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## THIS WEEK IN SCIENCE

edited by PHIL SZUROMI

#### Welding under water

Pyroclastic volcanic explosions on land, such as occurred at Mount St. Helens, produce huge amounts of ash that can settle into large tuffs; as the thick layers of hot ash settle and slowly cool, glass and pumice shards commonly weld together and form a distinct texture in which air bubbles collapse and glass shards deform plastically. In contrast, subaqueous pyroclastic eruptions were thought to mix with water and cool too rapidly to weld. Kokelaar and Busby (p. 196), however, describe evidence for welding in an ancient submarine ash flow tuff from California. To account for the welding, they suggest that in subaqueous eruptions, most material is incorporated into a steadily flowing particulate stream in which water is excluded.

# Attractive yet transparent

Most magnetic materials at room temperature are opaque. Mesoscopic materials-particles in the range of 10 to 100 angstroms-may be one route to incorporating magnetic properties into a transparent material. Ziolo et al. (p. 219) have synthesized and characterized an iron oxide-polymer nanocomposite that exhibits a high degree of light transmission for visible wavelengths. Measurements show that the iron oxide particles have unusual magnetic properties: they are small enough that bulk magnetic properties have vanished, yet they are strongly susceptible to magnetization by an external field. Potential applications might include magnetic storage of data and electro-optical device fabrication.

#### C<sub>60</sub> and C<sub>70</sub> in Precambrian rocks

Fullerene molecules have now been found in nature. Fullerenes might be present in the atmospheres of carbon-emitting stars, but the astrophysical data are still ambiguous and searches for fullerenes in meteorites have turned up nothing to date. Buseck *et al.* (p. 215; see news story by Amato, p. 167) report the discovery of  $C_{60}$  and  $C_{70}$  in a carbon-rich Precambrian rock found near the town of Shunga in Karelia, Russia. The authors obtained high-resolution transmission electron micrographs and mass spectra of carbon films from fracture walls inside the rock. The puzzle now is how the fullerenes formed in this geological environment.

#### Subsurface chemistry

Hydrogen can adsorb below the surface of metals and can show enhanced chemical reactivity compared with hydrogen adsorbed on the metal surface. Johnson et al. (p. 223) show that methyl groups (CH<sub>3</sub>) adsorbed on a well-defined nickel surface [the (111) face of a single crystal] react with subsurface hydrogen to form methane, but that hydrogen adsorbed at surface sites is unreactive under the same conditions. Molecular beam methods were needed to prepare a surface with only subsurface hydrogen. These studies help clarify the chemistry of subsurface hydrogen, whose role has been suggested from studies of industrially important heterogeneous catalysts.

#### Early eukaryotes

The time and origin of the eukaryotes has been uncertain; several estimates have been about 1.7 to 1.8 billion years ago. Han and Runnegar (p. 232) now describe coiled megascopic fossils that resemble *Grypania spiralis*, a probable eukaryotic alga, from 2.1-billion-year-old rocks in Michigan. Because *Grypania* are thought to be organelle-bearing eukaryotes, the eukaryotes most likely evolved much earlier.

## Wilms tumor targets

The p13 region of human chromosome 11 is associated with Wilms tumor, a hereditary malignancy of the kidney that occurs in children. The wtl gene has been isolated from this region and appears to function in the development of Wilms tumor as well as in kidney and gonadal development. Bickmore et al. (p. 235) studied the DNA-binding properties of alternative forms of the protein encoded by wt1. Binding to DNA occurs through zinc finger structures in these molecules, and alternative splicing of the gene produces molecules with different spacings between the zinc fingers. The minor product has high affinity for the binding site for the early growth response family of proteins, whereas the major product, which contain three extra amino acids between two of the zinc fingers, is specific for a binding site not recognized by the minor form. Thus the wtl gene products generated by alternative splicing may have different cellular targets.

#### 

#### Restoring immunity against CMV

In immunodeficient persons, such as persons with AIDS or those undergoing cancer chemotherapy or receiving trans-

plants, infectious agents that are normally kept in check by T cell responses can proliferate. For example, infection with cytomegalovirus (CMV) usually does not produce symptoms in healthy individuals, but CMV infection in immune-compromised individuals can cause blindness, pneumonia, and ultimately death . Riddell et al. (p. 238; see news story by Hoffman, p. 166) show that immunity against CMV in humans can be restored by adoptive transfer of T cells. Cytotoxic CD8<sup>+</sup> T cells specific for CMV were isolated from the bone marrow of donors who were infected with CMV. These T cells were cloned and propagated in an in vitro system and then infused into the bloodstream of bone marrow transplant recipients. The recipients did not show any toxic responses, and the cytotoxic effects of the clones appeared to be persistent.

