by suggesting that their results were equivocal and necessitated a larger follow-up. Atwood says that the earlier studies in fact found that the treatment was ineffective at preventing heart attacks.

In 2008, TACT was suspended after regulators learned that subjects were not being given calcium disodium EDTA, as implied on informed-consent forms — instead, they were being infused with the slightly different salt disodium EDTA, for which the FDA had revoked approval. The trial resumed after consent forms were reworded to include warnings, such as "death is a rare complication of EDTA infusions".

Josephine Briggs, director of the NCCAM, declined to comment on TACT until the results are published in a journal. The principal investigator, cardiologist Gervasio Lamas of Mount Sinai Medical Center in Miami Beach, Florida, says that the study's findings were a surprise and deserve following up. He adds that the trial consent forms were approved by the NIH and multiple institutional review boards. Gary Gibbons, director of the NHLBI, says that his institute stands by the study's methodology.

But critics charge that TACT is simply the latest example of dubious research into unproven therapies supported by the NCCAM. Some argue that even high-quality studies would have little value, because negative results are unlikely to sway ardent practitioners. "Show me one alternative medication or procedure that was studied, found to not work, and was abandoned by practitioners. I'm not aware of any," says Steven Novella, a neurologist at Yale University in New Haven, Connecticut. Briggs, who previously led the NIH's kidney-disease research, points out that echinacea sales fell after an NCCAM-funded study showed it was ineffective against colds (R. B. Turner *et al. N. Engl. J. Med.* **353,** 341–348; 2005). With the centre's research showing that Americans spend about $34 billion on alternative medicine each year, "we think it's really important to bring some science into this", she says.

Briggs adds that the NCCAM's critics often misrepresent the centre's research, focusing on studies of herbal supplements such as lavender oil but ignoring multi-million-dollar grants for more-mainstream science. Among the largest studies funded by the centre this year are a computational analysis of the human microbiome and an effort to use brain imaging to understand and treat chronic back pain.

Novella and other NCCAM critics do praise Briggs for bringing increased accountability to the centre, and for boosting the rigour of the research it funds. But "even if you did pristine research under the NCCAM", says Novella, "it's what you're studying that is the problem". ■

BIOTECHNOLOGY

Pig geneticists go the whole hog

Genome will benefit farmers and medical researchers.

BY ALISON ABBOTT

T. J. Tabasco is something of a porcine goddess at the University of Illinois, Urbana-Champaign, where her ruddy, taxidermied head looks down from the office wall of geneticist Lawrence Schook. Now she has been immortalized in this week's *Nature*[1] — not by name, but by the letters of her DNA.

Scientists are salivating. For the past couple of decades they have been slowly teasing information from the pig genome, applying it to breed healthier and meatier pigs, and to try to create more faithful models of human disease. This week's draft sequence of T. J.'s genome (see page 393), with its detailed annotation — a 'reference genome' — will speed progress on both fronts, and perhaps even allow pigs to be engineered to provide organs for transplant into human patients. "Agriculture in particular will benefit fast," says Alan Archibald of the Roslin Institute in Edinburgh, UK, one of the paper's lead authors. "The pig industry has an excellent track record for rapid adoption of new technologies and knowledge."

T. J., a domestic Duroc pig (*Sus scrofa domesticus*), was born in Illinois in 2001. The next year, Schook and his colleagues generated a fibroblast cell line from a small piece of skin from her ear and commissioned clones to be created from it, so that they could work on animals all with the same genome. One set of clones was created at the National Swine Resource and Research Center (NSRRC) in Columbia, Missouri, along with genetically engineered pigs with genes added or deleted to mimic human diseases. "Making such pigs has got increasingly easier as knowledge of the genome increases," says physiologist Randall Prather, a co-director of the NSRRC, which is funded by the National Institutes of Health (NIH).

The NIH launched the NSRRC in 2003 to encourage research in pig disease models. Pigs are more expensive to keep than rodents, and they reproduce more slowly. But the similarities between pig and human anatomy and physiology can trump the drawbacks. For example, their eyes are a similar size, with photoreceptors similarly distributed in the retina. So the pig became the first model for retinitis pigmentosa, a cause of blindness. And four years ago, researchers created a pig model of cystic fibrosis[2] that, unlike mouse models, developed symptoms resembling those in humans.

T. J. Tabasco, star of the show.

Geneticist and veterinarian Eckhard Wolf at the Ludwig-Maximilian University in Munich, Germany, has exploited the similarity between the human and pig gastrointestinal system and metabolism — like us, pigs will eat almost anything and then suffer for it — to develop models of diabetes. One pig model carries a mutant transgene that limits the effectiveness of incretin, a hormone required for normal insulin secretion[3]. Mice with the transgene developed unexpectedly severe diabetes, but the pigs have a more subtle pre-diabetic condition that better models the human disease. "This shows the importance of using an animal with a relevant physiology," says Wolf.

Pig models are now being developed for other common conditions, including Alzheimer's disease, cancer and muscular dystrophy. This work will be enriched by the discovery, reported in the genome paper, of 112 gene variants that might be involved in human diseases. Knowledge of the genome is also allowing scientists to try to engineer pigs that could be the source of organs, including heart and liver, for human patients. Pig organs are roughly the right size, and researchers hope to create transgenic pigs carrying genes that deceive the immune system of recipients into not rejecting the transplants.

Back on the farm, early knowledge about the pig genome led to the discovery in 1991 of a gene involved in porcine stress syndrome, in which the stress of overheating, being moved or even having sex causes the animals to die suddenly[4]. It then became possible to test for the ▶

gene and select pig stocks free of it.

