

# DÉTENTE IN THE LABORATORY

*OU Chemist Bruce Roe proves every day that teaching and research are not mutually exclusive territories.*

by **Randall Turk**

Photography by Gil Jain

Throughout their history, institutions of higher learning have undergone internal struggles involving two primary functions: instruction and research. At the University of Oklahoma and other large institutions, these functions compete for appropriations, grants and endowments.

Proponents of these two camps are often at odds about which function should be given priority in carrying out a university's mission of disseminating knowledge. Some charge that advances in research come at the expense of the undergraduate learning experience; they cite enormous class sizes, the proliferation of graduate assistants in teaching posts and the "publish or perish" principle.

Researchers counter that institutional budgets fall woefully short of providing the sophisticated equipment and attracting the first-rate talent required for significant advances in knowledge. Administrators attempt to placate by compromise, often resulting in universal dissatisfaction.

Is this apparent schism in the priorities of universities destined to grow wider? Will institutions be forced to sacrifice one function for another? Or will a heightened appreciation of the role of research as a teaching tool erode



*OU chemistry professor Bruce Roe, right, with Norman senior Judy Crabtree, is training a new generation of Ph.D.s to take his human genome sequencing research into the next century.*

the barriers dividing the two?

Since 1990, external funding for OU projects has risen from approximately \$60 million to \$100 million per year. Along with that growth in funding has come increased recognition of the research laboratory as a classroom.

Highly specialized research requires substantial amounts of funding, talent and time. To carry on the work, research professors are seeing a need to increase the number of talented stu-

dents in their programs. One example of this development at OU is the work of chemistry professor Bruce Roe, whose human genome sequencing project is part of a national effort that will require many years and hundreds of trained specialists to complete.

Over the past six years Roe and his colleagues have been developing methods for automated DNA sequencing, or deciphering the order of genes in the human body. They also are exploring mutations, or changes in the order of genes, that result in childhood leukemia, tumors and mental retardation. In September the National Institutes of Health awarded a \$1.7 million grant to continue the OU project for another three years.

"We're one of a handful of groups in the world—probably less than 10—doing what we

do," Roe says. "There are too few students trained in these techniques. Part of our role is to train the next generation of Ph.D.s who will take this project into the next century."

Working alongside Roe on the genome project are four postdoctoral students, eight graduate students and four undergraduates. Several dozen other students have worked on the project and moved on over the past three years. The current group of students is the





largest Roe has had at one time in his laboratory. "They work with each other and with me to develop techniques, improve accuracy and interpret data," he explains. "Most critical teaching occurs one-on-one. Lecturing to 200 students is, of course, critical, but you're not the mentor, you're the lecturer."

Roe maintains that research projects not only enlarge the world's body of knowledge but also serve as a teaching medium to help students develop research skills. Actually it is the students who "play in the sandbox," doing the actual research under the leadership and training of professors, he emphasizes. "Projects like mine need hands to do the work and brains behind the hands. If I train 10 students to do these experiments, we can answer 10 times the questions."

Roe has found that the teamwork

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*In Bruce Roe's laboratory, research is the teaching medium with students doing the work under his guidance and leadership. At left, Norman doctoral student Stephanie Chissoe loads samples into a centrifuge, later removed later by Kala Iyer, below, a doctoral candidate from India.*

