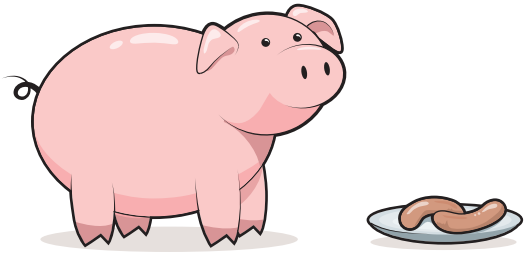


A taste of things to come?

Researchers are sure that they can put lab-grown meat on the menu — if they can just get cultured muscle cells to bulk up.

BY NICOLA JONES

Mark Post has never been tempted to taste the 'fake' pork that he grows in his lab. As far as he knows, the only person who has swallowed a strip of the pale, limp muscle tissue is a Russian TV journalist who visited the lab this year to film its work. "He just took it with tweezers out of the culture dish and stuffed it in his mouth before I could say anything," says Post. "He said it was chewy and tasteless."

Post, who works at the Eindhoven University of Technology in the Netherlands, is at the leading edge of efforts to make *in vitro* meat by growing animal muscle cells in a dish. His ultimate goal is to help rid the world of the wasteful production of farm animals for food by helping to develop life-like steaks. In the near term, he hopes to make a single palatable sausage of ground pork, showcased next to the living pig that donated its starter cells — if he can secure funds for his research.

Post started out as a tissue engineer interested in turning stem cells into human muscle for use in reconstructive surgery, but switched to meat a few years ago. "I realized this could have much greater impact than any of the medical work I'd been doing over 20 years — in terms of environmental benefits, health benefits, benefits against world starvation," he says. Largely because of the inefficiency of growing crops to feed livestock, a vegetarian diet requires only 35% as much water and 40% as much energy as that of a meat-eater[1]. Future 'in-vitrotarians' should be able to claim similar savings.

The prospect of an alternative to slaughtering animals led People for the Ethical Treatment of Animals based in Norfolk, Virginia, to announce two years ago a US$1-million prize for the first company to bring synthetic chicken meat to stores in at least six US states by 2016. In the Netherlands, where the vast majority of work has been done so far, a consortium of researchers convinced the government to grant them €2 million (US$2.6 million) between 2005 and 2009 for developing *in vitro* meat.

Such incentives have helped to solve some of the basic challenges, applying human tissue-engineering techniques to isolate adult stem cells from muscle, amplify them in culture and fuse them into centimetre-long strips. But far more money and momentum will be needed to make *in vitro* meat efficient to produce, cheap and supermarket-friendly. Post estimates that creating his single sausage will require another year of research and at least $250,000. So what still needs to be done?

CHOOSE THE RIGHT STOCK

The first question for researchers is which cells to start with. Embryonic stem cells would provide an immortal (and therefore cheap) stock from which to grow endless supplies of meat. But attempts to produce embryonic stem cells from farm animals have not been successful. Most work so far has been on myosatellite cells, the adult stem cells that are responsible for muscle growth and repair. These can be obtained by a relatively harmless muscle biopsy from a pig, cow, sheep, chicken or turkey; the desired cells are then extracted using enzymes or pipetting, and multiplied in culture.

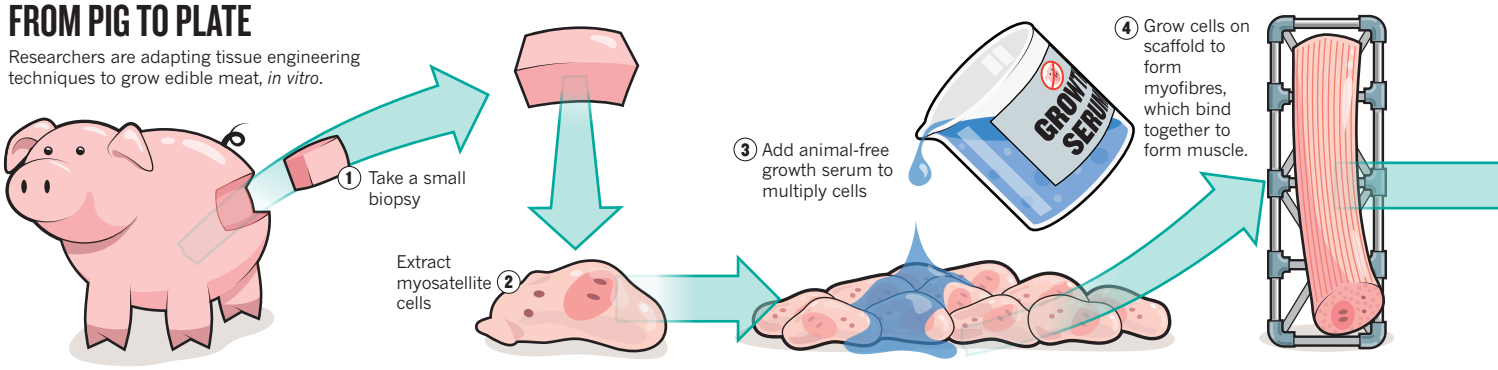
Morris Benjaminson, professor emeritus at Touro College in New York, prefers a different approach — planting the whole biopsy in a dish. "We use the whole business without the brain," he says. "We don't break it down to cells and put them back together again." He used this method to grow goldfish fillets in his lab in 2002, boosting the surface area by up to 79% over a week by adding a shot of extra cells from ground-up muscle[2]. It's not clear, however, whether this procedure could produce enough muscle for a commercial enterprise.

