ago, astronomers discovered an unusual class of objects that emit bursts of gamma rays; the nature of these "bursters" is still hotly debated. Eichler and Silk (p. 937) propose that these gammaray sources are related to another astronomical puzzle, a population of pulsars (pulsating neutron stars) outside but mov-

Hydrogen bonding and antigen binding

The major histocompatibility complex (MHC) molecules recognize and present the foreign peptides to the cells that mount the immune system's attack. Two studies address how class I MHC molecules recognize foreign peptides. Fremont et al. (p. 919) present x-ray structures of two complexes of the mouse MHC class I molecule H-2K^b with peptides, one with an eight-residue viral peptide and the other with a nine-residue peptide. Analysis of these structures by Matsumura et al. (p. 927) suggests that deep, highly conserved pockets at the ends of the peptide-binding groove form hydrogen bonds with the peptide that dictate its orientation. A deep polymorphic pocket in the middle of the groove plays a major role in binding and specificity. In a separate study, Latrone et al. (p. 964) studied the effect of mutating conserved residues in a human MHC class I molecule of known structure, HLA-A2, on presentation of influenza virus peptides to T cells. Mutations that appear to disrupt hydrogen bonding in the A pocket, which binds the amino terminal of the peptides, greatly reduced recognition (see news story by Barinaga, p. 880).

ing toward the Milky Way with high velocity. They suggest that the pulsars are formed by the coalescence of compact stellar remnants that may form part of the dark matter thought to be present in galaxies. The mysterious gamma-ray bursts might be produced when these coalesced neutron stars release some of their stored energy.

8

Greener chemistry

Fluoropolymers and chlorofluoropolymers, such as Teflon, are usually synthesized in chlorofluorocarbon (CFC) solvents (freons) to maintain solubility. DeSimone et al. (p. 945) synthesized these polymers through free-radical chemistry using supercritical CO_2 as the solvent. The advantage of the very high solubility that many compounds have in supercritical CO_2 has normally been exploited in chromatography. The extension to synthesis may allow a reduction in the use of CFCs, which harm the ozone laver when released to the atmosphere.

Stark results

A direct measure of the electric field at the amino terminus of an α -helical peptide has been made by Lockhart and Kim (p. 947). They took advantage of the Stark effect; an electric field shifts the absorption spectrum of a covalently attached probe molecule between its ground and excited states. The field at the amino terminus of the peptide was about an order of magnitude greater than what would be expected from the dielectric properties of bulk water. The electric field at the amino terminus did not increase with peptide length.

A well-timed event

The 180-kilometer-diameter Chicxulub structure buried beneath sediments on the Yucatán Peninsula has emerged as the most likely candidate for the Cretaceous-Tertiary (K-T) boundary impact site. Its age, however, has been poorly constrained, and thus the identification has been uncertain. Swisher et al. (p. 954) used ⁴⁰Ar/ ³⁹Ar incremental heating to date impact melt rock obtained from drill cores into the structure and to perform an intralaboratory comparison of tektites (glassy droplets likely produced by an impact) from nearby K-T boundary sites. The best ages obtained, 65.0 million years, are indistinguishable from ages for the tektites. Kerr (p. 878) discusses the age and the 15-year search for the impact site.

Cultural advance

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Molecular analysis of the life cycle of viruses requires the propagation of viruses in tissue culture rather than in animals: Meyers et al. (p. 971) have developed an in vitro system for the production of human papillomaviruses (HPVs), which are associated with a number of different anogenital tumors. Organotypic (or raft) cell cultures, which re-create aspects of the cellular environment, have not been able to duplicate all of the stages of epithelial cell differentiation linked to virion production. The HPV's life cycle proceeds through the formation of keratinocytes, the epidermal skin cells that contain fibrous proteins such as keratin. Addition of 12-O-tetradecanoyl phorbol-13-acetate to the culture induced morphological differentiation and expression of keratin 10, and also induced virion production.



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■ CircumVent[™] DNA Sequencing Kit



Tube worms at 2010 meters around a hydrothermal vent where the native organism containing Deep Vent_R["] DNA Polymerase was isolated.</sup>

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Vent[™] DNA Polymerase

High fidelity thermostable DNA polymerase with fidelity levels up to 20 fold higher than Tag DNA polymerase due to a $3' \rightarrow 5$ proofreading exonuclease activity.

- Discovered and cloned at NEB
- High fidelity
- Primer extensions up to 13 Kb
- Stable up to100°C
- Half life of 6.7 hours at 95°C

Deep Vent[™] DNA Polymerase NEB's second thermostable DNA polymerase with a 3' \rightarrow 5' proofreading exonuclease activity. Originally isolated from an ocean submarine thermal vent at 2010 meters, Deep Vent, ** DNA Polymerase is even more thermostable than Vent_R[™] DNA polymerase at temperatures of 95°C to 100°C.

- Discovered and cloned at NEB
- Superior stability up to 100°C
- Half life of 23 hours at 95°C

These products do not carry a license to perform the Polymerase Chain Reaction (PCR) process. PCR is covered by U.S. patents issued to the Cetus Corporation.



Reversion frequency reflects error rate in DNA synthesis and was measured by the opal codon reversion assay. Kunkel et al. (1987) Proc. Natl. Acad. Sci. USA 84, 4865-4869. Mattila P. et al. (1991) Nucleic Acids Res. 19, 4967-4973.

Vent[™] (exo[−]) DNA Polymerase Genetically modified form (exo-) of the cloned Vent_R[™] DNA polymerase with fidelity levels up to 2-fold higher than Taq DNA polymerase. Preferred form for hightemperature dideoxy DNA sequencing and thermal cycle DNA sequencing.

- Discovered and cloned at NEB
- High temperature dideoxy sequencing
 Primer extensions up to 13 Kb
- Stable up to 100°C

CircumVent[™] DNA Sequencing Kit The only thermal cycle sequencing kit that uses the Vent_R^{∞} (exo⁻) DNA polymerase.

- Easier than conventional methods
- Fast no need to collapse double stranded plasmids, eliminates centrifugation steps and independent priming steps. You save valuable research time.
- Requires only nanograms of template (only femtomoles when using ³²P end labelled primers)
- Allows direct sequencing from colonies, plaques, cosmids, or DNA fragments isolated from agarose gels
- Diminished secondary structure effects due to high temperature reaction
- Compatible with radiolabel or chemiluminescent detection

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