



MCDB Newsletter

Yale University

July 2001

Corporate Partners Program Launched

The Departments of Molecular, Cellular & Developmental Biology; Molecular Biophysics and Biochemistry; and Chemistry are establishing an interdisciplinary industrial affiliates program. This effort is called the Yale University Partnership in the Biological and Chemical Sciences (YPBCS), designed to increase interactions between Yale scientists and members of the biomedical/biotech industrial community. The goals are to promote closer ties between academia and industry and to communicate Yale's scientific excellence in biomedical and biotechnology research in order to benefit society. The first three members of this partnership are Boehringer Ingelheim, Schering-Plough and Merck.

YPBCS Features

- Annual research presentation event for YPBCS members and Yale faculty

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Welcome to New Faculty

Dr. Christine Jacobs arrived at Yale in January of this year. She was awarded an



MS in Biochemistry at the University of Liège in Belgium. She received her doctoral training under the shared supervision of Dr. Jean-Marie Frère at the Center for Protein

Engineering, University of Liège, Belgium and Dr. Staffan Normark (Microbiology and Tumor Biology



Dr. David Wells arrived at Yale in January to join the MCDB department as an assistant professor. He completed his undergraduate and Ph.D. work at The University of Vermont, receiving a Ph.D. from the Department of Anatomy and Neurobiology. He

then went to the Biology Department at the University of Michigan for two years as a post doc in the lab of Dr. Richard Hume.

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YPBCS continued

- Invitations to departmental retreats
- Invitations to departmental symposia
- Invitations to seminars
- YPBCS members recruiting, including intern ships, among Postdoctoral Fellows and Graduate Students
- Quarterly newsletter
- YPBCS website
- Preprint/reprint service
- Special-Topics Meetings. Half-day work shops attended by YPBCS members and Yale faculty in small groups (sample topics follow).
 - a) Current Advances in Nucleic Acid Chemistry/Biology
 - b) Genomics/Proteomics
 - c) Recent Advances in Organic Synthesis
 - d) Plant Molecular Biology
 - e) Computational Chemistry/Biochemistry
 - f) Frontiers in Structural Biology/Biochemistry
 - g) Current Topics in Molecular Recognition
 - h) Pharmaceutical Target Validation
 - i) State of the Art Imaging Technology
 - j) Genetic Model Systems of Disease
- Access to:
 - a) Visits-in-residence for YPBCS scientists; exchange opportunities between corporation scientists, university students, post-doctoral candidates, and faculty
 - b) Special tutorials for YPBCS scientists
 - c) Participation in research centers, opportunities for research collaboration
 - d) Participation on Corporate Advisory Committee (in formation).

For more information, visit the website at <http://research.yale.edu/ypbcs>.

**MCDB Research Funds
Continue to Grow**

1997-98	\$9,657,947
1998-99	\$12,255,317
1999-00	\$12,337,621

Christine Jacobs, continued

Center, Karolinska Institute, Sweden). She was the 1997 Grand Prize Winner of the Amersham Pharmacia Biotech and Science for her PhD work on β -lactam antibiotic resistance and cell wall sensing in Gram-negative bacteria. To acquire knowledge in bacterial genetics and cell biology, she then joined as a postdoctoral fellow the laboratory of Lucy Shapiro at Stanford University where she studied cellular polarity and cell cycle control in a prokaryotic model system. At Yale, The Jacobs lab is using the bacterium *Caulobacter crescentus* to unravel the regulatory mechanisms controlling differentiation and cell cycle progression. The lab is occupying space on the 10th floor of the Kline Biology Tower.

David Wells, continued

Here, he examined synapse formation using intracellular and patch clamp electrophysiology. He pursued the study of synapse formation at a more molecular and cellular level upon joining the lab of Dr. Justin Fallon in the Department of Neuroscience at Brown University. While at Brown University, Dr. Wells began studying how mature synapses in the brain are able to modify based upon activity, a process that is thought to play a critical role in learning and memory. At Yale, the Wells lab is continuing to examine how sensory experience and neural activity can induce changes in neuronal synapses. Dr. Wells' lab is located on the newly renovated second floor of the Kline Biology Tower.

New Staff in MCDB

Jureen Li - Administrative Associate in the Deng Li Lab for the Yale Peking Center.

