

Cabilly patent invalidated

Genentech's stronghold on monoclonal antibody production techniques may slip if a recent US Patent and Trademark Office's (USPTO) initial ruling is upheld. In late September, the USPTO rejected the company's ubiquitous Cabilly 2 patent on the grounds that it extends the life of another patent called Cabilly 1, which would have expired next year. Genentech plans to appeal the decision. Cabilly 2, scheduled to expire in 2018, covers principle processes in manufacturing antibody drugs such as Johnson & Johnson's Remicade, Abbot's Humira, ImClone's Erbitux, and MedImmune's Synergis. Each of these companies pays significant royalties to Genentech, and without a patent, Genentech would miss out on between \$220 and \$300 million dollars a year in license revenue, according to analyst's estimates. Some analysts question the enforceability of the patent beyond the 2006 expiration date of Cabilly 1. "March 2006 is like a stop sign at three in the morning and no cop around," says Thomas Kowalski, a partner in the law firm Frommer Lawrence & Haug in New York City. At that point, companies paying license fees may make their own rules, he says. Some may pay a portion of their fees and some may not pay at all, he adds, "and Genentech will have to go chasing down all the people who ignored the patent." *EW*

Stem cell bank to link three continents

Nuclear transfer pioneer Woo Suk Hwang will lead a new international stem cell hub, which will be headquartered at Seoul National University. On October 19, the group announced plans to open regional banks in the San Francisco Bay Area (which has already filed for incorporation) and near London. Stem cell expert Gerald Schatten, director of the Division of Developmental and Regenerative Medicine at the University of Pittsburgh, has been asked to lead the centers. Their remit will be to distribute quality-controlled cell lines created in Hwang's laboratory in Korea to basic researchers at cost. Hwang announced in June that he had derived a dozen patient-specific human

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France restarts GM vine rootstock field trials

Ending a six-year suspension, researchers at the National Institute for Agricultural Research (INRA) in Colmar in the Alsace region of France resumed field experiments on grapevines in the beginning of September. Similar fields were last uprooted in 1999. INRA is now testing genetically modified rootstocks designed to resist infection by the devastating grapevine fanleaf nepovirus. Far-reaching biosafety measures were implemented for France's only genetically modified (GM) grapevine field trial. Over 1,500 non-GM rootstocks surround 70 GM plants—the lot being protected by a high fence. Non-GM scions of *Pinot Meunier*, a grape not otherwise used for wine making in the Alsace region, will be grafted on top of the rootstocks. Floral buds will be cut, so no grapes—let alone wine—will be produced. Apart from the French ministry of agriculture, which declared the experiment safe, a local steering committee including researchers, neighbors, consumer groups and anti-GMO activists, decided on the biosafety requirements. Olivier Lemaire, the research project's leader at INRA, believes the trial is important because no naturally occurring resistance genes have been found in wild vines, rendering traditional breeding methods powerless. "We are at a dead end with this disease," Lemaire says, but for the strategy now being tested. If successful, the technique will not be patented, enabling all wine growers to use GM rootstocks. The scion will remain nontransgenic, says Lemaire, "making the acceptability of such a strategy easier for society." *PV*



embryonic stem cell lines using an improved somatic cell nuclear transfer technique that generates lines that yield a tenfold efficiency (30%) compared with previous attempts which only generated lines three percent of the time. With this method, the hub plans to derive an additional 100 patient-specific lines in 20 diseases during 2006. Cambridge Institute for Medical Research's Roger Pedersen, who left the University of San Francisco in 2001 to pursue his research in the UK, supports the idea but warns that adding new cell lines is only part of the solution. He explains, "The true test of the concept will be whether knowledge of the new techniques is transferred to Western collaborators." Meanwhile, the Catholic Church in Korea announced, early in October, its plans to donate 10 billion won (\$9.61 million) for adult stem cell research to counter the burgeoning studies on embryonic stem cells. *CTS*

Biotech chiefs could face jail in patent disputes

The European Commission's (EC) plan, backed by big pharma, to make patent infringement a criminal rather than a civil offence—as part

of the EC's IP [intellectual property] Rights Enforcement Directive (officially called COM(2005)-276)—is running into strong opposition. Detractors of the criminalization measure, including biotech startups and biogenerics companies, claim it will hamper innovation by forcing entrepreneurs to decamp to the US rather than risk a jail sentence. The UK-based Foundation for Information Policy Research (FIPR) is leading the opposition to the draft directive. FIPR chairman Ross Anderson, a professor at Cambridge University, noted that all technology entrepreneurs currently take risks with IP, knowing that many patents do not stand up in court. "Making patent infringement a crime will undermine this, especially as it will happen only in Europe, not in the USA," he says. Peter Cozens of the UK Biotechnology Industry Association agreed that the move could damage innovation in the bioscience sector. But European biotech IP expert Bo Hammer Jensen says many patent attorneys agreed with the EC that extra measures are needed to deter organized criminals. "However, safeguards do need to be in place to protect people who infringe IP rights in the normal course of business, which does happen in the biotech industry," he says. The proposal will also criminalize the abetting and incitement of patent infringements, which could turn IP attorneys and consultants into outlaws. *PM*

