# Fortieth Annual Briefing **NEW HORIZONS IN SCIENCE**

October 27 through 30, 2002 The Ritz-Carlton Hotel St. Louis, Missouri



Program by: Ben Patrusky, Executive Director, CASW

Sponsored by: Washington University in St. Louis

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### Saturday, October 26 6:00 p.m.

REGISTRATION CASW Hospitality Suite, The Ritz-Carlton Hotel

# Sunday, October 27 9:30 a.m. to 12:30 p.m.

RNA-ANCHORED TARGETED THERAPY John-Stephen A. Taylor, Ph.D., Professor of Chemistry, Washington University in St. Louis, MO

Karen L. Wooley, Professor of Chemistry, Washington University in St. Louis, MO

Talk about "smart" biobombs, how's this for an ingenious idea? Find RNA that's uniquely expressed or overexpressed in diseased cells for use as anchorage for side-by-side docking of two oligonucleotides (snippets of precisely coded nucleic acids), each packing a complementary payload. Hitched to one: an inactive form of a cell-destroying drug; to the other: an activating catalyst. Transported to targeted cells, each of the pair homes in on its respective landing site. The prodrug, sparked by the now-adjacent catalyst, springs to lethal life. What beckons, should the full clinical potential of this RNA-as-trigger strategy be realized, is a revolution in cancer and viral-disease therapy. In a companion study, researchers are seeking to splice RNA-docking molecules to a novel breed of nanoparticles

— specially structured "nanocages" — for on-the-mark, stay-put delivery of diagnostic and disease-fighting agents. Said nanoparticles, dubbed knedels for their similarity to a Polish dumpling, also hold promise for other, non-medical applications (e.g., as a foil to maritime fouling).

### TAMING MICROBIAL BIOFILMS

J. William Costerton, Ph.D., Professor of Microbiology and Director, Center for Biofilm Engineering, Montana State University, Bozeman, MT

Infectious-disease specialists were baffled. Why, they wondered, were certain microbial diseases — e.g., otitis media (earache) in children and prostatitis in adults — so fiercely resistant to antibiotics? Stymied in their search for answers, they began to call the very notion of bacterial causation into question. But not of late, not since they acquired the technology needed to make sense of it all. The pathogens responsible for these chronic ills, they found, live for the most part not as free-floating "loners" but as colonialists, as members of intricately structured communities — assemblages that form biofilms, slimy matrices impermeable to antibiotics. Under certain circumstances, however, the aggregates disengage; the bacterial cells revert to the loner, now-antibiotic-vulnerable state. Armed with fresh details about the genes and molecular cues governing these lifestyle conversions, researchers are on the verge of bringing a novel class of drugs to the bedside — behavior-modifying agents designed not to kill but rather to render the microbial population harmless (so as to preclude development of resistance to these new agents).

# Sunday, October 27 2:30 p.m. to 5:30 p.m.

### IN SEARCH OF COSMIC MAYHEM

In place or soon to be: a remarkable set of complementary tools — observational, experimental and computational — for exploring violence in the universe. A look at what's ahead.

#### THE TeV SKY

James H. Buckley, Ph.D., Associate Professor of Physics, Washington University in St. Louis, MO

It's the most intense form of radiation known to science, gamma rays with energies measured in trillions of electron-volts, testimony to cosmological paroxysm *in extremis*. At least six TeV-emitting sources have been spotted to date. More will certainly come to light once two next-generation, ground-based gamma-ray observatories are up and running.

### GRAVITY WAVE ASTRONOMY

Wai-Mo Suen, Ph.D., Professor of Physics, Washington University in St. Louis, MO

LIGO, the gravity-wave observatory, has finally come on line, poised to capture the ripples in the fabric of space-time that speak of near-unimaginable cataclysm. For the project to succeed, however, scientists need to know what to expect — i.e., the vibrational "signatures" characteristic of black-hole collisions, say, or the big bang itself. Efforts now underway to solve Einstein's equations of general relativity on supercomputers, as a prerequisite to simulation of neutron-star and black-hole mergers, should help.

