

M C B Transcript

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Newsletter for Members and Alumni of the Department of Molecular & Cell Biology at the University of California, Berkeley

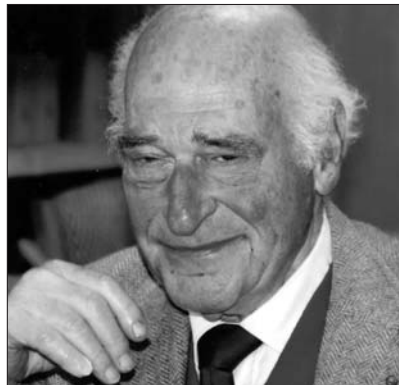
Gunther Stent, Generalist,

Feted at 80

Neurologist Oliver Sacks, chemist Manfred Eigen and biologist Sydney Brenner were among the scientific notables who gathered in Koshland Hall on a sunny April Saturday to celebrate the life and work of Professor Emeritus Gunther Stent. The rare congress of luminaries and Nobel-prizewinners from diverse fields was intended to represent Stent's wide-ranging interests and contributions over the course of his career, which has lasted more than half a century.

Organizers Michael Botchan and David Weisblat originally wanted the symposium to coincide with Stent's 80th birthday last year, but coordinating the visits of so many top scientists proved more challenging than expected, Botchan says. In the end, the April 9 symposium featured seven speakers who spoke on subjects as diverse as genome expression, free will and visual perception. Besides the many local friends, colleagues and interested students who filled Cox Auditorium, former post-docs and graduate students of Stent's turned up from around the country. Throughout the day, Stent looked radiant. "I was completely overwhelmed," he said a week later in his office in LSA.

Stent was among the handful of pioneering scientists whose work launched the discipline molecular biology after the second world war. Having fled Nazi Germany in 1940, Stent went to school in Chicago and later studied physical chemistry at the University of Illinois. But after graduate school, his interests turned to biology. Like many of his contemporaries, he was deeply



Gunther Stent

influenced by physicist Erwin Schrödinger's book *What is Life?*, which suggested that undiscovered laws of physics might be necessary to explain heredity. The book mentioned Max Delbrück as a young physicist with interesting ideas along these lines. So Stent wrote Delbrück to ask if he could join his lab at the California Institute of Technology as a postdoc.

As Stent tells it today, he hardly knew what he was getting into. Delbrück was using bacteriophage to study the nature of genes, and when he offered the young Stent a position, he said: "Do you want to work on phage?" "Yes sir," Stent replied, "that's exactly what I want to work on, but could you refresh my memory as to just what phage is actually all about?"

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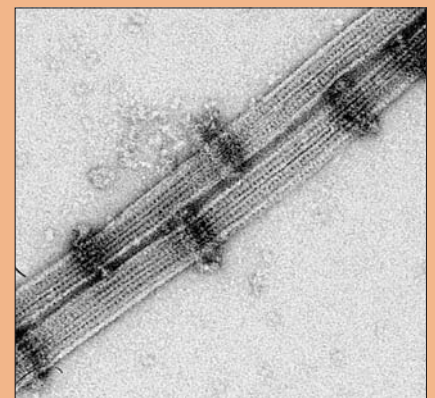
Chromosome

Mystery Solved

Few sights are as awe-inspiring as a cell in anaphase. Seen through the microscope, the replicated chromosomes, having lined up neatly along the midline of the dividing cell like a row of tiny X's, are simultaneously yanked apart. Each X splits into two sideways V's careening in opposite directions, folded at the middle like a running back receiving a flying tackle. It all happens in the blink of an eye in a space smaller than a speck of dust.

The orderly segregation of chromosomes is absolutely essential to ensure that every cell has a complete set of genes. Errors in segregation can sometimes lead to cancer or birth defects. Yet how every cell pulls this off without a hitch nearly every time is poorly understood.

continued on page 4 . . .



Collared: Dam1 rings bound to microtubules
(Courtesy of Stefan Westermann)

... Gunther Stent continued from page 1

Stent came to UC Berkeley as an Assistant Biochemist in 1952, around which time DNA had just become generally accepted as the chemical basis of heredity. At Berkeley, he continued to study the nature of genes and their expression through the use of DNA radio-labeling techniques in bacteriophage and *E. coli*. He helped establish and shape the Department of Virology in 1957 and the Department of Molecular Biology in 1964. He chaired that department from 1980 to 1986 and then served as the founding chair of MCB, which subsumed molecular biology and biochemistry, until 1992.

