IN brief

GM beets approved—finally

Genetically modified (GM) sugar beets reached the end of a rocky regulatory road when the US Department of Agriculture (USDA) in July fully approved the variety for commercial cultivation. The fate of the beet had been in limbo for nearly three years. Developed by St. Louis–based Monsanto, the Genuity Roundup Ready beet is genetically modified to tolerate the herbicide glyphosate through the insertion of a gene encoding the enzyme 5-enolpyruvylshikimate-3-phosphate synthase protein. The plant was initially approved, or deregulated, by the USDA in 2005. But in 2009, after a lawsuit brought by the Center for Food Safety, a US district court judge ruled that the USDA failed to examine the likelihood of transmission of the genetically modified gene to conventional and organic sugar beets and beet relatives, and the socioeconomic effects on growers of these crops. The court ordered the agency to address these issues in an environmental impact statement and voided the USDA's 2005 approval of the crop. To allow GM beet cultivation to continue while it worked on the environmental review, the USDA in February 2011 partially deregulated Monsanto's beet but with strict planting restrictions. The agency completed its impact study in June and the following month fully approved the crop. *Emily Waltz*

FDA prevails in stem cell trial

In August, the US district court for the District of Columbia sided with the US Food and Drug Administration in a four-year-long dispute with Regenerative Science, a company in Broomfield, Colorado, over clinical uses of an unapproved stem cell product. On 23 July 2012, the court issued a permanent injunction against the use of the company's Regenexx procedure, consisting of culture-expanded autologous bone marrow stem cells, to treat orthopedic injuries. The FDA had tried to stop the company Regenerative Science from offering the unapproved Regenexx program. The company countersued, claiming that autologous stem cells are not drugs and hence outside the FDA's purview. The court concluded that Regenexx is a drug, and that its clinical use constitutes interstate commerce, which is captured in the Federal Food, Drug and Cosmetics Act. While the case was being decided, Regenerative Sciences took the offending therapy off their US product line but continues to offer unexpanded cells, removed and reinjected on the same day. Whereas Dave Audley, executive director of the International Cell Medicine Society, believes that the ruling clearly defines cell expansion as a regulated product, some still feel the agency has not provided a roadmap for cell therapies. The next battleground, according to Audley, may be stromal vascular stem cells processed from fat tissue. The FDA has already tipped its hand; last March, it issued a warning letter to Intellicell BioSciences, a New York–based firm that offers adipose tissue–derived stem cells for various uses from breast augmentation to osteoarthritis. *Laura DeFrancesco*

Clinical setbacks reduce IGF-1 inhibitors to cocktail mixers

The news that Thousand Oaks, California–based Amgen halted the phase 3 trials of ganitumab (AMG-479) in metastatic pancreatic cancer appears to have pounded a nail in approaches attempting to target the insulin-like growth factor 1 receptor (IGF-1R) in cancer. No safety concerns popped up, but the interim data provided no evidence the fully human monoclonal antibody (mAb) would benefit patients, echoing other studies with IGF-1R inhibitors. The only sliver of hope for the field may now lie in drugs acting against IGF-1 itself or against downstream signaling pathways.

Christine Regan, Amgen's director of Corporate Communications, refused to comment on the company's future plans for IGF-1 programs, although data from the study will be made public at an upcoming conference, she says.

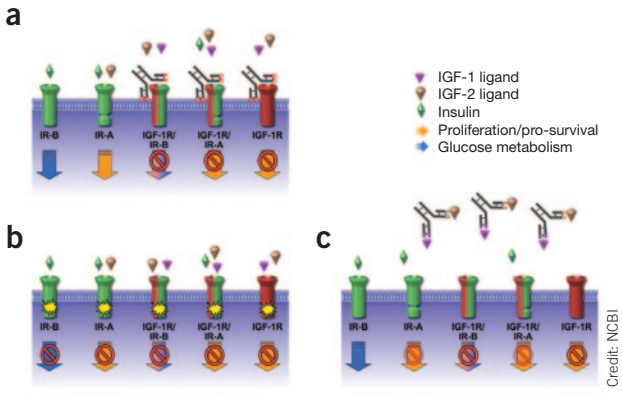
AMG-479 is the latest in a string of mAbs targeting the IGF-1R to fail in cancer-treatment trials. "If this was the first failure, it might suggest there were other issues," says Michael Yee, managing director at RBC Capital Markets in San Francisco. "Given that there have been failures in multiple different tumor types, this suggests the target isn't what we had hoped." The disappointment is particularly pointed because at one time anti–IGF-1 drugs were thought to hold much promise as anti-neoplastic agents, with a rationale built around a substantial scientific literature.

IGF-1 is a target that came to the party rather late, eventually attracted a lot of attention and then broke a bunch of hearts. The target first got attention in the mid-1980s, when Genentech's Axel Ullrich cloned the receptor. Because IGF-1 is a growth stimulant, it was initially regarded as a potential target for wound healing. In 1987, the first cancer connection emerged from the lab of IGF-1 pioneer Michael Pollak, a professor in oncology at McGill University in Montreal. That paper underscored the presence of IGF-1Rs in human breast and colon cancers (*Cancer Lett.* **38**, 2223–2230, 1987). Soon after that, Carlos Arteaga of Nashville, Tennessee–based Vanderbilt University described evidence that IGF-1R inhibition slowed tumor growth in mice.

The field really took off in 2008. At least seven drugs targeting IGF-1R were in clinical trials for various cancers, most of them in phase 2 (*Nat. Biotechnol.* **26**, 719–720, 2008). Not long after, the bad news started to roll in. ImClone of Bridgewater, New Jersey, Pfizer of New York and Merck of Whitehouse Station, New Jersey were among those who placed big bets on IGF-1R and faced serious disappointment.

Leonard Saltz, of Memorial Sloan-Kettering Cancer Center, New York, was one of the authors of a 2010 paper that delivered an early 'warning shot' that problems were afoot (*J. Clin. Oncol.* **28**, 4270–4246, 2010). The paper was based on a phase 2 study of ImClone's IMC-A12, an IGF-1R–targeting fully human mAb. IMC-A12 had been administered as a monotherapy in some patients and in combination with Erbitux (cetuximab; a chimeric mAb that targets the epidermal growth factor receptor; EGFR) in others. All the patients had metastatic colorectal cancer that was refractory to Erbitux and to Vectibix (panitumumab), Amgen's fully human IgG2 anti-EGFR mAb. Of 64 patients, only one achieved a response.

Just a few months earlier, Pfizer had terminated a trial in non–small cell lung cancer of figitumumab (CP-751871), another fully human IgG2 mAb targeting IGF-1R, because that drug did not appear effective. Last year, Merck also discontinued its IGF-1R targeting mAb for colorectal cancer. This time, the drug appeared to worsen the patients' prognosis.



Three ways to skin an IGF-1. (**a**) A lack of efficacy for mAbs targeting IGF-1 receptor arises presumably because other pathways can upregulate to overcome receptor blockade; (**b**) small molecules may be able to inhibit tyrosine kinases; (**c**) ligand sequestration strategies are plausible.

It is hardly surprising that even some of the field's pioneers are now pessimistic. "In the case of IGF-1R, one can protest that proper studies have not yet