### LABORATORY X-RAY ASTROPHYSICS

Peter Beiersdorfer, Ph.D., Research Scientist, Lawrence Livermore National Laboratory, Livermore, CA

The Chandra and XMM observatories have been delivering information in such spectrographically exquisite detail as to allow scientists not only to differentiate among various X-ray emitters but also to unravel the astrophysical processes that are at work when stars explode or matter falls into black holes. For that to happen, however, they must first fill in some of the remaining blanks in current atomic models. With an expanding arsenal of new laboratory devices, they have begun to do just that.

PROBING STELLAR VIOLENCE WITH RADIOACTIVE BEAMS Michael S. Smith, Ph.D., Senior Scientist, Oak Ridge National Laboratory, Oak Ridge, TN

After the big bang, most of the normal matter in the universe consisted of hydrogen and helium, with only trace amounts of lithium, beryllium and boron. All the rest was cooked up by thermonuclear fusion in stellar cores and spewed into the void when stars exploded. Scientists are working with sophisticated computer models of stellar flameout to ferret out the details of how the other members of the periodic table came to be. But they require information that can only be obtained using beams of unstable nuclei.

6:30 p.m. to 8:30 p.m.

WELCOME RECEPTION The Ritz-Carlton Hotel

# Monday, October 28 8:30 a.m. to 11:30 a.m.

### THE GENOMICS OF CRITICAL ILLNESS

J. Perren Cobb, M.D., Associate Professor of Surgery, Washington University School of Medicine in St. Louis, MO

The death spiral goes something like this. First: injury. Then: post-traumatic shock. Then: massive, uncontrolled systemic inflammation. Finally: multi-organ failure. That's pretty much the story of how 162,000 critically ill people die each year in the U.S. Medicine can help stem the tide, but only up to a point. Once the inflammatory state is reached there's little, if anything, to be done; either the condition proves self-limiting, or the patient dies. Not that researchers haven't labored long and hard to develop therapies to restore or support organ function, but, for the most part, they've failed. A newly launched initiative, however, could go a long way towards remedying this disheartening clinical picture. Its design rests on the presumption that critical illness is a complex disease demanding a deeper understanding of the host's full range of genetic responses to injury.

### AGROBIOTECHNOLOGY: NEW FRONTIERS

In light of the heady progress being made in plant science, several payoffs of major benefit to the developing world may be in the offing.

#### PLANT-BASED ORAL VACCINES

Terry Woodford-Thomas, Ph.D., Domain Associate Member, Donald Danforth Plant Science Center, St. Louis, MO

The idea: engineer into edible plants well-defined gene sequences derived from diseasecausing microorganisms for generation of proteins, which, following ingestion, would act to provoke a robust, full-scale (i.e., T- and B-cell) immune response. Among the prime targets: HIV, tuberculosis and malaria.

#### TAILORING CROPS FOR MARGINAL SOILS

Daniel P. Schachtman, Ph.D., Principal Investigator, Donald Danforth Plant Science Center, St. Louis, MO

With a deepening understanding of mechanisms involved in sodium, potassium and mineral intake by roots, plant scientists are at work developing micronutrient-enriched, salt-tolerant, less-fertilizer-dependent varieties capable of thriving in extremely challenging soils.

APPLIED EVOLUTION IN AGRICULTURE AND BIOLOGICAL CONTROL Mark D. Rausher, Ph.D., Professor of Biology, Duke University, Durham, NC

By applying Darwinian principles — "evolutionary engineering," they call it — researchers believe they can redirect the course of evolution so as to: keep agricultural pests from winning the plant-pest "arms race"; persuade pest populations to evolve to extinction; and create mating barriers to prevent transgenes from escaping into wild plant species.

