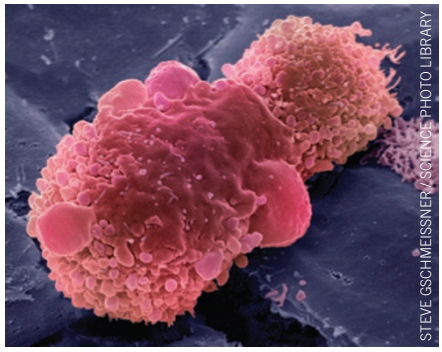
Sequencing firms vie for diagnostics market, tiptoe round patents

Genome sequencing companies are moving into clinical diagnostics, with the number of deals soaring, despite an uncertain patent landscape. This past April, Cambridge, Massachusetts–based personal genomics company Knome announced a strategic partnership with French company bioMérieux to develop sequencing-based *in vitro* diagnostics. A few weeks later, Helicos Biosciences, also based in Cambridge, restructured its financially struggling business to focus on diagnostic applications for its sequencing platform. Industry leaders Illumina and Life Technologies are also racing to apply their 'next-generation sequencing' platforms to the investigation of cancer and other diseases. At the same time, issues around patent ownership are being put aside, at least for the moment, in the deal-making flurry.

The idea of using genome sequencing as a diagnostic tool is catching on fast. In May, a collaboration between S. San Francisco–based Genentech and Complete Genomics of Mountain View, California, revealed a staggering 50,000 single-nucleotide genomic mutations in a tumor from the lung of a heavy smoker that were absent in unaffected lung tissue (*Nature*, **465**, 473, 2010). In another recent study, Victor Velculescu's team at Johns Hopkins Medical Institute in Baltimore partnered with Carlsbad, California–based Life Technologies to identify genomic translocations in colorectal and breast tumors that proved suitable as patient-specific biomarkers (*Sci. Transl. Med.*, **2**, 20ra14, 2010). In June, Life Technologies spearheaded The Genomic Cancer Care Alliance—a collaboration between the company and the Fox Chase Cancer Care Center, in Philadelphia, the Scripps Genomic Medicine in San Diego, and the Translational Genomics Research Institute in Phoenix, Arizona, to study whether whole-genome sequencing can help guide treatment decisions in oncology.

"In some ways, I think this has probably surprised all of us in the industry, and certainly me," says Shaf Yousaf, division president of molecular and cell biology at Life Technologies. He and others credit changes in price and throughput as the primary drivers. The price point of sequencing of individual genomes has fallen below $10,000 across many platforms, as manufacturers and service providers slash prices with the fervor of salesmen on a car lot. In parallel, these systems now deliver complete sequences in under a week. "We're getting to the point where a genome can be extracted in a single experiment in a short time at an affordable cost and at increasingly high quality and repeatability," says David Bentley, chief scientist and vice president at San Diego–based Illumina. In June, the company announced the launch of its individual genome sequencing service, which costs $19,500 but drops to $14,500 if a physician orders five or more at a time, and to $9,500 if an individual has a serious medical condition.



Smoker's lung tumors contain up to 50,000 single-nucleotide mutations. Sequencing offers an entirely new approach to cancer diagnosis, and manufacturers are jumping into the space.

Meanwhile, newcomers like Pacific Biosciences are promoting 'single-molecule' sequencing systems that offer longer read-lengths and faster turnaround times, although many of these instruments are still awaiting formal release. In June, Harvard University spinout GnuBio shook up this year's Consumer Genetics Conference by announcing plans for a microfluidics-based system capable of turning out a full human genome for around $30.

This fast and furious price-slashing suggests the ingredients may soon be in place for an entirely new approach to diagnostics. "At Massachusetts General Hospital, they're already doing genotyping for every tumor," says Ari Kiirikki, vice president of sales and business development at Knome. "There's no doubt that when the cost becomes a little bit more reasonable, they'll sequence every single tumor and sequence it multiple times throughout the course of treatment."

This enthusiasm, however, is increasingly tempered by awareness of a potential intellectual property (IP) minefield. Nearly 30 years of gene patenting have enabled individuals and institutions to lay claim to an estimated 20% of known human genes—and at least one study suggests this is an underestimate (*Science* **322**, 198, 2008). More importantly, these patents diverge wildly in terms of specified claims, ranging from isolated cDNA or genomic sequences to diagnostic platforms. The restrictions enacted by these patents also

IN brief

French IPO spate

Three French companies have floated on the stock market in rapid succession, in what appears to be a sign of financial maturity and investor interest in the local biotech sector. On April 21, Paris-based Neovacs listed on the New York Stock Exchange Alternext (part of NYSE Euronext for small and mid-sized companies). Industrial biotech Deinove, of Paris, floated next, on April 27, and within a month, medtech concern Carmat of Vélizy Villacoublay began the initial public offering (IPO) process, expected for July. The listings are surprising, given investors' current reluctance to bankroll small and medium-sized firms. "Selected top-notch companies can IPO even in shaky markets," says Philippe Pouletty, who sits on the board of the three companies and is managing partner for private equity firm Truffle Capital, Paris. What they have in common, he says, is "Strong proprietary technology, major product candidates for large markets, experienced management teams and committed historical investors wanting to reinvest upon IPO." Neovacs is developing vaccine-induced polyclonal antibody therapies. Deinove is exploiting *Deinococci* bacteria to develop biofuels and Carmat is developing an implantable artificial heart for heart failure. "In France, the past crunch has not significantly affected the ability to raise capital for mature biotechs," says France Biotech director, Andre Choulika. "The downturn in private rounds is more worrying." *Emma Dorey*

Industrial biotech to boom?

In the next 20 years industrial biotech will surge, according to a new analysis of The Organization for Economic Cooperation and Development (OECD). The report, entitled *The Bioeconomy to 2030*, forecasts that biotech will grow from the current 0.5–1% to 2.7% of gross domestic product, driven mostly by industrial biotech. "We should really be concentrating on industrial and agricultural biotech because these are areas that are going to be extremely important in the future," says report co-author David Sawaya, of the Paris-based OECD. Industrial biotech will contribute 39% to the sector agriculture, 36% and health, 25%. The numbers, however, are at odds with current R&D investment where 87% is focused on health and 2% on industrial applications. The report's potential weakness is that the data predate the economic crisis. The statistics were sourced from a 2008 US Department of Agriculture report, and these were, in turn, based in part on a 2005 presentation by Rolf Bachmann, then an analyst at global management consulting firm McKinsey & Co. To meet the report's predictions, the current 2% contributed by bio-based materials to the industrial chemical economy must rise tenfold. Growth will depend on rapid developments in fermentation techniques, favorable environmental legislation and high oil prices pushing for cheaper alternatives. "There might have been a bit of over-enthusiasm initially," says Jens Riese a partner at McKinsey, Bachmann's collaborator at the time, "but the overall trend is heading there." *Daniel Grushkin*