

The Jane Coffin Childs

MEMORIAL FUND FOR
MEDICAL RESEARCH

JCC Fellows Solve Vitamin Mystery

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No fewer than four Nobel Prizes have been awarded for research related to vitamin B12—one each for its isolation, structure, and *de novo* synthesis; and a fourth for a set of chemical rules inspired by one of its myriad biosynthetic steps. So it is perhaps surprising that until this year no one had any idea how one of B12's key components was made. The double-ringed chunk in question, known as dimethylbenzimidazole or DMB, helps coordinate the critical atom of cobalt at the vitamin's core. Yet in the 80 years since the discovery of B12, during which the biosynthesis of all its other



Nicholas Larsen and Michiko Taga

PHOTO: KEN TAGA

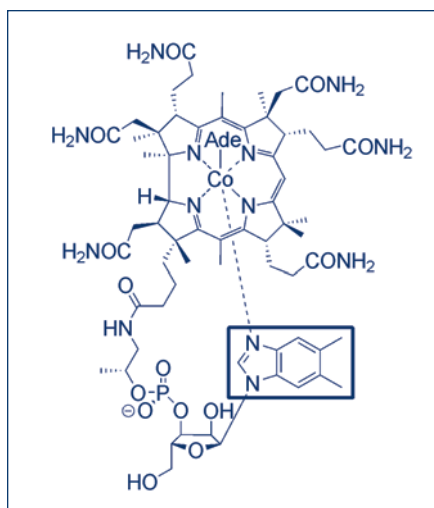
parts (not to mention all other essential vitamins) was fully elaborated, no enzyme for making DMB has been found.

Now, in a remarkable story of serendipity and teamwork, Jane Coffin Childs fellows Michiko Taga and Nicholas Larsen have found the last piece of the puzzle. They have shown that a bacterial enzyme named BluB generates DMB by cannibalizing part of vitamin B2—an unusual biochemical step analogous to stripping a car—and they have crystalized the protein to reveal its active site. Their solution to this lingering conundrum appeared in the March 22 issue of *Nature*.

DMB is only one small part of vitamin B12, among the largest non-polymer biomolecules known. The cobalt atom,

which is surrounded by a complex ring structure, is covalently linked to a variable side chain which determines the vitamin's role in the cell. One version, for instance, is a co-factor in fatty acid synthesis, while another supports production of the amino acid methionine. DMB, the so-called lower ligand of B12, is tethered at the end of a long tail in one of the final steps of synthesis (see diagram).

Only certain bacteria and archaea can make vitamin B12, alias cobalamin. Animals must get theirs another way. Some, such as ruminants, get it by hosting B12-synthesizing microbes in their gut. Others, including humans, must get it through their diets—ruminant muscle being a ready source.



Cobalamin, or vitamin B12.
The lower ligand DMB is boxed.

JCC FELLOWS SOLVE MYSTERY CONTINUED ON PAGE 2 . . .

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Plant cells don't need B12, but the compound does help microbes set up symbiotic relationships with certain plants. It is this function that led Graham Walker's lab at the Massachusetts Institute of Technology, where Taga is a post-doc, to the DMB biosynthesis story.

Walker's team studies the symbiosis between the soil alpha-proteobacterium *Sinorhizobium meliloti* and the root hairs of alfalfa. The nodules that result allow legumes like alfalfa and beans to fix atmospheric nitrogen into a form that plants can use. A few years ago, graduate student Gordon Campbell found a *Sinorhizobium* mutant that failed to initiate symbiosis unless it was given a dietary supplement of DMB. The mutated gene, *bluB*, thus became the first to be linked to DMB synthesis.

Clues to *bluB*'s function were already apparent in its sequence. The gene's RNA message included a riboswitch, a stretch of sequence capable of binding to vitamin B12. Riboswitches are a way for the ultimate product of a

biosynthetic pathway to turn down the genes involved once enough is made, suggesting that the BluB protein contributes to B12 synthesis. Also, the protein sequence of BluB revealed a similarity to known enzymes that bind flavin mononucleotide (a.k.a. FMN or vitamin B2), which is the biochemical precursor of DMB. So it seemed possible that BluB catalyzed the conversion of FMN to DMB.

