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The lamina propria of the rat duodenum, showing immune cells that unexpectedly express targets for anti-ulcer drugs. Plasmocytes that produce immunoglobulin G are shown in green, and cells that express M1 acetylcholine receptors are red; scattered immunoglobulin G-producing cells that also express M1 acetylcholine receptors are shown in yellow. See page 1662 and the News report on page 1579. [Photo: Ricardo Dreyfuss]


Production and Initial Characterization of Bionites: Materials Formed on a Bacterial Backbone N. H. Mendelson

Electrical Resistivity and Stoichiometry of C_{60}, C_{70}, and Sr,C_{60} Films R. C. Haddon, G. P. Kochanski, A. F. Hebard, A. T. Fiori, R. C. Morris

Charge Donation by Calcium into the t_{1g} Band of C_{60} G. K. Wertheim, D. N. E. Buchanan, J. E. Rowe

Electronic, Magnetic, and Geometric Structure of Metallo-Carbohedrenes B. V. Reddy, S. N. Khanna, P. Jena

Temperature and Size Variabilities of the Western Pacific Warm Pool X.-H. Yan, C.-R. Ho, Q. Zheng, V. Klemas

EMF, an Arabidopsis Gene Required for Vegetative Shoot Development Z. R. Sung, A. Belachew, B. Shunong, R. Bertrand-Garcia

A Homoeotic Mutant of Arabidopsis thaliana with Leafy Cotyledons D. W. Meinke


Expression of an Inward-Rectifying Potassium Channel by the Arabidopsis KAT1 cDNA D. P. Schachtman, J. I. Schroeder, W. J. Lucas, J. A. Anderson, R. F. Gaber

Thermal Stability Comparison of Purified Empty and Peptide-Filled Forms of a Class I HLA Molecule M. L. Fahnestock, I. Tamir, L. Narhi, P. J. Bjorkman

Localization of Targets for Anti-Ulcer Drugs in Cells of the Immune System E. Meze and M. Palkovits


Behavioral Lifetime of Human Auditory Sensory Memory Predicted by Physiological Measures Z.-L. Lu, S. J. Williamson, L. Kaufman

Structure of Src homology 3 (SH3) domain

Indicates accompanying feature

Communication

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Superconductivity Revisited

In 1987 the great excitement about high-temperature superconductivity was accompanied by a hype about applications. In hundreds of laboratories specimens of YBa2Cu3O7-x were synthesized and their superconductivity was confirmed. However, the solids were brittle and performed poorly in the presence of external magnetic fields. Practical applications seemed far distant. But since then substantial progress has quietly been made. Additional superconductors have been discovered. Experts state that advances in synthesis and processing of high-temperature superconductors (HTSCs) now make it justifiable to consider development of prototype devices and products.

Since 1987 thousands of compounds have been prepared and examined. More than 75 of these were found to be superconducting at temperatures greater than 21 K. These 75 belong to three general compound types: cuprates, bismuthates, and fullerenes. Of these three the cuprates are of special interest.

The limiting high temperatures for superconductivity (Tc) are important because of costs of refrigeration. A Tc of at least 77 K (boiling point of nitrogen) is desirable. Of the many cuprates having a Tc greater than 77 K, four have drawn the most attention. These are YBa2Cu3O7-x, Bi2Sr2Ca2Cu3O10, Tl2Ba2Ca2Cu3O8, and Tl2Ba2Ca2Cu3O8 (Tc is 125 K).

The Tc is only one factor in determining potential usefulness. Maximum current-carrying capacity (Jc in amperes per centimeter squared (A/cm²)) is important. The Tc at a given temperature cannot be exceeded; otherwise the material ceases to superconduct. A third factor is the behavior of a superconductor in a magnetic field. The crystalline structures of the various HTSCs respond differently to magnetic fields. Some Jc's are greatly diminished by fields of 1 tesla.

The current-carrying capacity of the various superconductors is closely related to the way in which they are processed. In turn, the configuration employed is dependent on the specific application. For example, thin films have potential for use in SQUIDs (superconducting quantum interference devices), Josephson junctions, and infrared sensors. The thin films (less than 3000 angstroms thick) are prepared by epitaxial growth on single-crystal substrates such as LaAlO3. The preparation methods include sputtering, molecular beam epitaxy, and chemical vapor deposition followed by heat treatment in an oxygen atmosphere. The Jc for highly oriented single-crystal thin films of YBa2Cu3O7-x has been found to be 5 x 10⁶ A/cm² at 77 K and 5 x 10⁷ A/cm² at 4.2 K.

Wires and tapes made from some of the cuprates are approaching the electrical and mechanical requirements for use in electromagnets and for prototype superconducting motors, generators, and power transmission cables. To be commercially useful, wires or ribbons must be capable of sustaining a Jc of at least 10⁴ A/cm². They must possess this Jc while being exposed to a magnetic field that is either self-generated or imposed. Power transmission cables would operate in a low magnetic field. Superconductors in motors or generators would be exposed to self-generated fields of at least several tesla.