Having the full genome should also help investigators to breed out susceptibility to porcine reproductive and respiratory syndrome (PRRS), a viral disease costing the US pig industry US$600 million per year. The PRRS Host Genetics Consortium, a network of US research groups, has identified a region on one chromosome that affects levels of virus in the blood during infection[5]. Archibald, who works on PRRS, says that the high-quality genome sequence should help investigators zero in on the genes responsible.

But the pig genome is not just about applications. Lead co-author Martien Groenen, a genome researcher from Wageningen University in the Netherlands, has resequenced the genomes of scores of different strains of wild and domestic pigs, and used the information to show that the pig was domesticated independently in Asia and Europe. He has also started to work out which genes were involved in the selection of desired traits — such as a longer spine to give more bacon — on different continents. "It's curiosity-driven research, but it may also help animal breeders in the future," he says. ■

1. Groenen, M. A. M. *et al. Nature* **491,** 393–398 (2012).
2. Rogers, C. S. *et al. Science* **321,** 1837–1841 (2008).
3. Renner, S. *et al. Diabetes* **59,** 1228–1238 (2010).
4. Fujii J. *et al. Science* **253,** 448–451 (1991).
5. Boddicker, N. *et al. J. Anim. Sci.* **90,** 1733–1746 (2012).

BUSINESS

Investment relief for biotech sector

Public markets provide cash injection for struggling field.

BY HEIDI LEDFORD

Robert Forrester gets a little giddy when he talks about the day his company went public. The otherwise understated chief operating officer of Verastem, a small biotechnology company developing drugs to target cancer stem cells, chuckles and bounces in his chair as he recounts key strategic decisions along the way to the company's initial public offering (IPO) on 26 January, which raised US$55 million.

Until recently, Verastem's IPO would have stood little chance. Few biotech companies have braved an IPO in the years since the global recession hit, and those that did often took a beating in the public markets. Venture capitalists began to pull out of the sector. Colleagues scoffed when Forrester told them that Verastem, a young company in Cambridge, Massachusetts, with no clinical data was going public. "Many people said, 'you've got to be kidding'," he recalls.

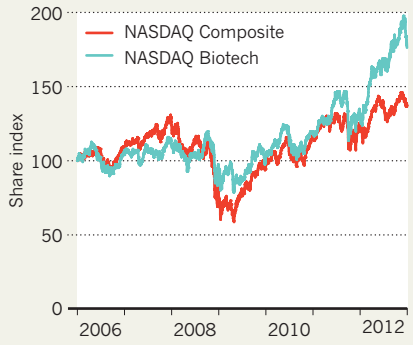
But the IPO drought may be ending. This year has seen 12 biotech IPOs, and others are in the pipeline. So far, this has pumped some $800 million into the sector, according to Renaissance Capital, an IPO-research company based in Greenwich, Connecticut. And biotech stocks are doing well — the NASDAQ Biotech Index has outperformed the NASDAQ Composite Index for the past 20 months (see 'Bullish on biotech'). "If this trend holds, it could be great news for the sector," says Josh Lerner, who studies venture capital at Harvard Business School in Boston, Massachusetts.

Restoring access to the public markets — particularly for young companies that have few fund-raising options left — can give companies the capital they need to expand research programmes, hire more researchers or even just survive. It can also grant them access to 'generalist' investors who do not specialize in health care. "Public investors who may have been out of biotechnology for the past couple of years have started to move back in," says James Healy, a general partner at venture-capital firm Sofinnova Ventures in Menlo Park, California.

Observers credit several factors for the rising investor confidence in biotech. Large pharmaceutical firms eager to restock drug pipelines are gobbling up smaller firms at high prices. Biotechnology companies have celebrated several high-profile successes in the past 18 months, with the US Food and Drug Administration approving groundbreaking drugs such as vemurafenib, a genetically tailored drug for advanced melanoma whose prowess in knocking out tumours is matched by its jaw-dropping price tag — more than $50,000 for six months of treatment.

BULLISH ON BIOTECH

An index fund of biotech companies is outperforming the NASDAQ composite index.



SOURCE: NASDAQ

Investors may also be drawn to the sector because of the poor performance of other industries, which are suffering more directly from the sluggish US economy, says Eric Schmidt, an analyst at investment bank Cowen and Company in New York. "Biotech earnings tend to grow independently of the economy, unlike electronics or consumer products," says Schmidt. "Everybody needs medicine."

The wave of public investment could help to offset the dearth of venture capital. A survey released last year by the National Venture Capital Association, headquartered in Arlington, Virginia, showed that nearly 40% of venture capitalists had decreased their investment in biotech during the previous three years, put off by the long timelines and high risks of drug development. Several prominent health-care funds have closed altogether. "Biotech is a money-eating machine," Lerner says. "The need for capital is so large, and given what's happened to venture capital, having alternatives is important."

Nowhere is that need greater than in young companies, the riskiest of all biotech investments, which have been among the hardest hit by the drop in venture funding. Verastem's IPO money advanced the company's business plan by two years; it should begin phase II trials of its leading compound by mid-2013, Forrester says.

But IPOs are not necessarily the answer for all struggling biotech ventures, cautions Brian Atwood, a managing director of Versant Ventures, a venture-capital firm in Menlo Park. He notes that many of the companies that pulled off IPO triumphs this year are unusual in some respect. Kythera Biopharmaceuticals of Calabasas, California, for example, is particularly appealing to investors because patients will have to pay out of their own pockets for its leading product — a fat-fighting injection designed to shrink double chins — rather than relying on health insurance and its accompanying cost controls. And Verastem's Forrester can barely utter a sentence without referencing the company's executives and scientific advisory board: a who's who of Boston's biomedical glitterati. Healy agrees: "It's a higher-quality set of companies that have recently gone public compared with those that may have gone public five years ago." ■