In the late 1960's, Stent's interest began to turn away from strictly molecular questions. He had decided that the really compelling problems—such as the structure of DNA and the genetic code— had all been solved. As Brenner told the audience at the symposium, Stent liked to say at the time that “molecular biology has such a great future behind it.” What grabbed his interest was neuroscience, and over the next 20 years

he published more than 100 papers on the neurophysiology of the leech.

At the same time, Stent began to explore more deeply his longstanding interest in philosophical questions. He published articles such as “Molecular biology and metaphysics” (*Nature* **248**, 779-781; 1974), and “Limits to the scientific understanding of man” (*Science* **187**, 1052-1057; 1975).

Philosophical claims often provoke controversy, and Stent's were no exception. One article, “Prematurity and uniqueness in scientific discovery” (*Sci Am.* **227**, 84-93; 1972), got him into hot water with colleagues because it described the classic 1944

experiments of Oswald Avery, which demonstrated DNA to be the genetic substance, as an example of premature science. Even though in retrospect the implications of the experiment were clear, Stent argued it had little impact on genetics at the time and few people talked about its significance until years later. But some scientists, including Nobel-prizewinning geneticist Joshua Lederberg, were annoyed by Stent's article, saying they knew full well the implications of the work right away. The paper still touches off philosophical arguments today, much to Stent's surprise. “I thought it was a simple point,” he says.



*Clockwise from top:
Seymour Benzer and Gunther Stent during a break;
Oliver Sacks prepares his talk;
Dale Purves discusses the nature of vision with Jim Watson;
Stent and Eric Wieschaus at lunch.*

Philosophical differences were in evidence at the symposium as well. Noted Berkeley philosophy professor John Searle, who has sparred with Stent on previous occasions, devoted his talk to their disagreement over the nature of consciousness and free will. “The highest compliment one philosopher can pay another is to try to refute something he says,” said Searle. “I’m now going to pay Gunther a compliment.”

The day’s wide-ranging and thought-provoking talks, punctuated with humorous anecdotes delivered in a roast-like manner, kept the audience well entertained. Brenner, Stent’s first postdoc in the early 1950’s and winner of the 2002 Nobel Prize for his work on developmental genetics, discussed his ideas about the relationship between ‘genome’ and ‘phenome.’ Neurologist Oliver Sacks, author of *The Man Who Mistook His Wife for a Hat* and *Awakenings*, described clinical cases of brain lesions that suggest human consciousness is much more modular than it seems.

Other speakers included Princeton University biologist Eric Wieshaus, who shared the 1995 Nobel Prize in Physiology or Medicine for his work on embryonic development, and Manfred Eigen from the Max Planck Institute for Biophysical Chemistry in Göttingen and winner of the 1967 Nobel Prize in Chemistry. Among the well-known figures in the audience were science writer Horace Judson, author of *The Eighth Day of Creation: Makers of the Revolution in Biology*, as well as James Watson and Seymour Benzer, who, with Stent, were members of Delbrück’s “Phage Group” at Cold Spring Harbor Laboratory in New York.

The day was appreciated by young and old alike. “Biology in general should pay more attention to his senior citizens,” said Professor Emeritus Harry Rubin. “It tends to forget its history in the rush to be up to date.” At least on this day, history was remembered.

Ruthild Winkler-Oswatitsch, Manfred

Eigen’s partner and frequent co-author,

took photographs throughout

the day and was kind enough to provide

copies to the *Transcript*. A sampling

appears below.

*Clockwise from right:
Stent unwinds at the end of the
day with Manfred Eigen;
John Searle delivers his critique of
Stent’s ideas on free will;
Stent converses with his former postdoc
(of 50 years ago) Sydney Brenner.*



Now a group of MCB researchers led by David Drubin, Eva Nogales and Georjana Barnes has opened a window to one of the most perplexing aspects of chromosome segregation. In a paper published in January, they describe a remarkable ring complex that attaches the segregating chromosomes to the microtubule fibers that lead to opposite poles of the cell. The rings appear to slide along the microtubule, keeping the chromosome connected even as the microtubule disintegrates and shortens rapidly during anaphase.