#### Syntaxins and synapses

Neurotransmitters are released when synaptic vesicles fuse with the presynaptic plasma membrane in response to an increase in the concentration of intracellular calcium. However, the molecular mechanisms by which vesicles associate with the membrane and fuse with it are not known. Bennett et al. (p. 255) describe two proteins called syntaxins that might participate in this process. The syntaxins directly associate with synaptotagmin, a protein that exists in the synaptic vesicle membrane, and also appear to interact with the N-type calcium channel. The syntaxins might take part in docking of synaptic vesicles near calcium channels in the presynaptic membrane.

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SDS-polyacrylamide gel electrophoresis of fractions from the purification of MBPparamyosin- $\Delta$ Sal. A:Lane 1:uninduced cells. Lane 2:induced cells. B:Lane 1:purified protein eluted from amylose column with maltose. Lane 2:purified protein after factor Xa cleavage. Lane 3:paramyosin fragment eluted from second amylose column.

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SHORT COURSES

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Gearing, A.J.H. et al, In Press, Annals N. Y. Acad. Sci.

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Harning, R. et al,Cancer Research (1991) 51, 5003-5005.

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Studies have shown differences in intensity related to age and to particular inflammatory conditions (Such as rheumatoid arthritis, systemic lupus erythematosus, metastatic cancer, and acute urolithiasis) of both ICAM-1 and VLA (unpublished).

Seth, R. et al, The Lancet (1991) 338, 83-84.

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- "New Matrices Extending the Biological Applications of Laser Desorption Time of Flight Mass Spectrometry" — John Yates, California Inst. of Technology. Monday, July 27th, Noon-1.30 p.m. Sheraton Harbor Island Hotel, San Diego.

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FINAL MEETING PROGRAM

# Ion Channels in the Cardiovascular System

 $\Rightarrow$  12–15 September 1992  $\Rightarrow$ 

Westfields International Conference Center, Chantilly, VA

Sponsored by National Heart, Lung, and Blood Institute, NIH and American Association for the Advancement of Science

Take part in an intensive conference that will synthesize the recent explosion of information on the function and dysfunction of ion channels in the cardiovascular system.

The conference will bring together leaders from three groups: basic scientists researching molecular aspects of cardiovascular channel structure and function, academic clinicians concerned with disease processes resulting from channel dysfunction, and pharmaceutical scientists involved in the design and testing of channel active drugs.

Discussion will focus on such issues as subunit function, modulation and control, mutagenesis and amino acid replacement studies, de- and repolarizing sodium and potassium channels, and channel involvement in disease processes (e.g., arrhythmias and sudden death). Participants will explore the ways in which this information could be used in the development of new pharmaceuticals to treat ion channel mediated diseases.

Westfields, a state-of-the-art conference center, will provide an atmosphere conducive to a high level of interaction among the participants and make you feel like a guest at one of Virginia's magnificient colonial estates. Yet, it's just minutes from Washington's Dulles International Airport.

Space is limited, so use the registration form on page 273 today!

**Program Committee:** Arthur M. Brown (*co-chair*), William A. Catterall (*co-chair*), Gregory J. Kaczorowski, Arnold M. Katz, Thomas W. Smith, Peter M. Spooner, Harold C. Strauss, August Watanabe, Robin Yeaton Woo

#### Saturday, 12 September

#### Noon – 3:00pm Registration

#### 3:00pm - 3:05pm Welcome

**Peter M. Spooner**, National Heart, Lung and Blood Institute **Robin Yeaton Woo**, American Association for the Advancement of Science

#### 3:05pm – 3:30pm **Opening Remarks**

**Arnold M. Katz**, Univ. of Connecticut Health Ctr. Ion channels and cardiology: Need for bridges across a widening boundary

#### 3:30pm – 5:30pm Ion Channels and Cardiac Disease: Dimensions of the Problem — Clinical Tutorial

**Harold C. Strauss**, *Duke Univ. Med. Ctr.* Conformational-dependent drug binding to cardiac potassium channels

**Robert J. Meyerburg,** Univ. of Miami Sch. of Med. Epidemiology of sudden cardiac death (SCD)

**Peter J. Schwartz**, *Univ. of Pavia* Autonomic markers of SCD

**Douglas P. Zipes,** *Indiana Univ. Sch. of Med.* Autonomic mechanisms underlying arrythmogenesis and SCD **A. John Camm,** *St. George's Hosp. Med. Sch.* Current pharmacologic and nonpharmacologic approaches to SCD

5:30pm - 6:00pm Break

#### 6:00pm – 8:00pm **Fundamentals of the Problem Basic Science Tutorial**

**William A. Catterall,** Univ. of Washington Introduction to molecular analysis of ion channel structure

**Arthur M. Brown,** *Baylor Coll. of Med.* Introduction to biophysical analysis of ion channel function

8:00pm Dinner

#### Sunday, 13 September

7:00am – 9:00am Breakfast

9:00am – 12:30pm Ion Channels and Cardiovascular Function

Chair: Harold C. Strauss, Duke Univ. Med. Ctr.

