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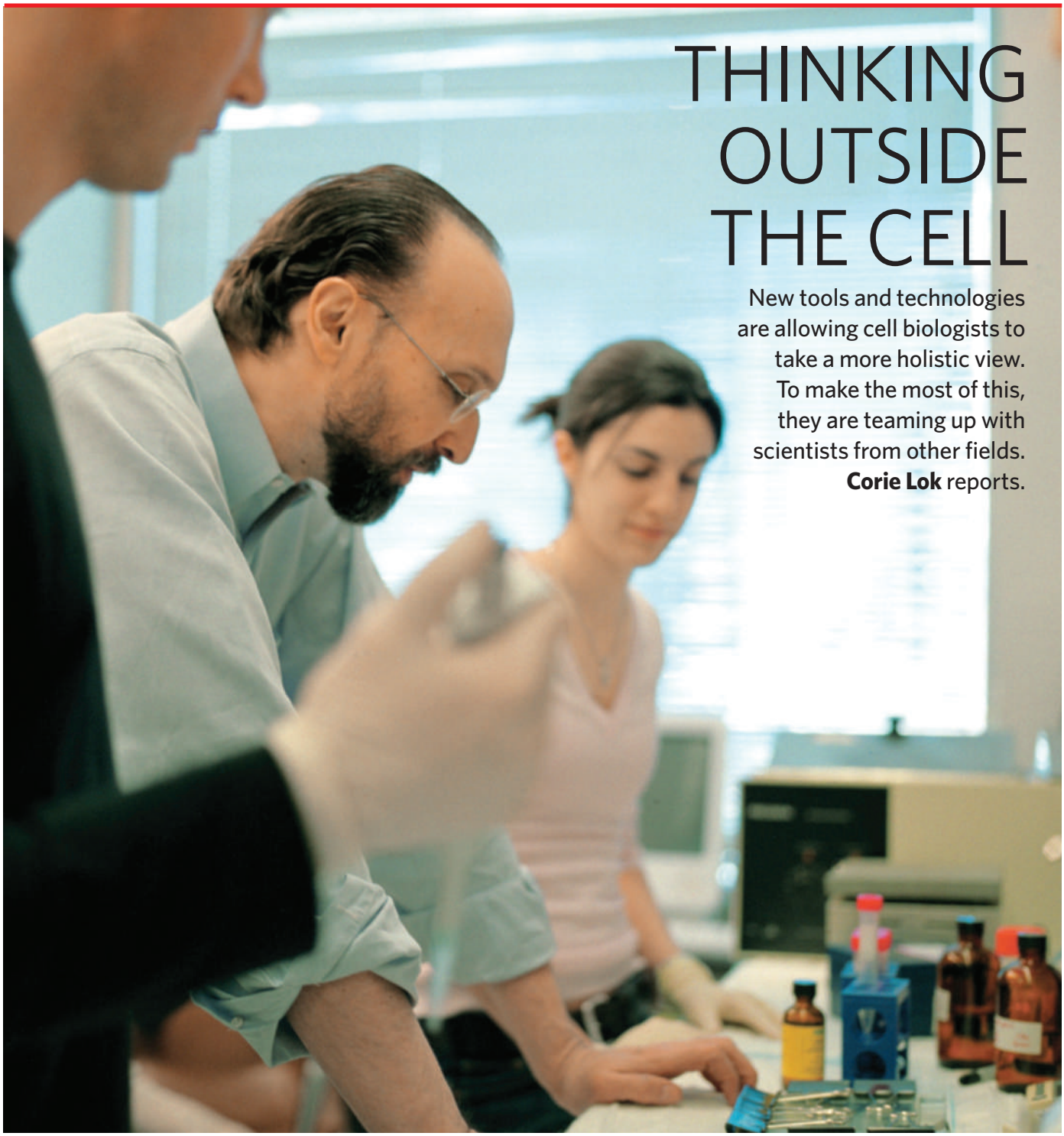

MEMORIAL SLOAN-KETTERING CANCER CENTER

THINKING OUTSIDE THE CELL

New tools and technologies are allowing cell biologists to take a more holistic view. To make the most of this, they are teaming up with scientists from other fields. **Corie Lok** reports.

For the past 20 years, Joan Massagué has been studying the growth factors and signalling pathways involved in cell proliferation and regulation. He has spent most of those years at the Memorial Sloan-Kettering Cancer Center in New York, but his research was still in basic cell biology.

"It was called cancer research because it was being done in the name of cancer, but it wasn't really research on cancer," says Massagué. Now that has changed.

About three or four years ago, Massagué began a project focused on the mechanisms underlying metastasis. Little is known about how tumour cells spread to other tissues and organs. But by then, Massagué felt he and his lab had accumulated enough knowledge and tools through years of basic research to start on the problem. "If I'd made this decision five or ten years ago, I would have gone nowhere," he says. "It's still very difficult and it costs a lot of money, but it can be done now." Earlier this year, his lab published a paper in *Nature* identifying genes that mediate the spread of breast cancer tumours to the lungs (A. J. Minn *et al. Nature* **436,** 518–524; 2005).

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— Kenneth Marians

Because of the new metastasis programme, Massagué has been recruiting more MD/PhD students and MDs as postdocs. Even those trained as basic biologists want to work on the more applied projects. He receives three times more applications for the metastasis projects than for his lab's ongoing basic-science projects.