"When I first saw the pictures, I thought, 'Wow,'" said BMB professor Jeremy Thorner, "because I was convinced it was a giant step in solving one of the long-standing puzzles about how chromosomes are faithfully segregated at each cell division."

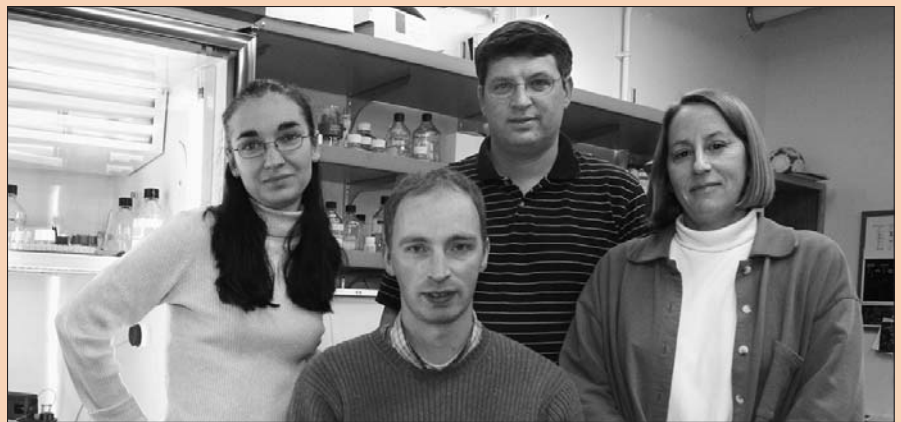
The puzzle has to do with the nature of microtubules. These dynamic rods make up the spindle fibers which guide the two sets of replicated chromosomes to opposite sides of the cell. Microtubules of the spindle apparatus connect to the chromosome via the kinetochore, a massive complex of between 70 and 100 proteins. Yet the microtubules themselves are continually growing and shrinking by adding and dropping subunits at both ends, making it hard to picture how the kinetochore manages to stay attached. "There is continuous flux," says Drubin. "How the

chromosome hangs on has been one of the big mysteries."

The first hint of a solution came in 1998 with the discovery of a protein called Dam1, mutations in which either cause the spindles to break down or produce defects in segregation (*J Cell Biol.* **143**, 1029-1040; 1998). Later, Iain Cheeseman, a former graduate student in the Drubin/Barnes lab, showed that Dam1 was part of a 10-member complex needed for microtubules to attach to the kinetochore (reviewed in *J Cell Biol.* **157**, 199-203; 2002). Postdoc Stefan Westermann, lead author of the new paper (*Molecular Cell* **17**, 277-290; 2005), purified

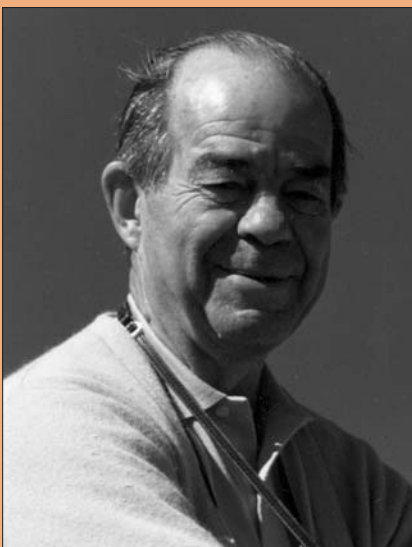
the 10 components and showed that they could form rings around microtubules in a test tube. In the electron microscope, these look something like curtain rings around a rod (see image on page 1). The rings stabilize the microtubules, and, perhaps most strikingly, are able to slide along them in a manner suggestive of the way the entire kinetochore may slide along the crumbling microtubule during anaphase.

Work is now continuing to show how the Dam1 ring fits into the whole kinetochore. But already anyone who peers through a microscope at a dividing cell can have a much clearer picture of what is likely to be going on.



From left: Nogales, Westermann, Drubin and Barnes

MORGAN HARRIS DIES AT 88



Morgan Harris

MCB mourned the loss of Professor Emeritus Morgan Harris this semester. Known for both his rugged outdoorsmanship and his contributions to cell biology, Harris died of pneumonia on February 14 at Kaiser Permanente Medical Center in Oakland. He was 88.