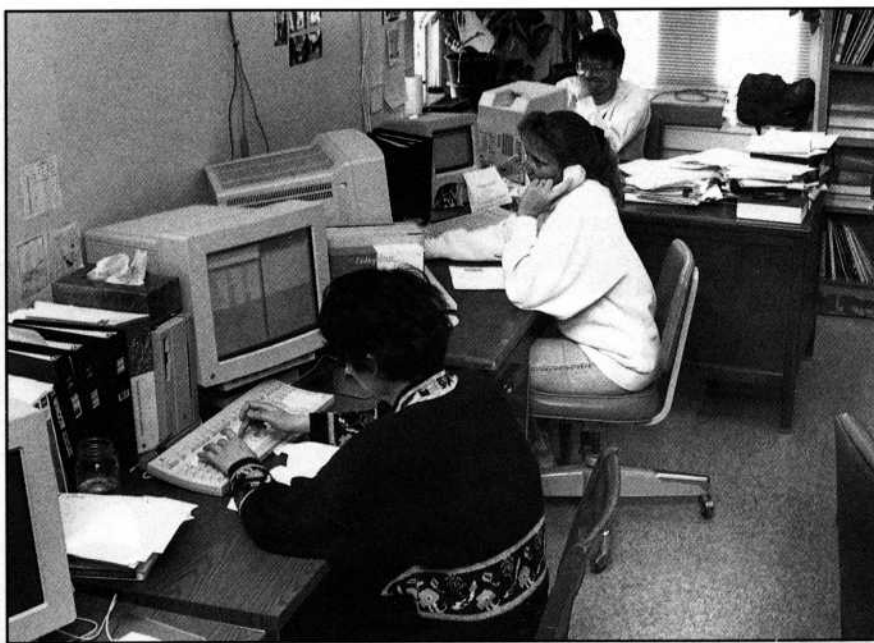




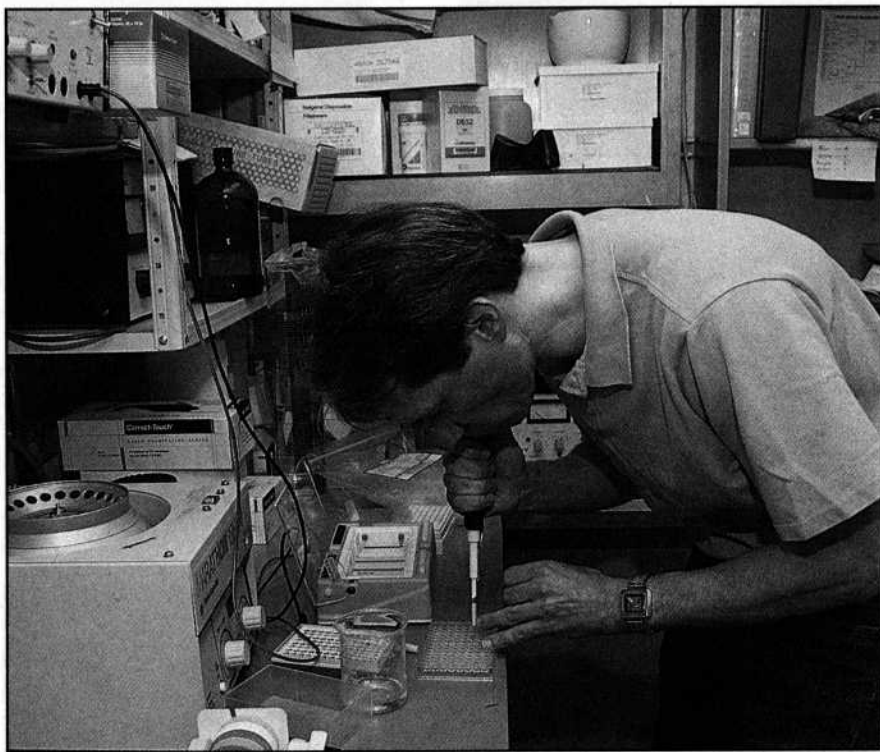
approach with students is crucial to perpetuating his project and laying the groundwork for major findings. "Ultimately it's the graduate student or undergraduate, or post doctoral fellow who works closely with the professor to make the discoveries," he maintains. "The people giving the money to my lab to do the experiments do so because we have outstanding students to do the work."

Roe points out that graduate and undergraduate students work together to improve their skills in interpreting data in conjunction with the project, "learning as they go."