# Monday, October 28 2:15 p.m. to 5:15 p.m.

### PREDICTING CATASTROPHES

Didier Sornette, Ph.D., Professor of Geophysics, University of California, Los Angeles, and a Director of Research, Centre National de la Recherche Scientifique (CNRS), University of Nice, France

Longstanding efforts to predict financial-market meltdowns — the 2002 sell-off, among them — have all essentially come to naught. Small wonder then, given this history of abysmal failure, that most economic experts view the search for such prophetic powers to be an inherently futile quest. But in a soon-to-be-published book, an eminent physicist argues otherwise. Drawing on ideas and tools from statistical physics and artificial/computational intelligence for modeling cataclysmic events, he has proposed a new theory on not only the how and why of crashes but also, more importantly perhaps, the when of them in time, it is hoped, to be able to introduce countermeasures against the build-up of conditions that bring the market to the tipping point. There's more. The predictive principle may apply as well to a host of other extreme events — including great earthquakes (the next California Big One, for example); precipitate changes in weather regimes, and maybe even large-scale epidemics.

CONTROLLING GLOBAL WEATHER: WHEN? HOW? SHOULD WE? Ross N. Hoffman, Ph.D., Principal Scientist, AER Inc., Lexington, MA

Pie-in-sky? Maybe. But to a growing cadre of scientists it's no longer a matter of if, but when — no more than a few decades, they say — before mankind has grasp at last of the means to control weather. That belief rests on some well-grounded assumptions that read like a syllogism. It goes like this. The atmosphere is chaotic. Chaos implies extreme sensitivity to small changes or "perturbations." A series of "just right" perturbations and — voilà — weather control. To create such perturbations: production of contrails (essentially solar and thermal radiation-modifying cirrus clouds) by aircraft flying precisely defined routes; solar reflectors in low earth orbit; space-based solar-power generators. The concept was recently put to simulated test. The aim: to deflect a hurricane — in this case, Hurricane Iniki, which in 1992 devastated Kauai in Hawaii. In their computer trials, the researchers were able to steer Iniki well clear of the island. It may not be too early, they say, to begin addressing the many social, economic and political issues — "weather wars," for one — that will go with the acquisition of this newfound power.

### 6:30 p.m. to 9:30 p.m.

CASW ANNUAL RECEPTION AND DINNER Donald Danforth Plant Science Center. Buses depart hotel beginning at 6:00 p.m.

Presentation of the Victor Cohn Prize for Excellence in Medical Science Reporting.

Featured speaker: Carl M. Bender, Ph.D., Professor of Physics, Washington University in St. Louis, takes on the Greenhouse Effect.

# Tuesday, October 29 7:45 a.m.

Buses begin departing for the Charles F. Knight Executive Education Center on the Washington University campus. Breakfast will be available at the Center.

### 9:00 a.m. to Noon

### NEW EYES ON BIOLOGY

Newly endowed with a breathtaking array of non-invasive imaging technologies, biomedical researchers now have it in their power to see biology at work in living animals at all scales — molecular, cellular and systemic — in unprecedented ways.

### MOLECULAR IMAGING

David Piwnica-Worms, M.D., Ph.D., Professor of Radiology and of Molecular Biology and Pharmacology, Washington University School of Medicine in St. Louis, MO

Working with an acronymic mix that includes PET, SPECT and MRI, molecular biologists are looking in on genes as they go about the business of generating proteins and on what it is proteins do in normal and diseased cells, prelude to discovery of new diagnostic and therapeutic approaches.

#### THE LIFE OF A SYNAPSE

Jeff W. Lichtman, M.D., Ph.D., Professor of Anatomy and Neurobiology, Washington University School of Medicine in St. Louis, MO

On the cellular level, neuroscientists can now monitor individual neurons and synapses over minutes, hours, months or years as a function of experience, aging and disease.

#### CORTICAL CARTOGRAPHY

David C. Van Essen, Ph.D., Edison Professor of Neurobiology and Head, Department of Anatomy and Neurobiology, Washington University School of Medicine in St. Louis, MO

On the systemic level, neurobiologists now have the capacity not only to observe wholebrain activity during thought, emotion and movement, but also novel brain atlases — flat maps akin to Mercator-projection maps — for viewing function as it relates to form.