"He was someone who did not go with the fashions," said longtime friend and colleague Harry Rubin. "He went with what he saw. He was a person of absolute integrity — granite solid."

Scientifically, Harris was best known for a series of experiments in the early 1980s which showed that epigenetics can have a profound effect on the phenotype of cells grown

in culture. This finding came at a time when much of the effort in molecular biology was focused on cloning individual genes for various cell and organismal traits. By showing that methylation of DNA could significantly alter a cell's sensitivity to drugs, Harris became one of the first to recognize the importance of epigenetic inheritance.

Harris also produced a classic volume on the behavior of cells in culture. Published in 1964, *Cell culture and somatic variation* is still used in some labs as a reference today.

In his earlier life, Harris was a pioneering rock climber in Yosemite. Together with frequent climbing partner David Brower, the

FACULTY NEWS

Carolyn Bertozzi (HHMI, Chemistry and BMB) has been elected to the National Academy of Sciences. → www.nas.edu

Carlos Bustamante (HHMI, Physics and BMB) made a number of award lists this past year. They include the 2004 Biophysical Society Founders Award, the 2004 Hans Neurath Award of the Protein Society, the 2004 Alexander Hollander Award of the National Academy of Sciences, the 2004 Southern Peru Copper Corporation National Science Prize, and the 2005 Richtmyer Memorial Lecture Award from the American Association of Physics Teachers. Bustamante has pioneered techniques for manipulating single molecules. → alice.berkeley.edu

Walter Freeman (Professor of the Graduate School) received the 2004 Distinguished Service Award of the Knowledge Engineering and Discovery Research Institute at the Auckland University of Technology. → www.kedri.info
He is also the 2005 recipient of the Dactyl Foundation's Annual Prize for applying Science to Literature. → www.dactyl.org

Jack Kirsch (Chemistry and BMB) will be a visiting professor at Uppsala University in June. → www.uu.se

Judith Klinman (Chemistry and BMB) will be awarded an honorary Ph.D. from the University of Pennsylvania in the Spring of 2006. → www.upenn.edu

John Kuriyan (HHMI, Chemistry and BMB) has received the 2005 Richard Lounsbery Award from the National Academy of Sciences "for his critical role in revealing the structural mechanisms underlying processivity in DNA replication and the regulation of tyrosine kinases and their interacting target proteins."

Michael Marletta (Chemistry and BMB) will become the Chair of the Department of Chemistry in July. → chem.berkeley.edu

Susan Marqusee (BMB) will host Visiting Miller Professor Carl Pabo, a structural biologist who has made numerous contributions to the understanding of how proteins bind to DNA. Pabo is Chairman of the Scientific Advisory Board of Sangamo BioSciences, Inc., in Richmond, California. Marqusee was also elected Executive Council member of the Protein Society. → proteinsociety.org

Eva Nogales (HHMI and BMB) is the second recipient of the annual Chabot Science Award, to be presented at the Chabot Space & Science Center's Gala on June 25, 2005.

The \$5,000 award was granted in recognition of Nogales' pioneering work on the structure of tubulin and the nature of its interaction with the cancer drug taxol. → www.chabotspace.org

George Oster (Environmental Science, Policy and Management and CDB) won the second annual Emerson Center Lectureship Award given by the Cherry L. Emerson Center for Scientific Computing at Emory University. → www.emerson.emory.edu

Randy Schekman (HHMI and CDB) has received a Dr. honoris causa from the University of Regensburg. → www.uni-regensburg.de