In human DNA, the biological polymer that is the building block of life, there are more than three billion nucleotides, or bases. It is the sequence, or order, of these nucleotides that determines how genes are encoded and used by cells of the body. Roe and his team first must determine in what order the nucleotides are assembled before they



*Computers perform millions of combinations to speed the exhaustive sequencing process necessary to decipher the order of genes in the human body and explore the mutations that result in childhood leukemia, tumors and mental retardation.*



*Roe sees each student in his laboratory as unique, some with more mathematical skills, some more comfortable with computers, others with more manual dexterity. Here Dennis Burian, Oklahoma City, is pipetting DNA sequencing reactions.*

can pinpoint aberrant combinations leading to various cancers and mental retardation. The number of possible combinations is staggering.

To speed up the exhaustive sequenc-

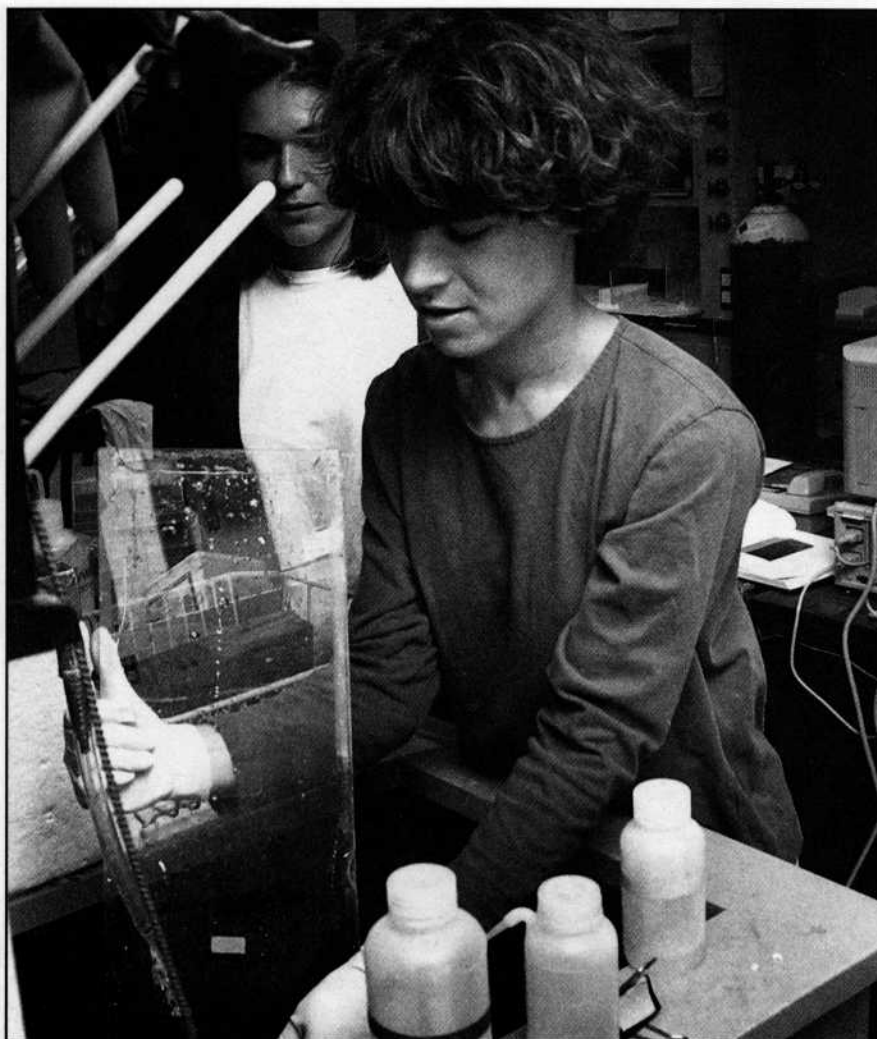
ing process, the project utilizes computers to perform millions of combinations. Computer-driven robots are used to prepare and isolate DNA samples for analysis. "To sequence 20,000 nucle-

otides manually takes a couple of people a year," Roe says. "Now it's possible to automate this process, letting machines collect the data." The computerized process can produce about 40,000 sequences per day.