### CATCHING CHEMISTRY IN THE ACT

Richard A. Loomis, Ph.D., Assistant Professor of Chemistry, Washington University in St. Louis, MO

In a first-of-its-kind effort, researchers are making "movies" of how two molecules mix and mingle in real time. Key to its production are powerful lasers capable of generating the femtosecond (10<sup>-15</sup>) "shutter speeds" required to see geometries changing, bonds breaking and new bonds forming as the reaction proceeds. Missing from the movie, however, are "shots" of events occurring at faster-than-femtosecond time scales. But reports of successful generation of attosecond (10<sup>-15</sup>) and zeptosecond (10<sup>-21</sup>) pulses suggest that those elements too will soon find their way into the movie. By parsing bimolecular reactions at these incredible levels of resolution, the moviemakers expect to open chemistry to dazzlingly new possibilities and novel applications. Example: increasing industrial chemical yield simply by shining powerful light at the right time in the production cycle.

# Tuesday, October 29 12:15 p.m.

Lunch

# 1:30 p.m. to 4:45 p.m.

### CAMPUS EXPLORATIONS

An opportunity to visit three special laboratories for vivid demonstrations of research aimed at: assessing the risk of head injury from soccer-ball impact; detecting and deactivating microbial and viral agents of biowarfare; developing novel construction techniques to safeguard buildings and bridges against earthquakes.

### 4:45 p.m.

Buses depart the campus for the hotel.

### 7:00 p.m. to 10:30 p.m.

### ROCKIN' AT BLUEBERRY HILL

An evening of fun, frolic and excellent dining hosted by Washington University at the club made famous by Chuck Berry, featuring music by St. Louis' own Soulard Blues Band. Buses depart the hotel beginning at 6:45 p.m.

### Wednesday, October 30 8:15 a.m. to 11:15 a.m.

### ULTRA-FAST SEARCHING OF MASSIVE DATABASES

Ronald S. Indeck, Ph.D., Das Family Distinguished Professor of Electrical Engineering, Washington University in St. Louis, MO

In the beginning was the word, and the word was *data* ... followed, almost immediately, by yet another — *multiply*. And it was done. And it was good. So begins a fable for our time, a story for the Information Age — a tale with no end in sight. But a pesky complication has recently come to light, an outgrowth of the ceaseless hunger for more — the need to store more detailed information, to store information for longer periods and to deal with the huge acquisitions of phenomenally data-dense enterprises, e.g., genome sequencing and intelligence gathering. Here's the hitch: database size is growing at a rate that far exceeds increases in data processor performance. Ergo: the search for and retrieval of select information from these ever more massive data sets are becoming increasingly time consuming. But now, with the advent of new technology that allows searches to be done 200 times faster than currently possible, the story is about to take a turn for the better.

### RINGS OF TRUTH: ANCIENT TREES, THE ENVIRONMENT AND HUMAN AFFAIRS David W. Stahle, Ph.D., Professor of Geosciences, University of Arkansas, Fayetteville, AK

The hunt's on. Aided by newly refined predictive models, tree-ring specialists are in a hurry-up search for the world's oldest inhabitants — imperiled but as-yet unrecognized remnants of the great forests primeval. These centuries-old stands, say dendrochronologists, will almost certainly have much to tell us about Earth's environmental history and its impact on human affairs. Thanks largely to recently developed tree-ring data, for instance, there's good reason to believe that the deaths of tens of millions of people in 16<sup>th</sup> Century Mexico stemmed not from non-native maladies introduced from Europe and Africa as is commonly presumed but from indigenous pestilences brought on by a 40-year "megadrought." And, based on newly completed tree-ring reconstructions dating back to the 8<sup>th</sup> Century, researchers now think that Teotihuacán, the once-flourishing center of Meso-American life, may have suffered a similar fate.

Contributors

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