The required wires or ribbons are made by a process in which tubes of silver are filled with fine-grained Bi2Sr2Ca2Cu3O8 and minor constituents. The tubes are drawn, heat-treated, and redrawn and ultimately treated with oxygen. (At high temperatures oxygen diffuses through the silver.) The minor constituents help promote a desirable crystal growth. Wire samples 100 meters or longer have been fabricated. Tests have shown that these will find application in producing very high magnetic fields at 4.2 K. The present technology uses NbTi and Nb3Sn. But the new superconductor wire is superior at fields greater than 15 tesla at low temperatures. Recently samples of HTSC wire have shown a Jc of 48,000 A/cm² (at 20.2 K and 20 tesla) versus 10,000 A/cm² for NbSn wire.

Scanning some of the recent relevant literature leads to the conclusion that progress is being made toward many applications. Scientists and engineers in the United States and elsewhere are accumulating the necessary knowledge and deep intuitive feeling for managing the behavior of tricky but reproducible substances. One is inclined to have faith in experts who have stated that only further incremental improvement is needed to achieve commercial equipment containing high-performance HTSCs by the end of the decade.

Philip H. Abelson

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Neuroscience at NIH

Regarding the ScienceScope item “Neuroscience tiff at NIH” (6 Nov., p. 879), let me correct any misimpression the reader may have received. Neuroscience was, is, and will continue to be a critical element of the strategic plan for the National Institutes of Health (NIH). It is singled out as a major objective in the critical science and technology area. To quote from the strategic plan, “Two particular areas of extraordinary importance and promise are neuroscience and developmental biology.” The plan goes on to identify not only basic neuroscience research but also analysis technologies, such as nuclear magnetic resonance imaging, and positron emission tomography, as areas of emphasis. The notion that neuroscience was left out of the strategic plan is incorrect.

Regarding the issue of space allocation on the NIH campus, as in most major academic and corporate institutions, such allocation is determined on the basis of merit, and merit alone. As in basic research, we must respond with flexibility to opportunities and to areas with promise.

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NIH Expenditures: Extramural Versus Intramural

A letter from Charles A. Gardner (23 Oct., p. 530) suggests that “no one has tried to compare the efficiency of a dollar spent on extramural versus intramural [NIH] research.” In fact, in response to that exact question, the intramural National Institutes of Health (NIH) record was documented in congressional testimony on 23 September 1992, before the House Budget Committee Task Force on Human Resources, chaired by Representative James L. Oberstar (D-MN). Even though the intramural program receives only 1 of every 10 NIH dollars, the output per dollar as indicated by citation frequency, publication impact in top journals, and speed of translation of discoveries from the bench to the bed was two to four times greater than that for extramural expenditures. More important, without the intramural NIH program, recent fundamental scientific discoveries, such as the development of gene therapy, of AZT, ddI, and ddC (the only approved drugs for the treatment of AIDS), of taxol treatment of ovarian cancer, and 200 other discoveries listed at the hearing might have been significantly delayed or might not have happened at all.

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Regulations for Genetically Engineered Foods

We appreciated the essay by David A. Kessler et al. of the Food and Drug Administration (FDA) elaborating on their reasons for deregulating oversight for genetically engineered foods (Policy Forum, 26 June, p. 1747), but we feel it is important to also present reasoned arguments in favor of stronger regulation than the Bush Administration has offered.

Our concern with the FDA’s approach—which allows the industry to decide which products should be evaluated for risks and which do not require any labeling or other consumer information about the presence of genetic modifications in the foodstuffs being consumed—is that the government’s approach does not follow what has been called “the precautionary principle.” The basis of this approach would be that, unless a novel technological procedure is assuredly free of risk, there ought to be assessment in advance of the impact, including estimation of risk probabilities. In addition, under this approach the burden of proof for demonstrating that the risks are acceptable would fall on the proponents of the new technology.

Underlying the reasoning in the Policy Forum by Kessler et al. is a scientifically questionable premise. In this view, if genes from one well-characterized and benign species, say peanuts, are inserted into the genome of another organism that is well characterized and benign, for example, tomatoes, the result is considered to be necessarily well known and benign and need not be assessed in advance. Yet in calculating any risk from a transgenic organism, one should consider four elements: the host organism, the foreign genes, the interaction between the foreign genes and the rest of the genome, and the environment in which the organisms will be used. Although the FDA’s proposed policy focuses on the first two elements, the literature contains many examples of genetic ma-
We examined three human serum-resistant strains of *E. coli*, including one freshly isolated from the blood of a bacteremic patient. We used an *E. coli* K12 strain as a control. The experimental conditions used were identical to those in (1), including the two culture media (BH1 and RPMI 1640). We used recombinant human IL-1β from BioSource International (Westlake Village, California) with a specific activity of 10^5 units per milligram. Three attempts to reproduce the findings reported in (1) were unsuccessful. IL-1β had no growth stimulatory effect on the tested strains. Although the strains grew much better in BH1 than in RPMI medium, the growth rate and final yield of cells after 10 hours of cultivation varied, which apparently reflected the characteristics of each strain.

