IN brief

RNAi patent jolt

The US Patent and Trademark Office has issued a patent for detection of RNA-mediated gene silencing to Sir David Baulcombe, University of Cambridge, and Andrew Hamilton, University of Glasgow, over a decade after their gene silencing findings in plants were first reported (*Science* **286**, 950–952, 1999). "The new patent has implications beyond plants," says Jan Chojecki, CEO of Plant Bioscience Limited (PBL), of Norwich, the tech transfer company that owns the patents. "Anyone in the US profiling short RNAs and their impact on gene expression in mammalian systems is likely to be interested. We think it will create quite a stir." The new patent recognizes Baulcombe and Hamilton's discovery that when genes are silenced complementary RNA strands of 20–30 bp accumulate—a finding that also proved critical to establishing short RNAs as a tool to manipulate gene expression. The initial patent for this technology, issued in 2004, was limited to plants, but the new patent broadens out to mammals. PBL expects to grant licenses to industry but will not enforce rights in academia, provided researchers use licensed detection kits. James McNamara, who directs the Office of Technology Management, University of Massachusetts Medical School, points out that Craig Mello and Andrew Fire, now at Stanford University, developed comparable RNA detection methods. "But if a company practices methods that might infringe on Baulcombe and Hamilton, they might take a license on it for reasonable terms," he says. *Charlie Schmidt*

Court voids HGS gene patent

In the first British case to deal with the validity of a gene sequence patent, a UK Court of Appeal struck down a patent held by Rockville, Maryland–based Human Genome Sciences (HGS) for lack of industrial application. The dispute in *Eli Lilly & Company v Human Genome Sciences, Inc.* centers around the validity of a patent for the neutrokine-α gene sequence. The outcome agreed on in February is expected to have a major bearing on future decisions on the scope of biotech patents, especially gene sequence patents. "The Court of Appeal's judgment will raise doubts over the validity of many biotech patents currently in force, as mere speculation [on] biological function—without experimental data—may not be sufficient, says intellectual property expert Robert Fitt at London-based law firm Bristows. "With pharma's increasing reliance on biotech drugs as a source of growth, the value of many patent portfolios may well be hit hard by this judgment," he says. HGS's patent was initially struck down by the UK Patents Court in July 2008 but later held valid by the Technical Board of Appeal of the European Patent Office. HGS is partnered with GlaxoSmithKline of London to develop an antibody to neutrokine-α called Benlysta (belimumab), for lupus. Lilly is developing its own antibody to neutrokine-α, having already spent some $50 million on its development, with plans to spend another $250 million in clinical trials. *Michael Francisco*

it all the more interesting. Some experts point to the impending comparative effectiveness package as one reason for the surge in personalized medicine approaches. Others are skeptical. "It takes as long as ten years for countries to set up comparative clinical effectiveness platforms," says Paul Keckley, executive director of the Deloitte Center for Health Solutions. "At the end of the decade, that is a strategic opportunity for personalized medicine, but it's a long way away."

Cost reduction is probably the main driver, Generation Health's Gardner believes. "[Genetic testing] addresses one of the areas where costs are growing the fastest and are still largely unmanaged," he says. Keckley agrees that the need to cut healthcare costs is most likely behind the surge in interest in personalized medicine. "Next-generation diagnostics, like Genomic Health's OncoDx, stand to profit from that trend, not drug companies making personalized medicines," he says.

Venture capitalist Dion Madsen and his colleague Stacy Feld at Physic Ventures, San Francisco, also see this as being a moment for diagnostics companies, not pharma. "We're interested in platforms and tools that will enable and inform decision making in the doctor's office or at the hospital," says Feld. The point-of-care aspect is critical in their view. "And we take a broader view of that," Madsen explains. "The point-of-care could be a retail clinic or the consumer themselves." In keeping with that strategy, the group recently invested in the personalized diagnostic firm On-Q-Ity, of Waltham, Massachusetts, which is developing a microfluidic device capable of detecting circulating tumor cells (based on work by Mehmet Toner's group at Harvard-MIT) and raised $26 million in a series A funding round.

The new focus on genetic tests will put drug companies in a predicament, says Peter Keeling, CEO of personalized medicine consulting firm, Diaceutics (Belfast, Northern Ireland). "This is a game changer for pharma, because now someone else will be determining how their drugs are used," Keeling says. Because they will control the testing and apparently much of the growing research in this field, the PBMs [pharmacy benefits managers] will start establishing which patients get which drugs, not the drug companies, as has traditionally been the case. Keeling also sees growing interest in personalized medicine on the part of payors. "A couple years ago they were all sitting on the fence," he says. "That's changed."

Nobody's expecting a stampede of pharmacy benefits managers or payors to follow Medco and CVS Caremark. "I think these companies are making these moves as part of their long-term strategies," says Philip Ma, director in McKinsey & Company's Silicon Valley office and the leader of the company's West Coast Healthcare Practice. "There is no pressing reason for them to enter this market now." Ma points out that there is a lot more "low hanging fruit" for them to squeeze money out of before they'll get noticeable savings from personalized medicine. "I expect they are a lot more focused on the basics, such as negotiating for lower drug prices, getting doctors and patients to comply with formularies, and working with physicians to control use," he says.

But optimism surrounding the feasibility of personalized medicine has been growing. In December, PricewaterhouseCoopers released a report estimating that the core market for personalized medicine—diagnostics and therapeutics—is already worth $24 billion and expected to grow by 10% annually, reaching $42 billion by 2015.

In the short term, however, McKinsey's Ma sees many hurdles to the personalized approach. Doctors may not have many reasons to change their practices yet, and patients can always switch doctors if they feel they are being denied a drug that might help them. Meanwhile, there is still tremendous uncertainty around regulatory issues. Personalized medicine is often spoken of by FDA staffers, but progress on critical issues, such as a drug and companion diagnostic approval pathway, has been very slow. As *Nature Biotechnology* went to press, the FDA's Pharmaceutical Science and Clinical Pharmacology Advisory Committee was meeting to discuss application of pharmacogenomics in the early stages of drug development. FDA commissioner Margaret Hamburg also recently spoke at a luncheon sponsored by the nonprofit, Washington, DC–based Personalized Medicine Coalition. According to a transcript, Hamburg said that the FDA would "issue draft process guidance on biomarker qualification" in the next few months. She also said, "We intend to clarify our expectations for the kinds of clinical trials and levels of confidence needed to satisfy us that a test is accurate and that it can be used to help shape clinical judgments."

If the FDA does take those steps, it might help convince a few more investors that it's time to jump on the personalized medicine bandwagon or risk missing the action. Keckley is optimistic, pointing to the fact that the FDA approved 26 drugs in 2009 and six of those are personalized medicines. "I think Margaret [Hamburg] inherited a fairly dysfunctional and inefficient operation, and she's already improved it," he says. The other missing ingredient, for investors at least, is knowing what direction healthcare reform will go. "There is tremendous hesitancy to move in any direction as long as there is such a big question mark about reform," Keckley says.

Malorye Allison *Acton, Massachusetts*