mAbs progress in MS

The issue of administering highly aggressive therapies to multiple sclerosis (MS) patients was highlighted once more when Genzyme, of Cambridge, Massachusetts, and Schering, of Berlin, announced on September 16 that one of three MS patients who had developed a clotting problem known as idiopathic thrombocytopenic purpura (ITP) during a phase 2 clinical trial of Campath (alemtuzumab) had died. Interim efficacy data of a head-to-head study against Rebif (interferon beta-1A) indicated that it reduced relapse rate by 75% and risk of disease progression by 60%, relative to Rebif. Indirectly, these data indicate that the product could be at least as potent as Tysabri (natalizumab), the monoclonal antibody targeting alpha-4 integrin, which was withdrawn from the market in February after publication of reports linking it to a rare demyelinating disorder, progressive multifocal leukoencephalopathy (PML) (*Nat. Biotechnol.* 23, 397–398, 2005). Moreover, ITP is more manageable and predictable than PML, says Yaron Werber, analyst at Smith Barney Citigroup in New York City, and further dose reduction could minimize concerns. “I personally do believe that Campath will become a very important seller in MS in the future and will potentially have game-changing implications in MS therapy,” he says, although he emphasizes that it is unlikely to gain approval until 2009 or 2010. Meanwhile, on September 26, Dublin, Ireland-based Elan and Biogen Idec of Cambridge, Massachusetts, announced they had filed a supplemental biologics license application for Tysabri, after completing a safety review of their MS phase 3

clinical trial. The two companies have sought a priority review of their application, which, if granted, would mandate the FDA to act within six months. CS

additional strategic step to reinforce its contacts with Asia. Meanwhile, the country has been trying to establish a free-trade agreement with China since 2003. MHT

Switzerland strengthens its biotech position in China

Switzerland is planning to open a ‘Swiss House’ in Shanghai in 2006 to give more opportunities to Swiss researchers and industrials to access Chinese biotech partners. This concept of ‘scientific consulate’ is the latest in a series of Swiss outposts dedicated to foster networking and collaboration opportunities in regions with a high scientific potential such as Boston, San Francisco or Singapore. The planned Swiss House, however, is only a prelude to “the likely launching of a government fund in 2008, endowed with a hundred million Swiss Francs (\$77 million) over a four-year period”, explains Claudio Fischer, head of the bilateral cooperation unit for research in Berne, who is attached to the Swiss secretary of state for education and science. This government fund—a rather uncommon initiative for Switzerland—would be used to finance joint Sino-Swiss scientific projects, mainly in the field of biotechnology. Chinese partners will be expected to match the level of investment committed by the Swiss. After the opening, in March 2002, of a Swiss Business Hub, which is a platform that offers to small and medium-sized Swiss enterprises services to develop their business relations in Beijing and Shanghai, Switzerland has now taken an

Kauffman patent settled

Ending a four-year long legal dispute about its alleged infringement on the famous ‘Kauffman patent’ in the US, human antibody biotech MorphoSys of Martinsried, Germany, announced on September 23 it had settled court claims filed by Applied Molecular Evolution of San Diego, California, a subsidiary of Eli Lilly & Co. of Indianapolis, Indiana. The Kauffman patent, named after researcher Stuart Kauffman, describes the use of randomized DNA sequences to enhance proteins, a technique now widely used in biopharmaceutical research (*Nat. Biotechnol.* 18, 373, 2000). Without confessing to actual infringement, MorphoSys agreed to give researchers at Lilly access to technologies for developing therapeutic antibodies. In return, Lilly gave MorphoSys a license to continue generating and screening peptide and protein libraries under its Kauffman-Ballivet patent for stochastic DNA, RNA and proteins, including the right to commercialize products. No financial terms were disclosed. Lilly declined comment on the settlement, but MorphoSys spokesperson Mario Brkulj says the company had initiated settlement negotiations last April after it realized it preferred “getting a new partner over paying more fees to lawyers.” The German company had earned a favorable ruling in 2003 from a magistrate judge in Massachusetts, which was, however, nullified in October 2004 by an appellate district judge. PV



Selected research collaborations

Partner 1	Partner 2	\$ (millions)	Details
Sirna Therapeutics (San Francisco)	Allergan (Irvine, California)	\$5	A deal to develop Sirna-027 and additional RNAi-based therapeutics to treat age-related macular degeneration and other ophthalmic diseases. Sirna will develop optimized lead compounds against Allergan's identified gene targets. Allergan will provide its ocular drug delivery technology and develop and commercialize Sirna-027, which is in Phase I trials. Sirna is eligible for additional royalties and up to \$245 million in milestones.
Amsterdam Molecular Therapeutics (AMT; Amsterdam) & Galapagos (Mechelen, Belgium)	Netherlands Institute for Brain Research (NIBR; Amsterdam) & Vrije Universiteit (Amsterdam)	\$4.5	A partnership to develop therapeutics to promote nerve regeneration and to diminish the effects of neural scarring. Galapagos will provide access to its functional genomics platform on a fee-for-service basis. AMT will use its gene therapy capabilities to analyze identified targets. The NIBR will contribute its microarray technology and Vrije will analyze nerve cell growth to further develop therapeutics. The Dutch government will contribute \$2.4 million to fund the research.
Cryptome Pharmaceuticals (Melbourne, Australia)	University of Virginia (UV; Charlottesville, Virginia)	*	A collaboration to discover compounds to treat vascular leak, an essential component of inflammatory disorders and a contributing factor to tissue damage. The university will make new peptide compounds based on analysis of the Pak signaling pathways. UV will also develop improved variants of CR014, a peptide discovered by UV. Cryptome will help with structural analysis and testing in animal models, and will develop some peptide candidates. Cryptome has first option to in-license intellectual property produced at the university.

*Financial details not disclosed

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