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Author

Lawrence Berkeley National Laboratory

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LAWRENCE BERKELEY LABORATORY LOG

VOLUME 4 ISSUE 1 • SPRING 1991

Excerpts from a Journal

by Mary Connolly

A view from the other side

"Sixty teenagers? Two weeks in the residence halls? And teaching, too? You must be crazy!" I just nod my head in agreement. It's lectures and labs, bus rides and breathtaking views. It's July and time for High School Honors at Lawrence Berkeley Lab.

As I walk into the dining room for the orientation dinner on Sunday I hear echoes of voices inside the people around me, "Will I make friends? Will I fit in? Am I going to have any fun? Am I smart enough? What am I doing here?"

I am a stranger, too. There are a few silent pauses at first but soon the room is filled with the buzz of conversation. The speakers promise a challenging and busy schedule for the next two weeks. As a returning counselor I have an appreciation for what that really means and I think this group will develop a better sense of that as the days unfold.

On Monday we are badged, bussed, tested, and toured. We work on basic technique in the lab and spool DNA from herring sperm while exchanging stories about where we live and what we do. In the evening we cut and paste paper plasmids and explain the multitude of "options" for off-campus walks, stargazing, and nightly volleyball and softball games. It's only Monday and we're off to a good start.

By Friday we have digested and fingerprinted DNA, toured the inside of Chiron, explored the Exploratorium, and reviewed the rigors of the required proposal. Mina Bissell has inspired us and Allan Wilson has provided some molecular evidence for human origins. Roger Wilson (no relation to Allan) has demonstrated the usefulness of the ubiquitous paper clip while Larry Lack



During a sightseeing trip through the Bay Area, some of the students gathered near the Golden Gate Bridge for a group photograph.



Visiting High School Honors students Anna Bruckner and Robert Danley — lab work was just one of the many aspects of the two-week program.

has investigated the nuances of tautomeric shifts.

Down time

The weekend arrives amid calls for more "down time" and some sightseeing. There's Pier 39, Marine World Africa USA, and a breezy day in Golden Gate Park. A few souls brave the chilly Pacific at Ocean Beach while others play football and frisbee. Some just sit in the sand. Who can forget our own version of "Saturday Night Live"? Hans and Franz pump us up for Paul's palindromes, and we are treated to song, poetry, and a piano piece. Bottle musicians give a whole new meaning to Handel's "Water Music" while Ron and the gang perform a recombinant rap. It is the best show in town!

Weather report for week two

Expect highs in the lows with brainstorms provided by Glenn Seaborg, Charles Cantor, and the Lawrence Hall of Science, followed by intermittent labs, gusts of Greenhouse Gases and Earthquakes by Friday morning. Partly cloudy skies are expected in some areas

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DUB-66

CMB Researchers Study Role of Growth Factor in Tumor Formation

by Diane LaMacchia

Cancerous tumors are not caused simply by the presence of cancer-causing genes, LBL scientists have long contended. The host micro-environment also plays a crucial role.

Now, a close look at that environment by graduate student Michael Sieweke of LBL's Cell and Molecular Biology Division supports the contention that tumor formation is not a simple, one-step event. Working in the laboratory of division director Mina Bissell, Sieweke found that a wound-associated protein called transforming growth factor beta (TGFbeta) helps create the conditions that lead to tumor formation. The results of the study, carried out in collaboration with colleagues at the National Cancer Institute, were published in Science (June 29, 1990).

Most cancer research in the past 15 years has focused on the role of oncogenes, or cancer-causing genes, Sieweke says. But according to findings by Bissell and her associates more than a decade ago, cancer development by oncogenes (in animals as well as humans) is a multi-step process analogous to chemical carcinogenesis.

In the mid-1980s, Bissell and her colleagues identified the role of wound healing in cancer genesis. By wounding chicks previously infected with the Rous sarcoma virus, RSV, (the first and best known oncogene-bearing virus), they induced tumor formation at the wound site. The researchers concluded that the wounding process itself acted as a cofactor with the oncogene to cause cancer.