**Harry A. Fozzard**, Univ. of Chicago Sodium channels and cardiac excitability

**Eduardo Marban**, *Johns Hopkins Univ.* Sodium and calcium channels in the heart **Michael C. Sanguinetti**, *Merck Research Labs* Delayed rectifier K+ channels of cardiac muscle

**Joseph R. Hume**, *Univ. of Nevada Sch. of Med.* Chloride channels

**David C. Spray**, *Albert Einstein Coll. of Med.* Cardiovascular gap junctions: Gating properties, function, and dysfunction

Discussion

12:30pm – 2:00pm Lunch and Poster Session

#### 2:00pm – 5:00pm Channel Modulation and Autonomic Control

Chair: Arthur M. Brown, Baylor Coll. of Med.

**Wayne R. Giles,** *Univ. of Calgary Sch. of Med.* Alpha-1 adrenoceptor effects in single cells and sarcolemmal membranes from rabbit atrial and ventrical myocytes

**Bruce Bean**, *Harvard Univ*. Beta-adrenergic modulation of cardiac calcium channels

**Martin Morad,** Univ. of Pennsylvania Regulation of cardiac sodium channels by cAMP receptors

**Arthur M. Brown**, *Baylor Coll. of Med.* Pore of a K+ channel and its regulation by G proteins

Discussion

6:00pm – 8:00pm Cocktails and Dinner

8:00pm - 10:00pm Poster Session

#### Monday, 14 September

#### 7:00am – 9:00am Breakfast

#### 9:00am – 12:30pm Structure-Function of Ion Channels I

Chair: Arthur M. Brown, Baylor Coll. of Med.

**Rod MacKinnon**, *Harvard Med. Sch.* Molecular physiology of potassium channels

**Richard Aldrich**, *Stanford Univ.* Mechanisms of voltage-dependent channel gating

**Peter Hess**, *Harvard Med. Sch.* Mechanisms of potassium channel gating probed by site-directed mutagenesis

**Michael M. Tamkun,** *Vanderbilt Med. Sch.* Molecular physiology of cardiac potassium and sodium channels

Discussion

#### 12:30pm – 2:00pm Lunch and Poster Session

#### 2:00pm – 5:00pm Structure-Function of Ion Channels II

Chair: William A. Catterall, Univ. of Washington

**William A. Catterall,** Univ. of Washington Structure and modulation of sodium channels

**Walter Stühmer**, *Max Planck Inst.* Extracellular potassium modulates a transient potassium current in rat atrial cells **Kurt Beam**, Colorado State Univ. Structural basis of calcium channel function in skeletal muscle

**Franz Hofmann**, *Tech. Univ. of Munich* Regulation of the L-type calcium channel by its subunits

Discussion

6:00pm – 8:00pm Cocktails and Dinner

8:00pm – 10:00pm Poster Session

#### Tuesday, 15 September

7:00am – 9:00am Breakfast

9:00am – Noon Molecular Pharmacology

Chair: William A. Catterall, Univ. of Washington

**Harold C. Strauss**, *Duke Univ. Med. Ctr.* Conformation-dependent drug binding to cardiac potassium channels

**Thomas Colatsky**, *Wyeth-Ayerst Research* Block of myocardial potassium channels by antiarrythmic drugs: Dependence on channel gating

**Robert S. Kass**, *Univ. of Rochester Med. Ctr.* Dihydropyridines and the molecular properties of heart calcium channels

**Jörg Striessnig**, Inst. for Biochemical Pharmacology Calcium antagonist binding domains of L-type calcium channels

Discussion

Noon – 2:00pm Lunch

#### 2:00pm – 4:30pm Drug Discovery

Chairs: August Watanabe, Eli Lilly & Co.; Gregory J. Kaczorowski, Merck Research Labs

**Gregory J. Kaczorowski**, *Merck Research Labs* Strategies to discover novel ion channel modulators

**Benedict R. Lucchesi**, Univ. of Michigan Med. Sch. Potassium channels, repolarization, and antifibrillatory drugs

**S. David Kimball**, *Bristol-Meyers Squibb* The design of new calcium antagonists

**William C. Lumma, Jr.,** *Merck Research Labs* Inhibitors of cardiac delayed rectifying potassium currents as potential novel anti-arrythmic agents

Discussion

#### 4:30pm – 5:00pm Concluding Observations

**Arnold M. Katz**, *Univ. of Connecticut Health Ctr.* Ion channels: Building the bridge

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