To obtain biochemical evidence for this conversion, Taga took a "sabbatical" to work in the laboratory of biosynthesis expert Christopher Walsh just across the river at Harvard Medical School in Boston. There she showed that purified BluB could convert FMN to a product that looked, like DMB. She also found that this product could rescue *bluB* mutant bacteria. The reaction also consumed molecular oxygen, a requirement found previously with cell extracts. And that the optimum concentration of FMN for the reaction was close to its physiological concentration.

Although the case implicating BluB as the missing enzyme looked good, to convert the bulky, three-ringed molecule

FMN to the modest, two-ringed DMB clearly required some complex chemistry. How could BluB do it all alone? To find out, Taga needed a crystallographer.

As it turns out, Larsen, an old friend from undergraduate days at Carleton College in Minnesota and now a trained crystallographer, happened to be completing a JCC-supported post-doc in Stephen Harrison's lab at Harvard Medical School. "We were just chatting about our work one day and he got interested in BluB. He offered to try to determine the structure," Taga says.

Although BluB proved somewhat finicky—one batch would crystallize easily and the next would not—Larsen was eventually able to solve the structure of the enzyme bound to its substrate FMN (strictly speaking the reduced form, FMNH₂). The active enzyme consists of two protein monomers clasped together into a dimer like a firm handshake, forming two flavin binding pockets in the space between. As expected, these pockets resemble active sites on known flavin binding proteins. But there is one intriguing difference.

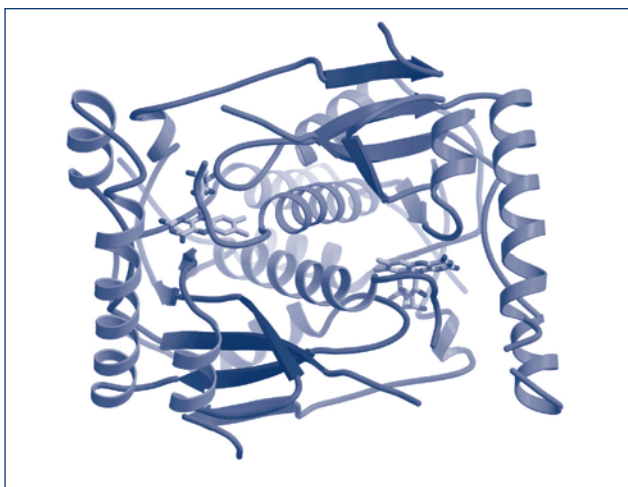
In enzymes such as flavin reductase of the luminescent bacterium *Vibrio fischeri* or NADH oxidase of the undersea vent microbe *Thermus thermophilus*, the binding pocket is easily accessible to the solvent, facilitating substrate exchange. BluB, by comparison, enfolds FMN and molecular oxygen in a closed reaction chamber that excludes all other molecules. In this way, the reaction can proceed without chemical interference. Water molecules, for instance, can deactivate the oxygen to some extent. Isolated, oxygen's full potential can be directed at dismantling FMN.

This may be important, as the conversion of FMN to DMB is more dramatic than the mere oxidation-reduction reactions catalyzed by BluB's relatives. "The substrate basically explodes," as Larsen puts it.

Of course the ultimate picture will likely be somewhat less chaotic than an explosion, but the mechanistic details of DMB's genesis remain to be worked out. Larsen and Taga hope to pursue a number of avenues, including making co-crystals of BluB and DMB. At the same time, both are continuing their original post-doc projects. Taga is examining bacterial enzymes that initiate symbiosis to try to understand why many species have both B12-dependent and B12-independent enzymes to do the same job. Larsen, now in Marc Kirschner's lab at Harvard Med, is attempting to crystalize the anaphase promoting complex or APC, a massive conglomerate that regulates a cell cycle checkpoint and has a role in cancer progression.

Why did BluB take so long to find when the enzymes that make every other vitamin, and every other part of B12, were tracked down years or even decades ago? According to Taga, most of the other vitamin synthesis genes were identified in genetic screens for mutant bacteria that lack B12. But *bluB* mutants are normal in such assays, apparently because other molecules can take DMB's place as the lower ligand, albeit less efficiently.