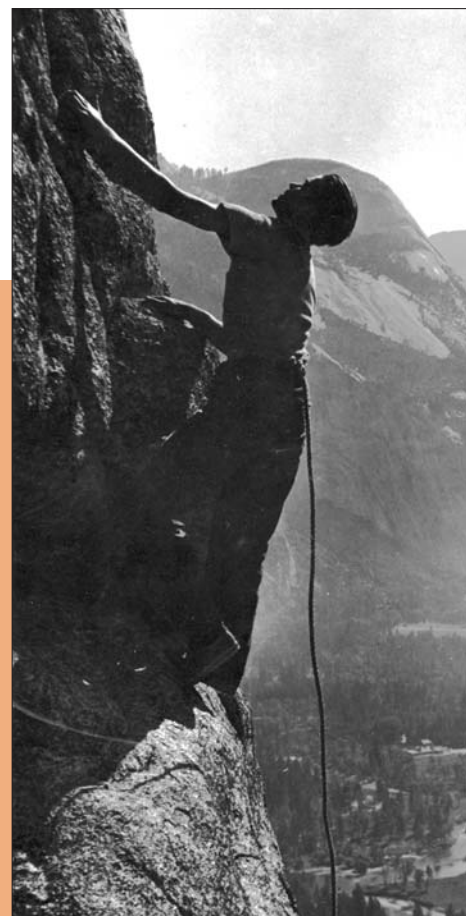
Loy Volkman (Plant and Microbial Biology and BMB) will host Visiting Miller Professor Kathryn Miller, who studies actin cytoskeletal proteins at Washington University in St. Louis. → www.biology.wustl.edu/faculty/miller

environmentalist and leader of the Sierra Club who died in 2000, Harris established 11 climbing routes in Yosemite Valley in the 1930s. Famed nature photographer Ansel Adams captured Harris and Brower reaching a summit in a photograph that later appeared on the cover of an early climbing guide. In 1936, Harris and his fellow climbers pioneered the pendulum traverse, the use of a rope to swing from point to point, during the first climb of Royal Arches. In all, Harris is credited with 14 first ascents in the valley and with establishing the "Shaky Leg Crack" route on the east face of Mt. Whitney.

Harris is survived by his wife, Lola, of Kensington, and two sons, Roger of Seattle and Ronald of Ithaca, N.Y., both of whom are also biologists. He is also survived by four grandchildren.

The family requests that, in lieu of flowers, donations be sent to the Golden Gate Chapter of the Audubon Society, 2530 San Pablo Ave., Suite G, Berkeley, CA 94702-2047.

— *portions adapted from an obituary by Robert Sanders, Media Relations*



Morgan Harris climbing in Yosemite Valley

AWARD WINNERS

GRAD INSTRUCTORS WIN AWARDS

This year, 15 MCB instructors received the Outstanding Graduate Student Instructor Award.



