IN brief

Kite and NCI partner on T cells

Kite Pharma and the National Cancer Institute (NCI) have partnered to develop and commercialize genetically engineered T cells as immunotherapies for advanced cancer. Under the leadership of Steven A. Rosenberg, the Surgery Branch of the NCI has pioneered the use of autologous T cells modified *ex vivo* to treat patients with multiple tumor types. The platform involves removing T cells from patients' peripheral blood, and genetically reprogramming them using recombinant retroviral vectors to contain chimeric antigen receptors (CARs). Most CARs consist of a single-chain antibody domain designed to recognize a tumor antigen, and a spliced-in co-stimulatory T-cell receptor to activate the modified T cells (*Nat. Biotechnol.* **29**, 853–855, 2011). Once re-injected into the patient, the engineered T cells traffic directly to the tumors and selectively eradicate them (*Blood*, **119**, 2709, 2012). Under a cooperative research and development agreement, the Los Angeles–based Kite will gain exclusive access to the NCI's current and future clinical product pipeline. Having raised $15 million of initial funding, Kite now plans to evaluate NCI's products and take them to phase 2 and 3 clinical trials. Although engineered T cells are remarkably potent, they can be coupled to serious and unexpected toxicities, says Martin Pule at University College London. Their bespoke nature is another constraint. "Currently a therapeutic product must be produced for each patient. This limits treatment to the few research medical centers...licensed to use integrating vectors," he adds. *Moheb Costandi*

Pan-African genomics

The US National Institutes of Health (NIH) and the London-based charity Wellcome Trust launched a new initiative designed to bolster Africa's genomics research capacity. The Human Heredity and Health in Africa (H3Africa) scheme announced on October 8 is a $38-million, five-year project aimed at studying diseases that affect the continent's people. "There is almost no cutting edge genomics in Africa. We can help correct that," says Jane Peterson, a senior NIH advisor based in Bethesda, Maryland. The first H3Africa projects aim to identify genetic risk factors in African populations for a number of diseases, including rheumatic heart disease, kidney disease, diabetes, African sleeping sickness and cardio-metabolic diseases. The project will fund two repositories for genetic samples—one in South Africa, the other in Nigeria. A pan-African bioinformatics network providing computational hardware and training for staff in genomics and population-based research are also included. The findings could have global importance, says Pat Goodwin, head of pathogens, immunology and population health at the Wellcome Trust. Africans are more genetically diverse than any other group on the planet, she says. This genetic variability could make it easier for scientists to identify genetic risk factors that would be hard to spot in a more genetically homogenous population. *Linda Nordling*

Threat to global GM soybean access as patent nears expiry

This October, five major seed companies came together to sign the first part of an agreement called the Generic Event Marketability and Access Agreement (GEMAA). Facilitated by the Biotechnology Industry Organization (BIO) of Washington, DC, and the American Seed Trade Association of Alexandria, Virginia, the accord is a legally binding contract that covers expirations of single-gene patents, and aims to ensure global access to genetically modified (GM) crops, even once they go off patent. "GEMAA is the most immediate concern," says Cathy Enright, executive vice president of BIO's food and agriculture section. "Farmers want to make sure that if they use a product that's under patent today they can continue to when it's off patent." Because regulatory agencies in some countries require reregistration of GM crops, the accord allays concerns that companies would fail to re-apply for registration of their products, once the patent expires.

The future global use of GM soybean is at stake as patent set to expire.

In 2014, the 20-year term for the gene patent on Monsanto's Roundup Ready soybean, which is used by >90% of US soybean farmers, will expire, and the looming deadline has raised fears among farmers that the expiration may disrupt trade. Their concern hinges on the disparity between how genetically modified organisms (GMOs) are regulated in the US and internationally. In the US, after a gene inserted into a crop is deregulated, the US Department of Agriculture (USDA) accepts its use in the crop indefinitely. But in the rest of the world, GM crops are approved for a specified time, which means that companies must periodically reapply with the regulatory agencies. In China, applications are submitted every three years, in Korea every five years, in Japan and Europe every ten.

Trade today moves smoothly because Monsanto maintains these approvals, but once the patent expires, Monsanto loses the financial incentive to continue filing. Nearly 60% of American-grown soy is exported abroad, mainly to China, Japan and Mexico, and almost all of it contains the Roundup Ready resistance gene. So in 2009, when Monsanto launched a second-generation GM soybean—Roundup Ready 2 Yield—farmers and other industry stakeholders realized that Monsanto had a *de facto* lock on the soybean trade. They feared that the seed giant would force them to adopt the next-generation trait by failing to file international approvals after expiration.

"There could be a terrible trade disruption if we had a product that was no longer registered in a foreign country. It could lock down ships. It could disrupt the entire trade system," says farmer Ray Gaesser, vice president and chairman of the regulatory committee of the American Soybean Association in St. Louis.

Monsanto acknowledges the problem and has pledged to continue filing until 2021. "There clearly were legitimate concerns from growers and grain handlers about what happens at the end of patent expiry. Quite honestly, we hadn't faced this situation ever before," says Jerry Steiner, executive vice president of sustainability and corporate affairs at Monsanto. "No one had prepared for that kind of thing."

Meanwhile, another wave of gene patents are scheduled to expire around 2020, including those owned by other companies. The industry had no strategy on how to maintain the regulatory approvals once off patent.

The accord requires signatories to announce their patent expiration three years ahead of time, after which patent

owners have three options: they may continue maintaining regulatory authorizations themselves, sign an arbitrated agreement to share responsibility with other companies, or discontinue maintenance by either transferring responsibility to another company or, failing that, announcing their intention to discontinue filing seven years hence.