Both Larsen and Taga intend to begin the search for faculty positions in the fall, fully cognizant of the realities of a competitive marketplace. But it certainly won't hurt anyone's prospects that a mere side-project has ended up putting such a neat period at the end of a long biochemical story. *



Ribbon structure of the BluB enzyme which cannibalizes flavin mononucleotide (FMN) to make DMB. The dimer structure creates two active sites, occupied here by FMN molecules (stick diagrams).

DIRECTOR'S CORNER

A Good Year



At least as far as funding is concerned, 2007 has been a great year to start a post-doc. Thanks to a generous gift from the Genentech Foundation and a favorable new post-doctoral policy at the Howard Hughes Medical Institute (HHMI), we were able to offer support to an additional six new fellows this year. The Genentech Foundation granted our request to fund two of those fellows—a request we plan to renew in future years. At the same time, HHMI extended a most generous offer to fund four of our top candidates who are in, or on their way to, HHMI labs, bringing the total number of JCC awards this year to 30. The HHMI support allows the endowment and gift support to be stretched to include fellows who might otherwise be below the cut-off, but who are still highly meritorious. HHMI has made a similar option available to three other highly selective agencies—the Helen Hay Whitney Foundation, the Damon Runyon Cancer Research Foundation and the Life Sciences Research Foundation. Between the Genentech Foundation and HHMI, that adds up to 18 new top-ranked post-docs who will receive financial support this year.

Although these new funds will allow us to extend support to a greater proportion of our highly-ranked candidates, the unfunded talent pool remains deep. With a mere 7% success rate in competition for Childs postdoctoral positions, we must make painful and sometimes arbitrary choices in the selection or exclusion of candidates that straddle our cut-off line. The combined funding available through private agencies pales in comparison to the census of scholars searching for postdoctoral stipend support. The situation is made much worse by the declining success rate for domestic postdoctoral candidates competing for NIH NRSA fellowships. Foreign scholars, who make up a large and important share of the biomedical work force, but who are ineligible for direct support from the NIH or the American Cancer Society, are left to find laboratories with funded positions. Needless to say, the current funding crunch at NIH makes these funded positions more difficult to secure. This problem requires a federal solution, but we are pleased to be able to help in our own small way.

In addition to helping us to secure funding, the members of the Board of Scientific Advisors (BSA) and the Fund Managers help through service in reviewing applications, organizing the post-doctoral fellow symposium and managing the portfolio. Members of the BSA serve four-year, once renewable terms. I am pleased to recognize the invaluable service and collegiality of Robert Eisenman, Ed Harlow and Jamie Williamson, whose terms on the BSA have concluded. With their departure, I am pleased to welcome our new members, Cynthia Kenyon, Charles Sherr and John Kuriyan. *

