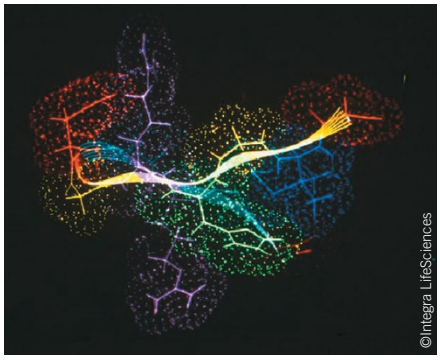
firms announced restructurings in the quarter to damp down their cash burn rates. And in Europe, Nasdaq announced on June 26 that it is shutting down Nasdaq Europe (formerly Easdaq) because of its failure to develop into an influential European IPO market (see p. 840).

Investor attitude toward the sector appears optimistic going forward, even in cash-starved Europe. "Some large funds are now beginning to return to the sector as there is a realization that there are sustainable businesses in Europe developing real products," says Redhead. In the United States, based on early statements of Q203 profits, confidence appears "solid if not strong," says Schmidt.

Peter Mitchell, London

US courts narrow patent exemptions

In June, the US Court of Appeals for the Federal Circuit (CAFC; Washington, DC) issued a ruling in the patent infringement lawsuit *Integra v. Merck KGaA* that is being praised as a victory for biotechnology companies and researchers holding patents protecting their research tool inventions. Despite victory cries in some circles, however, others are warning that this and another recent court ruling endanger the intellectual marketplace on which the biotechnology industry depends.



Integra's patented tri-peptide segment of fibronectin has been deemed a 'research tool'.

The CAFC ruling favored Integra LifeSciences (Plainsboro, NJ, USA) and other company collaborators in their 1996 lawsuit against Merck KGaA (Darmstadt, Germany) plus its former collaborators at the Scripps Research Institute (La Jolla, CA, USA) (*Nat. Biotechnol.* **21**, 725, 2003). The Integra patents cover the discovery and use of peptides that interact with integrins on cell surfaces. Under contract to Merck KGaA, David Cheresh and collaborators at Scripps studied these peptides for potential use as drugs to control tumors. When Merck KGgA refused to license the peptides, Integra sued for patent infringement.

The CAFC ruled that drug research and development activities, such as Merck KGgA's, are not covered by exemptions spelled out under the Hatch-Waxman Act of 1984. The CAFC thus interpreted this federal law narrowly, saying that it permits researchers to conduct studies on drugs (and medical devices) only to provide data to the Food and Drug Administration (Washington, DC, USA) for the purpose of applying for approval of generic drugs.

Another CAFC ruling, the October 2002 *Madey v. Duke* decision (see *Bioentrepeneur*, 13 February 2003, 10.1038/bioent719), focuses mainly on academic researchers who are using patented materials and techniques, threatening enforcement if those researchers do not work out licensing and royalty agreements for such uses.

Together, these two rulings appear to narrow the scope of what inquisitive researchers in industry, universities and nonprofit foundations may pursue without first clearing a path through ever-denser and tangled thickets of patents—a task that may require layers of licensing agreements for researchers to use multi-patent-encumbered techniques or materials whose control is scattered among many institutions.

Thus, the two rulings affect "a huge swath of science," raise policy concerns for both industry and academic institutions, and threaten the possibility that biotechnology researchers will begin receiving "cease-and-desist" letters, thereby interfering with their freedom to conduct experiments, says David Korn, a senior vice president of the Association of American Medical Colleges (Washington, DC, USA). "These issues have profound policy ramifications, and need to be debated outside the courts."

CACF Judge Pauline Newman, in her pointed dissenting opinion to this latest ruling, emphatically takes issue with her colleagues on the underpinnings of the entire decision. She argues that her colleagues are mistaken in calling Integra's patented technology "research tools" and says that it is "illogical" to block research, noting that the patent system traditionally only "bars activity associated with development and commercialization" and the "study of patented information is essential to the creation of new knowledge, thereby achieving further scientific and technologic progress."

Many agree that stifling academic research will not benefit biotech firms, and thus they seem unlikely to file masses of patent infringement lawsuits against universities. "It would be like shooting yourself in the foot," says Ybet Villacorta, an attorney with Katten Muchin Zavis Rosenman (Washington, DC, USA). The Integra case delineates a safe harbor where particular research on patented items is permitted, but wandering outside that harbor makes a researcher fair game for patent-infringement lawsuits, he says. "The big players were ignoring the little guys' patents. The CAFC said, 'this is what the law is about, and I hope that people will behave and observe others' patent rights.'"

Although the lower court told Merck KGaA to pay a $15 million "reasonable royalty" fee using those patented materials, the CAFC in June asked the lower court to reconsider this sum. Its forthcoming reassessment looms as important because it could influence whether other future 'infringers' of patented technology will forego licensing because the costs for ignoring a patent are deemed tolerable or, instead, will seek a license because too much money would be at risk. And when several different patents are being used at once, such costs could add up.

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For the moment, with the Supreme Court announcement in July that it is unwilling to review *Madey v. Duke*, and any changes through appeal of *Integra v. Merck KGaA* not expected anytime soon, these two rulings appear to set a new tone for researchers. "Anecdotally, people are worried" but these rulings "don't really change the status quo," says Lawrence Sung of the University of Maryland School of Law (Baltimore, MD, USA). "The research activities of faculty members can be patent infringements, but whether they're sued is another matter."

Jeffrey L Fox, Washington