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Response: We reported (1) a two- to tenfold increase in bacterial log phase growth when virulent bacteria were freshly obtained from the blood of bacteremic patients and exposed to IL-1; avirulent bacteria did not respond to IL-1. However, we subsequently reported that when the bacteria were passaged in serum or broth, or kept at −20°C for several weeks, they lost their responsiveness to IL-1 (2). This result has also been observed by other investigators (3). We did not appreciate these phenomena at the time of our initial report (1).

We have since tested IL-1-induced growth-enhancing effects on 64 *E. coli* strains. We have not found responses to IL-1 as high as those we originally reported in (1). We have isolated strains that respond to IL-1 significantly (P < 0.05), but growth was enhanced by a factor of only 1.5 to 2 (Fig. 1). These strains represent approximately one-fifth of the isolates. However, we believe that growth factors derived in vivo may contribute to the responsiveness to IL-1 and other cytokines.

Other investigators have observed increased growth of different microorganisms with the use of human cytokines (including IL-1, IL-2, and IL-6) or granulocyte-macrophage colony-stimulating factor and have found specific receptors for human cytokines on bacteria and fungi (4). Moreover, there are many reports of receptors for various mammalian proteins on bacteria (5).
Fig. 1. Growth of a virulent E. coli strain incubated in RPMI, with and without recombinant human IL-1α at 100 nanograms per milliliter, determined by direct colony counts. Results are expressed in mean colony forming units (CFUs) × 10^8 ± SEM with four experiments. *, P < 0.05, Student's t test.

We sent one of the newly isolated IL-1-responsive E. coli strains to Kim and Le, who did not confirm the growth-promoting effect in their laboratory. The strain was returned to us, and we again observed a growth-promoting effect of IL-1, using direct colony counts. We invited Kim and Le to come to Boston to observe our methods, but they declined our invitations. Therefore, we cannot explain this discrepancy.

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Corrections and Clarifications
In the letter of 23 October by Charles A. Gardner (p. 530), Dr. Gardner's address was incorrectly given as the Subcommittee on Human Resources and Intergovernmental Relations of the House Committee on Government Operations. Dr. Gardner was a AAAS Congressional Science Fellow assigned to that subcommittee through August 1992, but the views expressed in his letter were his own and not those of the subcommittee.
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As a complementary characterization technique to Edman Protein Sequencing — Apolipoprotein Al mutation Arg60 causes autosomal dominant amyloidosis; Ludwig Institute, London, UK; Proc. Natl. Acad. Sci., USA, 89, 7389-7393 (1992).

Characterization of recombinant proteins — Analysis of recombinant human ciliary neurotrophic factor (CNTF) by laser desorption time of flight mass spectrometry; Regeneron Pharmaceuticals, NY; presented at the Sixth Protein Society Symposium.

Verification of synthetic peptides, looking for deletions, additions and protecting groups that have not been removed — Optimized solid phase peptide synthesis of a 41 amino acid residue peptide sequence of GP41 envelope glycoprotein with significant high sensitivity against HIV-1 antibody positive sera; University of Tübingen, Germany; presented at the 22nd European Peptide Symposium.

Characterization of recombinant human ciliary neurotrophic factor (CNTF) by laser desorption time of flight mass spectrometry; Regeneron Pharmaceuticals, NY; presented at the Sixth Protein Society Symposium.

Characterization of variant proteins — Characterization of lysyl oxidase and TRAMP, distinct proteins that co-purify from porcine skin; Edinburgh University, UK; Matrix, in press.

Monitoring of enzymatic and chemical reactions — Studying advanced glycation processes using matrix assisted laser desorption; C.N.R. Padova, Italy, Policlinico University, Italy and Finnigan MAT, presented at Sixth Protein Society Symposium.

Characterization of glycoproteins and native oligosaccharides cleaved from glycoproteins — Glycobiology Institute, Oxford University, UK; Glycoconjugate J., 9 1-12 (1992).

Analysis of oligonucleotides — Matrix assisted laser desorption of oligonucleotides; California Institute of Technology; presented at 40th ASMS Conference on Mass Spectrometry.

Detection of peptides eluting from RP-HPLC — Predominant naturally processed peptides bound to HLA-DR1 are derived from MHC-related molecules and are heterogeneous in size; Harvard University, Cambridge, USA; Nature358, 764-768 (1992).

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