— Randy Schekman, Director of the Board of Scientific Advisors

Fellows Awarded Spring 2007

- **Bassem Al-Sady**
Investigating the core mechanism of heterochromatin formation, with Geeta Narlikar, Department of Biochemistry and Biophysics, University of California, San Francisco
- **Aurelie Y.O. Bertin**
Structure and dynamic of assembly of septin filaments, with Eva Nogales, Department of Molecular and Cell Biology University of California, Berkeley
- **Aparna Bohil**
ParM plays a central role in bacterial plasmid segregation, with Dyche Mullins, Department of Cellular and Molecular Pharmacology University of California, San Francisco
- **Anne-Kathrin Classen**
The polycomb family of epigenetic transcriptional repressors and their role in *Drosophila* growth control, with David Bilder, Department of Molecular and Cell Biology, University of California, Berkeley
- **Jichao Chen**
Mechanism of airway tube size control during lung development, with Mark Krasnow, Department of Biochemistry, Stanford University
- **Gregory M. Cooper**
Stratifying genomic variation to increase power in genetic association studies of common human diseases, with Evan Eichler, Department of Genome Sciences, University of Washington, Seattle
- **Dion K. Dickman**
Genetic dissection of synaptic homeostasis, with Graeme Davis, Department of Biochemistry and Biophysics, University of California, San Francisco
- **Jeffrey B. Doyon**
Investigation of dynamin's role in the temporal regulation of actin remodeling during endocytic vesicle formation, with David Drubin, Department of Molecular and Cell Biology, University of California, Berkeley
- **Morten Ernebjerg**
Probing complex microbial communities: structure and response to perturbations with antibiotics, with Roy Kishony, Department of Systems Biology, Harvard Medical School
- **Donald T. Fox**
Drosophila hindgut stem cells: uncovering their roles in tissue formation as well as tissue maintenance, with Allan Spradling, Department of Embryology, Carnegie Institution of Washington
- **Stephanie Hammill**
Structural and functional studies of the RNA quality control TRAMP4 complex, with Karin Reinisch, Department of Cell Biology, Yale University
- **Chun Han***
Identification of the repulsive signals mediating dendritic tiling of class IV *Drosophila* da neurons, with Yuh Nung Jan, Department of Physiology, University of California, San Francisco
- **Gunther Hollopeter***
Is PIP2 required for synaptic vesicle exocytosis or endocytosis?, with Erik Jorgensen, Department of Biology, University of Utah, Salt Lake City
- **Erik Hom**
Experimental evolution of symbiosis, with Andrew Murray, Department of Molecular and Cell Biology, Harvard University
- **Andrew A. Horwitz**
Synthetic chromatin: Exploring the design principles of cellular memory, with Wendell Lim, Department of Cellular and Molecular Pharmacology, University of California, San Francisco
- **Shigeki Iwase**
Roles of a histone demethylase SMCX in neuronal function, with Yang Shi, Department of Pathology, Harvard Medical School
- **Seyun Kim**
The role for nuclear GAPDH in the regulation of p300/p53 activation, with Solomon Snyder, The Solomon H. Snyder Department of Neuroscience, Johns Hopkins University
- **Alexei Korrenykh**
Taking apart a molecular switch: structure, regulation and specificity of the bifunctional kinase-ribonuclease IRE1, with Peter Walter, Department of Biochemistry and Biophysics, University of California, San Francisco
- **Hubert Lam**
Polarity and pathogenesis: identification and characterization of cell polarity determinants in *Vibrio cholerae*, with Matthew Waldor, Department of Medicine, Brigham and Women's Hospital
- **Gwangrog Lee**
A single molecular study of the exosome to understand RNA 3'-5' processing, degradation, and polymerization, with Taekjip Ha, Department of Physics, University of Illinois at Urbana-Champaign
- **Dayu Lin***
Neural substrates underlying aggressive vs. sexual behavior in mice, with David Anderson, Division of Biology, California Institute of Technology
- **Joseph J. Loparo**
Single-molecule enzymology of the replisome, with Antoine van Oijen, Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School
- **Daniel A. Lutterman**
Identification of transient reactive intermediates in RNRs and potential role in therapeutics, with Daniel Nocera, Department of Chemistry, Massachusetts Institute of Technology
- **Gregory T. Reeves**
Spatial regulation of the NF-kappaB pathway in *Drosophila* embryogenesis, with Angelike Stathopoulos, Division of Biology, California Institute of Technology
- **Nicolas Reyes**
Conformational changes of the glutamate transporter accompanying the release of ligands to the cytoplasm, with Olga Boudker, Department of Physiology and Biophysics, Weill Medical College of Cornell University
- **Eirini D. Trompouki**
The role of prostaglandins and Wnt signaling on hemopoietic stem cell renewal, with Leonard Zon, Division of Hematology/Oncology, Children's Hospital of Boston
- **Karen Wu**
The contribution of neuroligin and neuroligin diversity to synaptic specificity, with Peter Scheiffele, Department of Pathology, Columbia University
- **Xiaoyang Wu**
Coordinated cytoskeletal dynamics and epidermal polarity: implications in skin cancer, with Elaine Fuchs, Laboratory of Mammalian Cell Biology and Development, The Rockefeller University
- **Yasuo Yoshikuni***
Computational redesign of cytochrome P450 function and applications to synthetic biology, with David Baker, Department of Biochemistry, University of Washington, Seattle
- **Ivan A. Yudushkin**
Imaging molecular interactions upon ephrin-Eph receptor-mediated adhesion/repulsion responses in live cells, with Ronald Vale, Department of Cellular and Molecular Pharmacology, University of California, San Francisco

*HHMI award recipient

A Conversation with James Childs

James (Jamie) E. Childs, grandson of Jane Coffin Childs, has sat on the Board of Managers since 1987. He is one of the few scientists on this board, which mainly handles the Fund's finances. An epidemiologist, Jamie served for more than a decade at the Centers for Disease Control and Prevention in Atlanta, ending up as chief of the Viral and Rickettsial Zoonoses Branch from 1998 to 2003. After a brief stint at Emory University, he joined the faculty at the Yale University School of Medicine where his title is Senior Research Scientist.



