Growth industry

Drug companies are seeking help in their efforts to use the new understanding of cancer's complexities, says Ricki Lewis.

Discoveries in cell and molecular biology, new tools such as gene-expression profiling, and information from the human genome sequence are converging to brighten employment prospects in industrial cancer research. Two of the first cancer drugs to use these sources for 'rational' design — Herceptin, a protein-based treatment for breast cancer, and Gleevec, a small-molecule chemotherapeutic for some forms of leukaemia — are proving successful, and others such as Avastin and Erbitux are already following in their footsteps. This trend has created some bright spots in cancer R&D recruitment, even though drug discovery in general has been adversely affected by mergers, a few high-profile failures and a shaky US economy.

"Everyone is recognizing that there are going to be a lot of opportunities with all of the new information," says Jeff Hanke, vice-president for cancer research at AstraZeneca R&D Boston in Waltham, Massachusetts. Strong medical demand and a tremendous amount of new science makes this the time for a big push, he says. With that in mind, the company has taken on R&D staff in the United States and Britain during the past few years and built a new cancer facility in Waltham. And although opportunities are patchy, with some companies expanding cancer research and some not, there is currently a general upswing in hiring.

A GROWING MARKET

Signs of growth beyond AstraZeneca are clear. About 25% of biotech companies raising venture capital during the third quarter of 2003 listed cancer as their primary focus, according to online newsletter *VentureReporter*. And according to the Pharmaceutical Research and Manufacturers of America, 402 medicines were in development for cancer in 2002, up from 215 in 1996.

One catalyst is the Food and Drug Administration's accelerated drug-approval timetable: its evaluation of Novartis's Gleevec took just three months compared with the standard 10–12 months. But it is the staggering profits of early successes that attract most attention. In 2003, $1.9 billion of the $3.3 billion in revenue collected by Genentech in South San Francisco came from oncology products, mostly the monoclonal antibody-based drugs Rituxan, used to treat non-Hodgkin's lymphoma, and Herceptin.

NOVARTIS

Successes of individual drugs are having "a ripple effect throughout the industry", says Vishva Dixit, vice-president, molecular oncology, at Genentech. And those ripples are reaching the job market. "Oncology is the most active area in pharmaceutical R&D. The job market in cancer research is pretty good at the moment," says Steve Projan, assistant vice-president at Wyeth Oncology Discovery in Pearl River, New York.

Cancer is more of a problem in ageing populations, and the number of cases in the United States is expected to double by 2050, according to the National Cancer Institute (NCI) — unless there are changes in risk, improved diagnosis or new treatments. Although cancer cases are on the rise, so too are pharmaceutical success stories, and these have encouraged private funding. "The sometimes spectacular results with Herceptin have reinforced the idea that there is much to hope for as more biologics are brought to market," says Paul Schimmel, a molecular biologist at the Scripps Research Institute in La Jolla, California. "Much private capital has gone into developing biologics, and this has generated tens of thousands of jobs — many of them high-paying."

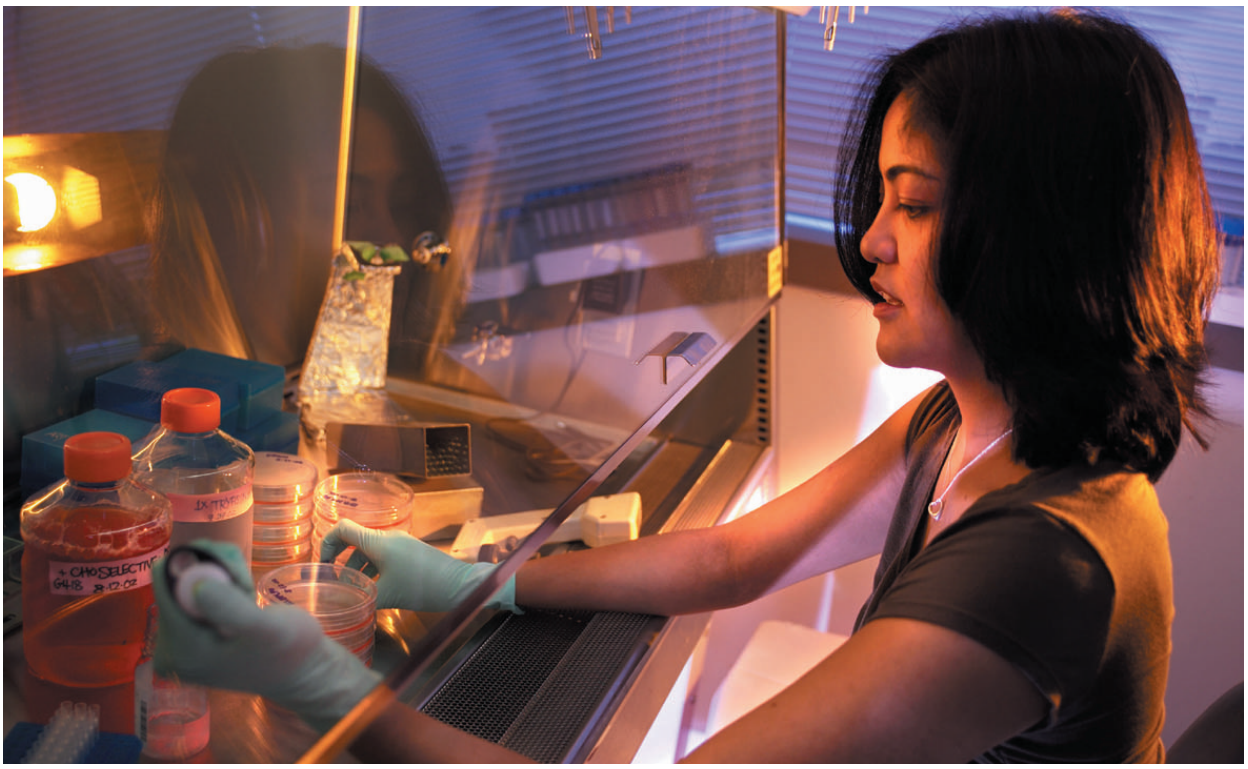
Increased understanding of carcinogenesis is providing new ideas, but market demands and profit potentials are also driving forces. "The ability to fund cancer research fluctuates and is greatly dependent on both internal and external economic factors, which drive hiring," says John Barnes, senior director of human resources at ILEX Oncology in San Antonio, Texas.