The fundamental problem is that myosatellite cells will only divide dozens of times, probably because their telomeres — the protective ends of the chromosomes — wear down with age. There are ways of boosting their proliferation. One is to add a gene for the repair enzyme telomerase. Another, being investigated by the start-up company Mokshagundam Biotechnologies in Palo Alto, California, involves inserting a tumour-growth-promoting gene. But genetically modified lab-grown meat might be too much for consumers to swallow. "Try selling that," laughs Post. An alternative is to get cells from a young

ILLUSTRATIONS: NIK SPENCER

FROM PIG TO PLATE

Researchers are adapting tissue engineering techniques to grow edible meat, *in vitro*.



animal and perfect the rest of the system, such as the culture medium, to maximize growth.

For now, Post uses regular cell-culture medium to grow his pork myosatellite cells. This contains fetal calf serum which, as it currently comes from dead cows, largely defeats the point of synthetic meat. It also contains antibiotics and anti-fungal agents that might not be good for human consumption. "Supposedly you could be allergic to these; you never know," Post says. To get the cells to differentiate into muscle, he shifts to horse serum, which has the same list of problems.

Animal-free media made from a slurry of plants or microbes are commercially available for biomedical work such as *in vitro* fertilization. But like animal-based media, they're expensive — right now, growth media account for about 90% of the material costs of lab-grown meat. And their composition is proprietary, making them difficult to customize. One alternative might be to use ground-up maitake mushrooms, which Benjaminson found works just as well as calf serum for his fish fillets. At the University of Amsterdam, researchers working on *in vitro* meat have been developing a cheap medium made from blue-green algae, with added growth factors made in genetically modified *Escherichia coli*. But no one has yet developed a way of making a cheap, animal-free growth serum in large quantities.

BEEF IT UP

Myosatellite cells grown on a scaffold will fuse into myofibres, which then bundle together to make up muscle. But lab-assembled muscles are weak and textureless. "It's like when you take off a cast after six weeks," says Post. To get the muscle to bulk up with protein requires exercise. Assembling the myofibres between anchor points helps, as this creates a natural tension for the muscle to flex against. Post uses this type of arrangement to boost the protein content of a muscle strip from 100 milligrams to about 800 milligrams over a few weeks. He also administers 10-volt shocks every second, which can bump protein content up to about a gram. This much electricity would be expensive in a scaled-up industrial process, so his group is hoping to learn how to mimic chemical signals that tell muscles to contract.

Vladimir Mironov of the Medical University of South Carolina in Charleston is instead using a scaffold made of chitosan microbeads — chitosan can be sourced from crabs or fungi — that expand and contract with temperature swings, thus making a natural fitness centre for his muscle strips.

If lab-grown muscle gets more than about 200 micrometres thick, cells in the interior start to die as they become starved of nutrients and oxygen. Post simply grows many small strips that could be ground up into a sausage. Others, including Mironov, are using blender-sized bioreactors of the type developed by NASA to study muscle growth in low gravity. These conditions help prevent cell clumping and improve transport of oxygen and nutrients.

Growing meat on an industrial scale would require large, customized bioreactors like those used by biopharmaceutical companies.

> **"This could have much greater impact than any of the medical work I'd been doing over 20 years."**

Mironov estimates that a commercial *in vitro* meat facility would need a five-storey building of bioreactors; with a similarly huge investment. And all that is just for manufacturing ground meat. The prospect of growing steaks is a much bigger challenge, requiring a system of fake 'blood vessels' built into the meat. That is decades away.

MARKET IT

The thing that enthusiasts for fake meat talk least about is its taste, perhaps because they haven't tried it. In the United States, researchers have largely avoided eating anything grown in the lab for fear of violating a Food and Drug Administration regulation (it's unclear whether it is actually forbidden) or being seen as publicity hounds. When Benjaminson grew his goldfish fillets, his team dipped them in olive oil, fried them in breadcrumbs and gave them to an 'odour and sight' panel who said they seemed edible, but who weren't allowed to try them.

Researchers generally believe that if they can get the texture right, taste will follow — particularly once flavouring is added. Fortunately, myosatellite cells can also turn into fat, which would add to the taste. At Mokshagundam Biotechnologies, the goal is to make a spam-like mix of different muscle and other cell types that provide the 'umami' taste that characterizes meat. Scientists will also have to find a way of adding nutrients such as iron (which comes from blood) and vitamin B12 (which comes from gut bacteria).

The process won't be cheap. By one rough estimate, first-generation lab meat could cost €3,500 per tonne (compared with €1,800 per tonne for unsubsidized farmed chicken meat)[3]. Mironov thinks the best way to secure an early market is by turning *in vitro* meat into a 'functional' food attractive to the rich and famous, perhaps by filling it with compounds that promote health or suppress appetite. "Only Hollywood celebrities like Paris will be eating this," he says. Alternatively, one could get an edge on the market by making meat products from exotic or even extinct animals, assuming a few of their cells could be saved. In the long run, advocates see a market in vegetarians and others who want guilt-free and environmentally friendly meat.

Researchers such as Post believe that the scientific and technical advances needed to make and sell *in vitro* meat are worth the fight — but convincing funders remains the biggest obstacle. Post's funding from the Dutch government ran out in 2009; he came out of that with hundreds of pork strips, not the thousands he needs for a sausage. Today, a couple of umbrella organizations promote the cause, including the non-profit New Harvest, which provides small funds for US- and Europe-based work, and a new commercial company, California-based Pure Bioengineering, which aims to raise venture capital. But no windfalls have arrived as yet.

Post will keep seeking funding for his demonstration sausage — but he knows that raising enough to commercialize the entire process will be a huge ask. "I usually say €100 million," says Post. "That's the number I forward to the government, and then they faint." ■

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