What is the job of the Board of Managers?

Our main tasks are to increase the size of the fund through management of the assets and to pursue other ways of obtaining sponsored fellowships. The Board of Managers also acts on and approves the recommendations of the Board of Scientific Advisors with regard to the number of new fellowships offered and the annual stipend. We want the award to be attractive in comparison with other fellowships, and we want to fund enough positions so that the excellent individuals who make up the BSA will feel it's worth their while to go through the numerous applications. The BSA gives us a list of between 20 and 30 candidates and we decide how far we can lean into the wind in terms of drawing down the capital to support as many of the recommended candidates as possible. It's a delicate balance.

It has been a challenging decade for investors.

How has the fund held up?

We have professional financial advisors to inform our decisions, but we also have on the board people like Bill Gridley and my brother John who have worked extensively in financial fields. At the moment, we have some 30 to 40 percent of the funds in overseas investments that have given very high rates of return. So even in hard times the fund has maintained and even grown. We also owe a great deal to the efforts of Randy Schekman who heads the BSA for his work in finding outside sources for fellowships.

The Board of Managers has always been made up principally of Childs family members and friends. Why?

The family is very interested in the whole process. It's very personal and very high in the family's priorities to

maintain and grow the fund going at the level of excellence it has attained. We meet with the scientific board twice a year, once at a joint dinner in New Haven, and once at the fall symposium in Connecticut. At the symposium board members and their families get to meet the fellows and hear about their work.

Tell us a bit about your epidemiological research.

Do you track down viruses where they live?

All my career has been spent on zoonotic pathogens, those that move between animals and humans. I have worked extensively on a number of viral systems, including hantaviruses and other viruses causing hemorrhagic fevers. I led the field investigation that identified the rodent reservoir species in the 1993 hantavirus outbreak in the four corners region of the southwestern US. I have also done research on Lassa and Ebola viruses in Africa and on Junin virus in South America.

More recently you have concentrated on rabies.

It was at the CDC that I started working extensively on rabies. At the moment I'm working with Les Real at Emory University on mathematical models of how rabies infections drive the population dynamics of its wildlife hosts and how these changes drive cross-species infections among domestic

animals and humans. We have also sequenced a large number of viral genomes obtained from different wildlife reservoirs over time, to see if the virus spreads mainly by local diffusion or if features of the host and its environment affect the pace of viral evolution.

I have also been interested in economic modeling of the cost-effectiveness of distributing rabies vaccine for wildlife. Right now there are vaccine barriers running hundreds of miles through Ohio and Pennsylvania where vaccine is set out in odorant packages that attract wildlife. It's an expensive program, but the consequences of viral spread are expensive too.

It has been 70 years since your grandfather Starling Childs and your great aunt Alice Coffin established the Fund in your grandmother's memory after she died of cancer. What do you think will be the JCC Fund's legacy in the development of cancer therapies?

I think the Fund has an extraordinary history of funding the best and brightest, but it is not necessarily outcome based. I couldn't say a Coffin Childs fellow will cure cancer, but I think by funding basic research, we raise the probability that some of this knowledge will be translated into effective treatments. I'm a strong believer that people will find ways to translate outcomes from basic science into practice. *

JCC Welcomes Three New Members to the Board of Scientific Advisors

Charles J. Sherr

Charles J. Sherr is the Herrick Foundation Chair of the Department of Genetics & Tumor Cell Biology at St. Jude Children's Research Hospital in Memphis, Tennessee. He has devoted much of the past 35 years to understanding the cellular and molecular origins of cancer, most recently with emphasis on cell cycle control. Among his many contributions to the field are the discovery of D-type cyclins and CDK4, which help regulate the cell's entry into the DNA synthesis phase of the cell cycle, and the characterization of ARF, a protein with a pivotal role in keeping cells from becoming cancerous.