Although it sounds straightforward, representatives from the companies and industry organizations have been gathering since 2010 for weekly meetings, sometimes several days long, to outline the legal framework for the 38-page document. "It's been a long journey," says Matt O'Mara, director of international affairs at BIO.

O'Mara believes that at the end of most patents' lives, consortiums will form to cover the costs of maintaining approvals. So far, however, the only signatories include seed giants, BASF Plant Science of Raleigh, North Carolina, Bayer CropScience in Monheim, Germany, Indianapolis' Dow AgroSciences, DuPont Pioneer of Johnston, Iowa, and Monsanto. None of the smaller seed companies have joined. Enright remains hopeful. "If you look at the signatories in six months, I think you're going to see new names."

"O'Mara believes that at the end of most patents' lives, consortiums will form to cover the costs of maintaining approvals."

Whereas GEMAA covers half the framework necessary for maintaining approvals, the signatories are now working on a second agreement called the Data Use and Compensation Agreement (DUCA) to be completed in 2013. Companies must periodically submit new data in order to maintain international approvals on crops that combine several foreign genes, or gene stacks. For gene stacks in Europe, for example, companies must submit data on the foreign genes in all their permutations. Therefore, as the number of genes in stacks rise, these data packages become exponentially larger and more expensive to maintain. With 100 pages written so far, the accord specifies that DUCA mandate signatories to share their data in return for managing the data, for which they will collect a designated fee. "We've got to make sure in the post-patent environment that someone is answering the phone calls from regulators, or trade is going to stop," says O'Mara.

Of the stacked seeds on the market, about half are the result of cross-licensing between companies. Monsanto's Smartstax corn, for example, incorporates an insect protection gene from Dow (Herculex Xtra), an herbicide resistance gene from Bayer (LibertyLink) and its own glyphosate resistance gene in Roundup Ready 2. DUCA will ensure that a single gene going off patent won't jeopardize the other licenses in a stacked product. "Cross-licensing is the lifeblood of the seed breeding industry," O'Mara says.

The accord emerged out of a morass surrounding Monsanto in 2009–2010, when it first commercialized Roundup Ready 2. The company became embroiled in a legal battle with DuPont over DuPont's program to stack the Roundup Ready 2 gene with DuPont's own glyphosate resistance gene. Monsanto sued for patent infringement. DuPont countered with an antitrust suit that prompted the US Department of Justice and a number of state's attorneys to begin their own antitrust investigations. "There was a lot of confusion at that time. I think a lot of competitive pressure and actions were causing some of that confusion," says Monsanto's Steiner.

Those allegations have since faded. A Missouri judge awarded Monsanto $1 billion in its suit. And DuPont's antitrust suit, which will go before the same judge next year, will likely fail, according to legal experts. "It's just gone away after they did the dog and pony show," says Tamara Nelsen, senior director of commodities at the Illinois Agricultural Association in Bloomington, Illinois.

After patent expiration, with GEMAA in place, the seed companies that now license Roundup will have one less bill to pay. "We still have some 600 small seed companies in the US. What we expect some of those smaller companies to do is look for more of a niche," says Nelsen. For smaller farms without the ideal farming conditions, "you are not going to worry about buying the latest and greatest."

At stake is the question, with a majority market share in most of America's staple crops, is Monsanto stifling competition and a potential generics market? "Ninety-three percent of soybean production is Roundup Ready," says Nelsen. "It's still like everyone is on a Microsoft system—at least, that's how farmers feel."

Daniel Grushkin, *Brooklyn, New York*

IN brief

Banking iPS cells

Ten pharma companies led by Roche of Basel are to set up a human induced pluripotent stem (iPS) cell bank in collaboration with 23 academic groups coordinated by Zameel Cader, of the Stem Cell Institute at Oxford University. The €55.6 ($72)-million project known as StemBANCC is part of Europe's public-private Innovative Medicines Initiative (IMI). At the same time, the UK will launch a national iPS cell bank, Human Induced Pluripotent Stem Cell Initiative (HIPSCI), with £12.75 ($20.5) million in funding from the Medical Research Council and the research charity Wellcome Trust. Both projects aim to develop standardized, genetically defined iPS cell lines and protocols for use as research tools. The biopharma industry has recognized the value of using iPS cells for high-throughput screening, toxicity testing and disease research, but views the generation of cell lines as precompetitive work. The IMI, whose brief is to improve the environment for pharma research in Europe, decided to set up a pan-European iPS cell repository after assessing the situation in the US. There, many small, privately funded cell banks, struggle to be viable despite an exponential increase in stem cell research such that demand outstrips supply. This points to a "unique opportunity," according to an IMI document, to create an industrial-scale, not-for-profit cell bank that will act as a pan-European storage and distribution center for iPS cells. The StemBANCC aims to generate 1,500 standardized, genetically defined iPS cell lines from 500 patients to develop models to study a range of diseases. It has a business plan to become self-financing in the next six years. The UK's national iPS cell bank HIPSCI aims to generate iPS cells from over 500 healthy individuals and 500 people with genetic disease. The goal is to use these cells to study the effects of genomic variation on cellular phenotypes. The aim of both projects is to standardize protocols for differentiating iPS cells to specialized cell types; neither mention potential clinical applications of the cells themselves. However, Keith Thompson, CEO of the UK's national Cell Therapy Catapult Centre, said that advancing the use of iPS cells as tools will also "inform strategies around the development of therapies." The UK national stem cell resource project will be led by King's College London and the Hinxton, Cambridge–based Wellcome Trust Sanger Centre.

Nuala Moran

IN their words

"Science is politics and the politics of amyloid won," says Claude Wiischik, founder of TauRx Pharmaceuticals, of Aberdeen, UK, whose company works on an alternative hypothesis that tau tangles drive Alzheimer's disease. (*The Wall Street Journal*, 9 November 2012.)