*Annaliese Beery
(Neuroscience Grad Group)*



*Raymond Chen
(Thorner Lab)*



*Benjamin Freedman
(Heald Lab)*



*Oron Frenkel
(Health and Medical Sciences)*



*Lindsay Garrenton
(Thorner Lab)*



*Erin Green
(Kaufman Lab)*



*Katherine Harris
(Beckendorf Lab)*



*Han Lu
(Bilder Lab)*



*Nicole Meyer-Morse
(Portnoy Lab)*



*Sarah Munchel
(Weis Lab)*



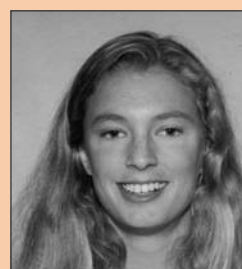
*Yuko Nakajima
(Drubin/Barnes Lab)*



*Catherine O'Connor
(Collins Lab)*



*Rachel Shreter
(Nogales Lab)*



*Jessica Shugart
(Shastri Lab)*



*Peter Woodruff
(Bertozzi Lab)*

CLASS NOTES

- **Derrick Brazill** (PhD 1995) is an Assistant Professor in the Department of Biological Sciences at Hunter College in New York City. (brazill@genectr.hunter.cuny.edu)
- **Elwyn Cabebe** (BA 1992) is finishing his residency in Internal Medicine at Santa Clara Valley Medical Center in San Jose. He will be a Hematology/Oncology Fellow at Stanford starting in July 2005. He is married to a fellow MCB graduate, Emily Lim (1994). They have a one-year-old son, Isaiah.
- **Yu Chin Christine Chen** (BA 1996) received her Master's in Public Health from the Columbia University Mailman School of Public Health (class of 1999). This year she is completing her M.D. at SUNY Syracuse, Upstate Medical University. Her residency will be in Obstetrics and Gynecology. In 2003 and 2004, she was proud to serve as a National Vice President for the International Federation of Medical Students' Associations. At Berkeley, Chen was one of the first students to participate in the Biology Scholars Program (BSP) and the Ronald McNair Scholars Program. She says she attributes her academic and research success to the "solid education" she received from her Berkeley MCB major. Chen welcomes email from classmates and her former faculty mentors. (obgyn05@hotmail.com)
- **Thomas Cunningham** (BA 2000) Is working on his Ph.D. at the University of Illinois, Champaign.
- **Susan DeLong** (BA 1999) is pursuing her masters and PhD in Environmental Engineering at the University of Texas, Austin. Her research is related to bacterial genetics and gene expression for pollutant degrading bacterial cultures in engineered pollutant treatment systems. (susan_delong@mail.utexas.edu)
- **Alexandra Dusa** (BA 2001) received her Master's in Chemistry from UC Santa Cruz in June 2004, and has begun working towards a Ph.D. in Biomedical Sciences at the Université Catholique de Louvain in Brussels, Belgium. (alexandra_dusa@yahoo.com)
- **Christine Fang** (BA 1999) is a fourth-year medical student at the University of Utah and is planning to go into radiation oncology. She will be married in the spring of 2005. (christinefang@gmail.com)
- **Justin Liu** (BA 1995) completed his residency in Physical Medicine & Rehabilitation at Stanford University Medical Center in June 2004. He is now Chair of Back & Trauma Rehabilitation and Vice-Chair of Neurorehabilitation at St. Mary's Medical Center in San Francisco where he runs both an inpatient rehabilitation unit as well as an outpatient clinic. He says despite having trained at Stanford, he has always been die-hard Cal fan at heart. (justinliumd@yahoo.com)
- **Deepak Sarpangal** (BA 2000) is an MBA candidate at the Stanford Graduate School of Business. He is concurrently pursuing a Master's in Education at the Stanford University School of Education. Previously, Sarpangal was an investment banker and private equity investment professional for Goldman Sachs in Menlo Park, New York, and London. (deepaks@stanford.edu)
- **Rommel Suratos** (BA 1996) worked for seven years at Chiron doing mammalian and microbial fermentation as well as protein refolding with the title of Specialist I/Pilot Plant Supervisor. He is currently working at Genentech in South San Francisco where he has been involved in manufacturing technical transfers to the company's plant in Spain. At Cal, he was the Drum Major of the Cal Band in 1994. He is now the proud father of a nine-month-old boy. (rqsuratos@yahoo.com)

CLASS NOTES WANTS TO HEAR FROM YOU

Do you have a Bachelor's, Master's or PhD in Molecular and Cell Biology from Berkeley? Let your classmates know what you are up to by sending in a Class Note for publication in the next issue.

To send your Class Note, you can

- Clip and mail this form
or
- go to mcb.berkeley.edu/alumni/survey.html
or
- Send e-mail to tscript@berkeley.edu

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AWARD WINNERS

UNDERGRADUATE AWARDS

Department of Molecular & Cell Biology

Departmental Citation:

- Huiyi Chen (Bertozzi Lab)

Outstanding Scholar:

- Jamie Harrington
(Andrew Jackson Lab, PMB)
- Kentson Lam (Harland Lab)

Division of Biochemistry & Molecular Biology

Grace Fimognari Memorial Prize

- Aaron Lay (Bilder Lab)

Kazuo Gerald Yanaba & Ting Jung Memorial Prize

- May T. Cho
(Priscilla Cooper Lab, LBNL)

Division of Genetics & Development

Spencer W. Brown Award

- Frederick Ling (Beckendorf Lab)

Division of Immunology

Outstanding Undergraduate

- Calvin Hang (Gregory Aponte Lab, Nutritional Science and Toxicology)

Divisions of Cell & Developmental Biology and Neurobiology

Chaikoff Memorial Awards

- Brandon Beamer (Calendar Lab)
- Caterina Equinozio (Firestone Lab)
- Jamie Harrington
(Andrew Jackson Lab, PMB)
- Gunjan Pantangay (Forte Lab)
- Jeffrey Huang
(Brian Staskawicz Lab, PMB)
- Tsang Lau (Bob Buchanan Lab, PMB)
- Daniel Lo (Firestone Lab)
- David Nguyen (Martin Lab)
- May Wong
(Brian Staskawicz Lab, PMB)
- Ian Kratter (T. Don Tilley Lab, Chemistry)
- Zhenwen Tina Tan (Winer Lab)
- Wendy W. Wong (Dan Lab)

MCB Transcript

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