Each student in Roe's laboratory is unique, with different knowledge, skills and background. "I have a very international laboratory," he notes. "Some students are more mathematical, some more comfortable with computers, others with more manual dexterity. Each one has to be treated differently and taught as an individual."

From the student perspective, the genome project is the source of invaluable research experience. "Dr. Roe likes to talk to you every day. He encourages you to ask questions and solve problems on your own," says Stephanie Chissoe, a Norman doctoral student. For the past two years Chissoe has been analyzing the sequencing data to "close the gaps" and link related parts of the project. "Every day Dr. Roe is teaching us this thought process," she explains. "All of our projects are interrelated. If one group has a problem, it affects all of us. To be a scientist, you're constantly thinking. He never lets you forget that."

In leukemia, genes become translocated or swapped between the 9th and



*Veronique Baud, Paris, France, in back, and Alexandra Freeman, Chevy Chase, Maryland, washing up after a day in the lab, are part of an international group of students Roe has gathered in his effort to train scientists who will make the discoveries and develop the methods to cure the diseases involved in his research.*

22nd chromosomes. Currently the project researchers are studying the "break point" regions of the altered 9th and 22nd chromosomes. That involves determining the sequence of a half million nucleotides.

"We're trying to compare the break point regions in several leukemia patients to see if there are common themes and determine whether there's a predisposition to leukemia," Chissoe says. "This is one of the first ways to establish what causes this kind of cancer."

Guo Zhong, from China, says he has worked for a year to learn the techniques involved in the genome project. A doctoral candidate, Zhong insists that "new students learn from the old" in the laboratory. "We're encouraged to talk to Dr. Roe on what to learn and

the next step in the process. He regulates how the work is to be learned and from whom. It makes the process much easier."

Sandy Clifton, a graduate student in botany-microbiology, was invited by Roe to conduct another gene sequencing project in his laboratory, working as a research assistant on the genome project. She is sequencing a recombination gene in *Haemophilus influenzae*, a bacillus that causes 95 percent of all bacterial meningitis among children in the United States. Her object is to determine how DNA "spills out" of *Haemophilus* cells to invade other cells. The result could be a more effective vaccine.

In her work, Clifton maintains cultures of bacterial clones sent to Roe's

laboratory from around the world. "I confer with Dr. Roe practically every day," she says. "He's generous with his time and very helpful if I have problems with a project or an idea I want to try."

Kala Iyer, a doctoral candidate from India, is working to develop a technique termed "primer walking" to employ fluorescent primers that may speed up the sequencing process. "Every doctoral candidate has to come up with a novel idea," she says. "You have to think critically, analytically."

Like others, Iyer thrives on the informal learning environment in Roe's laboratory. "Anytime you have a problem you can just barge in and talk to Dr. Roe," she says. "You can ask for suggestions. Problems are attacked right on."

Roe is the first to acknowledge that "examining the structure of genes is in its infancy," and much is left to learn before a true picture of human genetic makeup is determined. But, he says, "I would hope in the next 10 to 15 years we will know all the genes in a human being and will be able to compare them."

Once the gene sequence for leukemia is completed, the next step will involve screening leukemia patients to determine "what their real differences are," he says. "Once you get the sequence, you have the initial vocabulary—the words. Right now we've just got the alphabet randomly scattered on the pages."

Will specialized research programs assume the function fulfilled by more traditional classroom instruction? That hardly appears likely, yet emerging changes in approaches to research, particularly the "research laboratory as a classroom," could begin to soften the distinction between these university functions. The object for both is knowledge.

Says Roe of his program: "We're just now developing the tools and training the students to use them to make discoveries about these diseases and develop methods to cure them."

"It's this next generation of students that has to be trained to break new ground. That can be done only in a research environment."

"The University of Oklahoma's attempt to attract external funding for research programs is strengthening the quality of education in our state." 