Taking the study to the molecular level, Sieweke decided to look at the growth factors released as part of the healing process. He knew that one of the most potent was TGFbeta, a protein secreted by macrophages and granulocytes — cells that rush to the site of a wound and cause its typical swelling and redness. TGFbeta enhances the formation and tensile strength of collagen (the fibrous constituent of connective tissue) and can induce the formation in normal skin of new tissue that resembles granulation tissue in wound repair.

TGFbeta causes fibrotic tissue to grow during wound healing, says Sieweke. This interested him because he knew that other research had established that the formation of fibrotic tissue could be a precursor to tumor formation. For example, a person who has a fibrotic or scarred liver (due to genetic reasons or disease) has a greater predisposition to liver cancer. If TGFbeta were the crucial factor, he hypothesized, then either wounding or providing this factor should contribute to tumor growth.

In this study, researchers worked again with the RSV-virus and its

oncogene known as "src." TGFbeta was carefully injected into RSV-infected chicks in small doses via very fine needles so injury would be minimized. Tumors formed according to the level of TGFbeta applied. Other growth factors the researchers tested did not elicit the same response. The study concluded that TGFbeta is indeed a "molecular mediator of wound tumor formation" and "can substitute completely for wounding in tumor induction."

"There may be other factors," Sieweke says, "but this is certainly one crucial one." He cautions, however, that TGFbeta is "a curious factor. It does different things to different cell types." For example, it stimulates the growth of *continued next page*



Graduate student Michael Sieweke working in LBL's Cell and Molecular Biology Division, shown here with division director Mina Bissell.

continued... Excerpts from a Journal

on Thursday accompanied by some enlightening and a sprinkling of frustration about proposals. Friday afternoon should be clear and sunny with a slight chance of tears by Saturday morning.

P.S., I had a terrific time!

Like you, I made some new friends and learned some new things. I wish each of you the very best and hope that you will always have fond memories of your summer in Berkeley. Hey Jean, I miss our evening chats!

Two LBL Honors Students Win Rhodes Scholarships

by Adrienne Kopa

Studying at Oxford as a Rhodes Scholar is a dream that many American college students harbor. This year, for 32 of them, that dream has become a reality. Among the 1991 Rhodes Scholars are Goodwin Liu and Theresa Simmonds, both former High School Honors Program participants at LBL.

During the summer of 1987 — the first year LBL hosted the Honors Program in the Life Sciences — Liu was the California representative to the program, and Simmonds was the Pennsylvania representative.

During the two-week program, Liu worked with ChemBio researcher Jim Bartholomew, studying DNA sequencing techniques and the replication cycle of viral DNA in human cells. This was his first laboratory experience, and he found it "fascinating" to watch scientists at work and to see the high-tech equipment at LBL. He also says it was inspiring to be among a group of his peers who share similar aspirations and are idealistic enough to believe they can make an impact on the world.

Liu originated an Honors Program newsletter, because, he says, seeing a group of people who all had so much to offer — the future "movers and shakers" — made him decide that it was important to keep in touch.

Liu ranked first in his high school class, was editor of the yearbook, captain of the varsity tennis team, and senior class vice-president. He has also been a page in the House of Representatives and an intern for Rep. Robert Matsui (D-Calif.). Now a Stanford University student, he organized an education conference at Stanford last year that brought together students and state government leaders.

Liu plans to spend at least two years at Oxford. He has submitted a proposal for studies leading to a Ph.D. in immunology, but he has many interests particularly in policy-making — that will take him beyond the laboratory.

Simmonds first met Liu during the 1987 Honors Program, then again last summer at Leadership America — a five-week program that focuses on exploring international issues and developing leadership skills. They will meet for the third time at Oxford in October of this year.

At LBL, Simmonds worked with Cell and Molecular Biology researcher Rick Schwarz, studying the production of collagen. She says the summer program at LBL offered an "amazing look at what's going on" — both the complexity of the research and the scope of the scientific work being done.