Xi (Lucy) Liu - Lab Assistant in the Snyder Lab.

Gladis Thomas - Research Assistant in the Wells Lab.

Wanling Zhu - Lab Assistant in the Dinesh-Kumar Lab.

Faculty Awards and Honors

Sidney Altman

Dr. Honoris Causa in the Sciences, Lake Forest College

Ronald Breaker

Plenary Lecture at the 7th International Meeting on DNA Based Computers in Tampa Florida (June 13). The presentation is entitled "Nucleic Acids as Catalysts and as Molecular Switches".

John Carlson

Presented a lecture in the NIH Director's Lecture Series 2000, entitled "Olfaction in *Drosophila*: Genetics and e-Genetics". The lecture was televised.

Xing Wang Deng

Keynote address on light control of plant development at the 6th International Congress of Plant Molecular Biology, Quebec.

Michael Snyder

Plenary Speaker at the Cold Spring Harbor *Arabidopsis* Genome Meeting, December 2000.

Faculty Promotions

Xing Wang Deng

Promoted to full professor.

Shirleen Roder

Eugene Higgins Professor of MCDB, an endowed professorship.

Michael Snyder

Reappointment as MCDB Chair for a term of 3 years.

Senior Awards Class of 2001

Edgar J. Boell Prize

"for excellence in undergraduate senior research"

Dustin F. Khiem, SM

Senior project title: Anti-thrombix Mechanism of *Schistosoma mansoni*.

William R. Belknap Prize

"for excellence in Biology"

Whitney Paige Bowe, MC
Alexander Iribarne, CC
Michelle Ju Yoon Lee, TC
Katherine Anne Mason, ES

Congratulations to MCDB Ph. D.'s

and their thesis titles

Theresa Hill

Analysis of the Cis-Regulatory System of the *Arabidopsis* Floral Homeotic Gene APETALA3.
Ph.D. advisor: V. Irish.
Currently a postdoctoral fellow at U. California, Davis.

Pablo Jenik

Clonal and Mosaic Analyses of the Floral Homeotic Gene APETALA3 in *Arabidopsis*.
Ph.D. advisor: V. Irish.
Pablo is a postdoctoral fellow at U. of Wisconsin, Madison.

Nina Matova

Studies on the Regulation of Final Cytoplasm Transport During Oocyte Development in *Drosophila melanogaster*.
Ph.D. advisor: L. Cooley.
Nina is a Research Fellow at Memorial Sloan-Kettering Cancer Center, NY.

Lihao Meng

Eponemycin and Epoxomicin as Probes of 20S Proteasome Function.
Ph.D. advisor: C. Crews.
Currently a Postdoctoral Associate, MCDB, Yale University.

Zia Ur Rahman

The Role of Regulator of G-protein Signaling (RGS9) Proteins in Drug Addiction.
Ph.D. advisor: E. Nestler.
Zia is a Postdoctoral Research Fellow at U. of Texas Southwestern Medical Center, Dallas.

Graduate Student Fellowship

Scott Kreher received a 3 year NSF Graduate Fellowship and will be working with John Carlson for his Ph.D. research.



Dustin Khiem and his senior thesis advisor, Michael Cappello, at the poster session for MCDB senior projects.

Photo: William Segraves

Faculty Profile

Shirleen Roeder

Professor Shirleen Roeder was a graduate student at the University of Toronto, where she studied the replication and packaging of the bacteriophage chromosome DNA in Paul Sadowski's lab. She was a post-doctoral fellow in Gerry Fink's lab at Cornell University, where she was one of the first researchers to identify transposable elements in budding yeast. Since her move to Yale in 1981, Dr. Roeder's research has focused primarily on meiotic chromosome metabolism using budding yeast as a model system.

Meiosis is a special type of cell division that produces haploid gametes from diploid parental cells. The reduction in chromosome number occurs at the first division of meiosis, during which sister chromatids remain associated but homologous chromosomes segregate to opposite poles of the spindle apparatus. Reductional chromosome segregation depends on a complex series of interactions between homologous chromosomes that occur during meiotic prophase; these include homolog pairing, genetic recombination and formation of the synaptonemal complex. The Roeder lab is interested in the entire spectrum of meiotic interhomolog interactions. They are also interested in the mechanisms that regulate meiotic cell cycle progression such that chromosome segregation does not occur until the necessary interactions between homologs have been successfully executed. In humans, meiotic chromosome nondisjunction leading to aneuploidy is the predominant cause of spontaneous abortions and a major source of birth defects. Thus, an understanding of meiotic chromosome behavior is of critical medical importance.