Massagué's foray into such 'translational' research shows how cell biology is stretching beyond its

traditional borders. With the wealth of knowledge in basic cell biology and the rapid advance in powerful tools and technologies, cell biologists can now ask increasingly complex questions and find applications for the answers. After so many years of deconstructing the cell and its parts, researchers are putting the pieces together. To do so, they are turning to people outside the field — not just clinicians for translation help, but also physicists and engineers to build mathematical models illustrating the dynamics of cellular activities.

Even with this move towards interdisciplinary work, cell biologists emphasize that young researchers more interested in fundamental questions in biology are still in demand. Indeed, about half of Massagué's lab still conducts basic research. But now there is a need for a new kind of cell biologist: one who can, for example, work with human tissue samples and understand a disease process in patients; one who can think quantitatively and communicate with a mathematician; one who can co-author a paper with a physicist.

"What I'm looking for in my lab is interdisciplinary thinking; people who are fearless in pursuing new systems or new technologies," says Randall Moon, a biologist at the University of Washington in Seattle.

A trip to the hospital

Throughout the Sloan-Kettering Cancer Center, biology is shifting towards the clinic. The new Gerstner Sloan-Kettering Graduate School of Biomedical Sciences is recruiting its first class of graduate students, about a dozen, to begin in autumn 2006. The programme will train students to be strong bench scientists. "We also want them to acquire a strong clinical perspective and to understand patient-oriented research," says Kenneth Marians, chair of the molecular-biology programme at the cancer centre and dean of the new school.

The students will conduct full-time lab research, taking a cancer-biology class and working in different labs during their first year before selecting a thesis adviser and launching into their research project. But they can also choose a clinical mentor from the affiliated Memorial Hospital, which could enable them to attend clinical seminars and conferences.

At Stanford University's medical school, another PhD programme designed to bring basic biology and medicine closer will start in September 2006. The first class — six PhD students from Stanford's various biology departments — will take medical-school classes during the first year and a half. They will also take graduate classes and do lab rotations like the other PhD students. In the second year, they will begin their thesis work as usual. By the end, they will graduate with both a PhD and an MSc in medicine. Ben Barres, a neurobiologist who is spearheading the programme, says it is geared towards students who are interested in translational research, but who don't want to spend seven or more years in a MD/PhD programme.

A handful of other US medical schools, including Harvard, have established similar programmes to bridge the divide between basic and clinical sciences.

In Scotland, the Research Institute for Medical Cell Biology at the University of Edinburgh opened this summer and houses 600 bench researchers. It is located next to a new 900-bed hospital and teaching facility to encourage a 'bench to bedside' approach to biological research.

"Clinical research has had an image of being simple," says Alan Hall, director of the UK Medical Research Council's Laboratory for Molecular Cell Biology at University College London. But that is changing, he says. "I think there's a huge need for cell biologists in translational research," agrees Barres.

P. FETTERS

YIBIN KANG

Building bridges between disciplines: Kenneth Marians (opposite), biologist Raymond Deshaies (top), cancer researcher Joan Massagué (middle) and mathematician Alex Mogilner.

Cell biology is branching out not just into the clinical realm, but also into mathematics. Now that cell biologists have sophisticated tools to generate a plethora of data, they need mathematical models to put this information together in a meaningful and comprehensive way. And that means collaborating with engineers, physicists and mathematicians. Modelling is becoming more mainstream in cell biology, thanks to the growing sophistication of the models and the increasing amount of high-quality data to feed into them.

"The rate at which modelling is becoming acceptable has been amazing in the past few years," says Alex Mogilner, a professor in the maths department and the Center for Genetics and Development at the University of California, Davis.

Accommodating complexity

To foster this interdisciplinary work, Cornell University in Ithaca, New York, is building a cell and molecular biology institute, due to open in 2007. The building will house a dozen newly hired cell biologists, nine junior and three senior investigators, plus several other researchers from physics, nanotechnology and other physical sciences in which Cornell has traditionally been strong. "We've now come to appreciate the complexity of the questions we're asking," says Cornell biochemist Rick Cerione, who heads the committee seeking a director for the institute. "We need to bring multiple disciplines to bear."

At the Center for Integrative Molecular Biosciences at the Scripps Research Institute in La Jolla, California, engineer Gaudenz Danuser has teamed up with cell biologist Clare Waterman-Storer. Each mathematician in his lab is matched up with a biologist in Waterman-Storer's lab to work on problems in pairs. At Davis, Mogilner runs a lab jointly with biologist Jonathan Scholey, where they pool resources and students.

It is not clear what the best path is to computational cell biology, or even if there is one. Students can learn both biology and maths in the biological-engineering and systems-biology departments that are cropping up at universities such as the Massachusetts Institute of Technology and Harvard. Danuser says it is better for students to specialize in one or the other while being open to working with people outside their field. One option for a young cell biologist is to do a postdoctoral fellowship in a lab that does a lot of modelling or that collaborates with a lab such as Danuser's.

All those engaging in interdisciplinary research need to be open-minded, flexible and motivated, says Ivan Dikic, a biochemist at the Goethe University School of Medicine in Frankfurt, Germany.

Strengthening the quantitative background would be a potentially useful thing for young cell biologists, says Raymond Deshaies, a biologist at the California Institute of Technology in Pasadena. He lists physics, maths, statistics and even computer programming as important areas. "Even if you don't use them yourself on a day-to-day basis, you might end up collaborating with people from these fields," says Deshaies. "At least you'll be able to talk to them." ■

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