A National Merit Scholarship winner, Simmonds had attended the governor's



Working with ChemBio researcher Jim Bartholomew (left), Goodwin Liu studied DNA sequencing techniques.

school for science the previous year. Now a senior at the University of Pennsylvania, she is majoring in urban studies and environmental issues.

At Oxford, Simmonds plans to study philosophy, policy, and economics. She hopes in the future to earn both a Ph.D. and a J.D. and also has an intense interest in education, because of the potential for effecting change.

The Rhodes scholarships were established in 1902 by the estate of Cecil Rhodes. Rhodes, a British colonial statesman and diamond king in South Africa, left his fortune to public service.



Theresa Simmonds worked with biologist Rick Schwarz during the 1987 High School Honors Program, studying collagen production.

Each year, 75 scholarships are awarded to students in Britain, the U.S., and several other countries, on the basis of superior scholastic performance as well as outstanding character and leadership qualities.

continued... CMB Researchers

fibroblasts but it inhibits epithelial cells.

"Most of the vicious cancers in humans are carcinomas," says Sieweke. These are cancers that develop from the epithelial, or outer, cells. Because TGFbeta inhibits the growth of the epithelium, Sieweke says that "at first people were excited" about its potential in the treatment of those deadly carcinomas. But while it may inhibit the epithelial cells, the underlying mesenchymal cells are stimulated to create an environment favorable to tumor growth.

Because factors like TGFbeta have multifaceted effects, caution must be exercised before rushing into clinical trials, warns Bissell. And Sieweke hopes the importance of looking closely at these factors will be clear to other scientists through the publication of these results.

Disclaimer

Livermore to Receive Cray Supercomputer

Secretary of Energy James D. Watkins has announced that Cray Research, Inc., designer and manufacturer of large-scale computer systems, has agreed to donate a CRAY X-MP supercomputer to support the Department of Energy's (DOE) Lawrence Livermore National Laboratory's (LLNL) National High School Supercomputer program (NHSS).

The NHSS program is designed to improve high school math and science education throughout the nation by providing supercomputer time and instructional support for the students and teachers. Cray Research has announced that the CRAY X-MP system will be operated exclusively for the NHSS program. This collaborative arrangement provides the first national network dedicated exclusively to high school supercomputing. The NHSS will consist of three elements: the CRAY X-MP supercomputer; DOE's High School Honors Program in Supercomputing — called "Superkids" — which is a two-week summer supercomputing program for high school honor students; and, a new element — beginning summer 1991 the High School Teachers' Supercomputing Workshop.

The CRAY X-MP, which will be available immediately to students and teachers across the nation, has features such as electronic mail and bulletin boards so students, teachers and scientists can communicate. Cray Research has donated half of the annual maintenance cost of the CRAY X-MP and DOE will fund the other half.

If you are interested in learning more about this program, please contact Sue Wiebe at LLNL, (415) 423-9394. This document was prepared as an account of work sponsored by the United States Government. Neither the United States Government nor any agency thereof, nor The Regents of the University of California, nor any of their employees, makes any warranty, express or implied, or assumes any legal liability or responsibility for the accuracy, completeness, or usefulness of any information, apparatus, product, or process disclosed, or represents that its use would not infringe privately owned rights. Reference therein to any specific commercial product, process, or service by its trade name, trademark, manufacturer, or otherwise, does not necessarily constitute or imply its endorsement, recommendation, or favoring by the United States Government or any agency thereof, or The Regents of the University of California. The views and opinions of authors expressed herein do not necessarily state or reflect those of the United States Government or any agency thereof of The Regents of the University of California and shall not be used for advertising or product endorsement purposes.

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Editor: Eileen Engel Assistant Editors: Christopher Slye, Mary Connolly

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Lawrence Berkeley Laboratory Eileen Engel / CSEE Mailstop 90-1070 Berkeley, CA 94720 U. C. Lawrence Berkeley Laboratory Líbrary, Berkeley

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