The Roeder lab has used genetic methods to isolate and characterize yeast mutants defective in meiosis. In addition, they have used cell biological approaches to localize proteins within meiotic cells and to identify interactions between meiotic proteins. Using these methods, they have identified yeast genes that encode building blocks of the synaptonemal complex, and they have used mutants in the corresponding

genes to investigate the functions of the complex. They have shown that synaptonemal complex assembly initiates at the sites of meiotic recombination events. They have demonstrated that telomeres play an important role in the pairing of homologous chromosomes during meiosis.

Exciting research is currently underway in the Roeder lab. Jennifer Fung and Tomomi Tsubouchi are studying the distribution of meiotic crossover events along and among chromosomes. They have obtained evidence that at least two different mechanisms operate to regulate crossover distribution. In

contrast to expectation, their data indicate that crossover distribution is largely independent of synaptonemal complex formation. Laurent Maloisel has demonstrated that DNA polymerase d (an essential replication enzyme) plays a role in meiotic recombination by characterizing a novel allele of polymerase d that affects meiotic recombination specifically. Beth Rockmill has been studying the yeast Sgs1 helicase, a homolog of the human proteins involved in Bloom's and Werner's syndromes. She has obtained evidence that Sgs1 regulates the early pairing of homologous chromosomes prior to synaptonemal complex formation. Erica Hong has demonstrated that the DNA damage checkpoint

protein Ddc1 localizes to the sites of meiotic double-strand break repair, consistent with the hypothesis that Ddc1 acts as a sensor of DNA damage. Hideo Tsubouchi is studying a complex of meiosis-specific proteins, Hop2 and Hop3, that act to prevent synapsis between nonhomologous chromosomes. Studies of this complex are likely to provide insight into the mechanisms that distinguish genuine homologs from homologous sequences dispersed among nonhomologous chromosomes (e.g., transposable elements).

Dr. Roeder was appointed as an Investigator of the Howard Hughes Medical Institute in 1997. This year, she was named Eugene Higgins Professor of MCDB. Dr. Roeder holds a joint appointment in the Department of Genetics in the Yale School of Medicine.



ment. "Then you have a good idea of how a transcription factor turns cells into what they normally do. The transcription factors we tested govern the cell cycle. They tell the cell it's time to enter a new cell cycle, when it's time to make a new cell."

In the study, published in the Jan. 26th issue of the journal *Nature*, researchers in the Snyder lab in collaboration with researchers at Stanford University identified almost 250 genes that were bound by these key transcription factors. Many of these genes are known to play a role in the start of a new cell cycle. But many genes with unknown functions were also identified.

The principal authors of this study were Christine Horak, a graduate student in Michael Snyder's laboratory in MCDB, and Vishwanath Iyer, currently a professor at the Institute of Molecular and Cellular Biology at the University of Texas in Austin. Coauthors include Charles Scafe, a postdoctoral fellow in genetics at Stanford; David Botstein, a professor of genetics at Stanford; and Patrick Brown, a Howard Hughes investigator and professor of biochemistry at Stanford.

Christine Horak

New Postdoctoral Fellows in MCDB

Anapuma Dahanukar is a NIH Fellow in John Carlson's lab studying "Odorant Receptors and Olfactory System Development".

Ghia Euskirchen joined Michael Snyder's lab with a NIH Fellowship working on the "Transcriptional Circuitry of the Yeast Cell Cycle".

Stephanie Leuenroth was awarded an American Cancer Society fellowship working on "Identifying Triptolide Binding Proteins: Validating Antitumor Drug Targets". She is in Craig Crews lab.

A recent paper from the laboratory of **Dr. Craig Crews** looks at the active ingredient of a popular herbal medicine. Each year, more and more people around the world turn to traditional herbal medicines to supplement (or supplant) 'modern' pharmaceuticals. This significant increase in the use of herbal medicines has occurred despite continuing concerns over their efficacy.