Like several other members of the BSA, Sherr began his cancer research career with the study of tumor-associated retroviruses, once thought to be a principle cause of cancer. After completing his M.D. and Ph.D. at New York University in 1972, Sherr joined the National Cancer Institute where he identified and cloned oncogenes from feline retroviruses. These successes led to his recruitment to St. Jude in 1983 to help establish a new department of tumor cell biology. By then, viral oncogenes were known to be mutated copies of genes from the animal host, and Sherr's lab soon worked out the normal function of one of his cloned genes, FMS. The Howard Hughes Medical Institute began funding Sherr's work in 1987.

Sherr altered course a few years later when his discovery of



the D-type cyclins led him to begin thinking about the importance of cell cycle regulation in cancer progression. Much of the lab's effort is now directed at ARF, a protective gene that is mutated or deleted in many forms of cancer. ARF senses persistent cell-division-promoting signals of the sort that arise when cellular oncogenes are inappropriately activated and directs the cell to stop dividing or even to commit suicide if the damage is not repaired. "You can think of ARF as a fuse that recognizes mitogenic current. When the current gets too high, the fuse flips," Sherr says.

Although Sherr has never hosted a JCC fellow, he has attended the fall symposium and says he is well aware of the high caliber of the post-docs the fund supports. His four-year term begins this fall.

John Kuriyan

Structural biologist John Kuriyan is a Howard Hughes Medical Institute Investigator with a joint appointment to the Departments of Molecular & Cell Biology and Chemistry at the University of California,

Berkeley. His lab's two main thrusts are aimed at understanding the macromolecules that send and receive intracellular signals and the machinery that replicates DNA.

In the realm of signaling, Kuriyan has focused on tyrosine kinases, which pass messages within cells by adding phosphate groups to tyrosine residues on other proteins and are particularly relevant to cancer. In 1992, Kuriyan's laboratory became the first to work out the structure of a phosphotyrosine recognition domain (SH2) bound to a phosphopeptide, thereby elucidating the nature of one of the key "molecular handshakes" that transmit signals inside animal cells. The laboratory later determined how two cancer-related tyrosine kinases, Src and Abl, are shut down by SH2 domain interactions.

Hyperactive Abl signaling causes chronic myeloid leukemia (CML), and Kuriyan's work explained how the cancer drug Gleevec, made by Novartis, selectively hobbled Abl by binding exclusively to its inactive conformation. When Gleevec resistance emerged in some CML patients, Kuriyan helped show the cause to be Abl mutants that either blocked Gleevec binding or failed to adopt the inactive conformation. These and Kuriyan's ongoing structural studies of kinases are now aiding in the development of kinase inhibitors less likely to promote resistance.

Among Kuriyan's achievements in the study of DNA replication is the discovery and



cataloging of the sliding clamp component of polymerases. In the early 90's, he showed that the beta subunit of *E. coli* DNA polymerase III was in fact a closed circular structure that surrounds the DNA. This processivity factor, or sliding clamp, keeps the polymerase attached and mobile during replication and has proven to be essential to the action of DNA polymerases that replicate chromosomes. Kuriyan's team went on to determine the structure of the clamp loader complexes that open the clamp and position it on DNA, as well as the structure of the chromosomal replicase in bacteria.

Kuriyan holds a reputation as an engaging mentor and avid teacher of both graduate and undergraduate students, and he says he is eager to help choose the most promising candidates for JCC funding. "The Jane Coffin Childs fellowship program has been instrumental in allowing young scientists to take on challenging projects in laboratories such as mine," Kuriyan says. "I look forward to working with the JCC board in helping to select the very best people for this prestigious award".

2007



Cynthia Kenyon

Cynthia Kenyon, an American Cancer Society Professor in the Department of Biophysics and Biochemistry at the University of California, San Francisco, jump-started the study of the genetic regulation of aging 15 years ago when she described mutant roundworms with twice the normal life span. Since then her work has revealed that death is not just the end result of a gradual decline but an intricately regulated life stage inscribed in the genes.

Soon after her initial discovery in *Caenorhabditis elegans* of a life span regulator, which proved to be the insulin receptor DAF-2, Kenyon found that a second gene was needed for *daf-2* mutants to live so long. This gene, *daf-16*, encodes a transcription factor which has since turned out to be a linchpin for the entire system of life span control in *C. elegans*. In a tour de force, Kenyon's lab used microarrays to find out which genes are regulated by DAF-2 and DAF-16, and then knocked each one out in vivo using RNA interference in order to learn its function. They discovered that DAF-16 is

a master regulator of a wide range of proteins, from antioxidants to antimicrobials, each of which has an incremental effect on longevity.