SIGNAL STRENGTH

Gleevec led the way in exploiting signal-transduction pathways to treat cancer — it blocks tyrosine kinase enzymes that can help to trigger out-of-control cell division. "Kinase inhibitors can be given safely and with minimal toxicity and have dramatic clinical effects," says Charles Sawyers, a Howard Hughes Medical Institute professor at the Jonsson Cancer Center at the University of California, Los Angeles, and part of the drug's discovery team.

The approach of targeting key signalling molecules is now spreading beyond the tyrosine kinases. For example, AstraZeneca's Iressa inhibits epidermal growth factor and is used to treat non-small-cell lung cancer. Thios Pharmaceuticals in Emeryville, California, focuses on the biochemical pathways that add sulphur atoms to molecules to activate their signalling capabilities. "As our efforts in sulphation targets progress, we will definitely be looking to expand the number of scientists devoted to oncology," says Thios president Bruce Hironaka. A cell biologist with experience in signal transduction could segue nicely into industry, as those pathways are the inspiration for new drug targets.

Subcellular systems other than signalling suggest new targets by revealing new points of vulnerability. The proteasome, for example, a structure that straightens out or dismantles misfolded proteins, is targeted by Velcade, a drug made by Millennium Pharmaceuticals in Cambridge, Massachusetts, that is used against refractory multiple myeloma.



GENENTECH

Hands on: industrial research into cancer therapeutics has received a boost from the recent flood of genome data.

Another new avenue in cancer research is to combine drugs. Wyeth's Mylotarg, for instance, links an antibody to a chemotherapeutic, and homes in on CD33 receptors on acute myeloid leukaemia cells. Expertise in biochemistry, cell biology and immunology is required to develop such a drug.

BACK TO THE FUTURE IN HIRING

The bread and butter of biology — considering entire organisms — is returning to prominence, after decades of focus on the cellular and molecular. New institutes and academic departments devoted to 'systems biology' or 'integrative biology' reflect this trend, and it is important in the industrial cancer-research lab, too (see *Nature* **427,** 568–569; 2004). A good example of the kind of person Genentech seeks is a researcher who can create a transgenic or knockout animal model of a human cancer, and can then image the animal as the disease progresses and it reacts to treatment with a drug candidate, says Dixit.

"Ten years ago, cloners were valuable," Dixit says. "Now we are back to people who have biological insight coupled to expertise in technologies such as transgenics or DNA microarrays."

Because cancer perturbs cells in many ways, expertise in molecular and cell biology is always in demand, as is an ability to wade through vast amounts of data. Not all companies require incoming staff to have a PhD. At AstraZeneca, new employees range from a BSc or MSc with little experience to researchers with decades of experience, says Hanke. At Genentech, employees without a PhD can become a research associate, with pay comparable to that of an associate professor.

In general, as company size increases, focus narrows and salary increases, says Barnes. In other words, a researcher at a smaller company must have broader skills, because there are fewer people to take a drug from concept to reality. "Opportunities are probably better in smaller biotech companies, as young researchers can take over responsibility faster," says Walter von Horstig, chief financial officer of Europroteome in Hennigsdorf, Germany. "Salaries are probably lower. A typical starting salary for a researcher with postdoc experience is about €45,000–50,000 (US$55,000–60,000)."

But those in big drug companies can still be creative, says Ronny Mosston, senior director for staffing at Millennium Pharmaceuticals. "We nurture independent thinking and innovation." Wyeth also encourages researchers to develop their own ideas, says Philip Frost, vice-president at Wyeth Oncology Discovery.

PERSONALIZED PRESCRIBING

In the past, cancers were classified by body part — breast, lung or colon, for example. Gene-expression profiling is changing that picture by splitting cancers into molecularly defined subtypes. This approach will eventually reach the clinic, although the transition from bench to bedside is expected to be slow.

Hanke says that the new strategy will not fragment the market, but reclassify it according to drug response, based on gene-expression patterns. Molecular targeting of drugs will increase efficacy, so that patients will use them for a long time, adds Frost. And increasing profits may translate into more jobs.

With cancer increasingly being seen as treatable, the future for cancer research is bright. "There is exciting science, opportunity, emerging successful clinical trials, and you know you are working in an area of such great medical need," says Hanke. "All of these coalesce and make cancer research a very attractive area." ■

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