One commercially available traditional medicine gaining in popularity is the medicinal herb, Feverfew, whose therapeutic properties were first documented in the Roman era. While long considered useful for arthritis and rheumatism, Feverfew extract is used primarily today for the treatment of migraine headaches. Despite its long history and current widespread use, the specific mechanism of Feverfew's biological activity has remained unknown.

Led by biology graduate student Ben Kwok and chemistry postdoc Dr. Michael Elofsson, researchers in the Crews lab have used a combination of chemical and biochemical approaches to investigate the mode of action of Feverfew. As reported in a recent issue of *Chemistry and Biology*, the Crews lab demonstrated that Feverfew's active component, the sesquiterpene lactone parthenolide, covalently binds to and inhibits the activity of a key protein involved in mediating the inflammatory response.

This protein, I κ B kinase beta (IKK β), is a critical player responsible for interpreting and transducing extracellular pro-inflammatory signals into intracellular responses. These responses include the expression of genes required to produce the familiar swelling and redness associated with inflammation. Given the importance of IKK β in the pro-inflammatory signal transduction pathway, these results provide both a novel molecular tool for IKK β investigation as well as may possibly serve as the basis for new anti-inflammatory therapeutics.

The paper can be found at: <http://www.elsevier.nl/gej-ng/10/14/33/36/56/article.pdf>



MCDB Office Staff

from left to right:

Brian Blake, Angela Lee, Nancy Carrigan, Bonita Potter, Valerie Butler (kneeling), Carol Hwang, Barbara Cangiano, Tara Noel.

photo: Greg Fitzgerald

the monthly grant status reports that go out to all faculty and for the departments quarterly operating expense reports.

Brian Blake – Accountant. Brian is a new addition to the MCDB Business Office and is responsible for almost all of the accounting functions done in the Business Office. He is responsible, in part, for

Valerie Butler - Financial Assistant / Purchasing Manager. Valerie has been with the office for 7 years and is responsible for purchasing items for all areas of MCDB. Any and all purchasing questions should be directed to Valerie and she is also the person to see about petty cash.

Barbara Cangiano - Sr. Administrative Assistant. Barbara provides support for MCDB faculty in OML and can be found in room 250A. She has worked for the department 10 years and is in charge of maintaining security access for personnel working in the building and preparing class work, manuals, and handouts during the academic year.

Nancy Carrigan – Sr. Administrative Assistant. Nancy has been with the office for 15 years and in addition to any administrative needs that are requested, she is responsible for the Casual and C&T Payroll along with the MCDB Seminar Series.

Carol Hwang - Facilities Coordinator. Carol has been with the office for over 5 years and is responsible for all facilities related situations (i.e. construction coordination, building maintenance, telephone & ethernet requests). Carol is also the person to see for room keys, photo ID activation, network access, email account activation and is the KBT PC Desktop Support Provider.

Angela Lee - Assistant Administrator. Angela has been with the department for 20 years. She started as a Financial Assistant and through the years has been promoted to Assistant Administrator. In addition to those duties as the Assistant Administrator she is the Grants Coordinator/Advisor for the department and is responsible for the Postdoctoral payroll.

Pat Marks - Financial Assistant / Purchasing Assistant. Pat has been with the office for two years now and in addition to many financial and office duties she is responsible for Travel and Employee Reimbursements. When Valerie is away, Pat is the person to see for all of your purchasing needs!

Tara Noel – Secretary. Tara has been with the office for just over a year. She is the person that greets you at the front desk and in addition to her normal office duties will help you with just about anything! In Carol's stead she can hand out room keys and is responsible for handing out C&T and M&P payroll checks on payday!



photo: G. Fitzgerald

Bonita Potter - Office Assistant. Boni has been with the Business office for 6 months and is responsible for Oracle JSA, Labor Distribution transactions and Oracle/Brio reports.

Donald Wiggin – Administrator. Don has been Business Manager for MCDB for almost 15 years. He is one of the chief coordinators for the KBT Renovations Project and is responsible for all MCDB business related decisions.

Tara Noel



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July 2001

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Next newsletter deadline: Dec. 1, 2001



What is this crane doing? As part of the KBT facilities upgrading, one of the largest cranes in CT was brought in to lift sections of duct work to replace connections to the roof air handlers.

Photo by Simon Bernard of Sordoni Skanska Construction Co.