Numerous signals, both endogenous and exogenous, have been found to affect life span through the action of DAF-2 and DAF-16. For example, Kenyon's group discovered that sensory perception controls the aging process, as do signals from the reproductive system. Remarkably, by perturbing several processes at once, it has been possible to increase the lifespans of healthy animals by six fold.

Most recently, Kenyon has advanced our understanding of how these life span regulators stave off the grim reaper. In a Science paper last year, she showed that life span extending mutations specifically antagonize tumor growth, rendering certain tumor-promoting mutations harmless. Thus the link between aging and cancer may be more direct than previously thought.

Kenyon is the director of the Hillblom Center for the Biology of Aging at UCSF, as well as a member of the National Academy of Sciences and the Institute of Medicine. As a member of the BSA, she joins a group of accomplished biologists that includes, as it happens, Graham Walker of MIT, who directed her PhD thesis 26 years ago. *

The Jane Coffin Childs

MEMORIAL FUND FOR
MEDICAL RESEARCH

Current Board of Scientific Advisers

2007-2008

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Berkeley
- **Dr. John Kuriyan**
Departments of Molecular & Cell Biology and Chemistry,
University of California,
Berkeley
- **Dr. Elizabeth Blackburn**
Department of Biochemistry and Biophysics, University of California, San Francisco
- **Dr. Susan McConnell**
Department of Biological Sciences,
Stanford University
- **Dr. Peter Cresswell**
Section of Immunobiology,
Yale University School of Medicine
- **Dr. Thomas D. Pollard**
Departments of Molecular, Cellular & Developmental Biology and Cell Biology,
Yale University
- **Dr. Elaine Fuchs**
Laboratory of Mammalian Cell Biology and Development,
The Rockefeller University
- **Dr. Charles Sherr**
Department of Genetics & Tumor Cell Biology,
St. Jude Children's Research Hospital
- **Dr. Tony Hunter**
Molecular and Cell Biology Laboratory, The Salk Research Institute for Biological Studies
- **Dr. Pamela A. Silver**
Department of Systems Biology,
Harvard Medical School
- **Dr. Cynthia Kenyon**
Department of Biochemistry and Biophysics, University of California, San Francisco
- **Dr. Graham C. Walker**
Department of Biology,
Massachusetts Institute of Technology

Fellowship Application Information

The Fund awards fellowships to qualified individuals for full-time postdoctoral research on cancer and related subject areas. Applicants should not have more than one year of postdoctoral experience and should hold either an M.D. or a Ph.D. in the field in which they propose to study. In some cases, evidence of equivalent training and experience will be accepted. The appointment normally lasts three years. The basic stipend for the 2008 recipients will be \$43,000 the first year, \$44,000 the second, and \$46,000 the third. Applications for 2008 must be received by Thursday, February 1, 2008.

Applications must be submitted electronically.

For details, please visit the Fund's website at www.jccfund.org

The 2007 Retreat

Challenges in Biomedical Sciences: Stem Cells

October 12–14, 2007

Interlaken Inn, Lakeville, Connecticut

HOSTED BY

Dr. Elaine Fuchs and Dr. Elizabeth H. Blackburn

SPEAKERS

Arturo Alvarez-Buylla
Department of Neurosurgery,
University of California,
San Francisco, California

Elaine Fuchs
Head, Laboratory of
Mammalian Cell
Biology and Development,
The Rockefeller University,
New York, New York

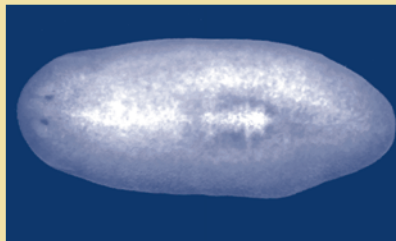
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Leonard Zon
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Stem Cell Research Program
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Planarians, like Schmidtea mediterranea, completely regenerate severed portions of their bodies. Now they are yielding insights into stem cells.

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The Jane Coffin Childs

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