Modern Agriculture Foundation: Accomplishments

<u>Sent 8/7/16</u>

- Initiation of first cultured chicken meat and first "whole-tissue" meat (of any kind) study, including laying the scientific and organizational structure for Supermeat. Full support behind the the crowdfunding initiative, including publicity, interviews, coalescing the scientific community and getting their approval (featured on the Indiegogo page) and answering questions both on PM and "walls". Bringing in investors for the first seed amount for the company, \$200k.
- 2. Mentions in 40 outlets including Reuters, Huffington Post, Mirror and Yahoo Tech
- 15 lectures including at 2 Vegan Congresses and 3 Universities (Tel Aviv, Ben Gurion, Hebrew),
- 4. 25 information booths at vegan/animal rights events, environmental events and scientific events 10k pamphlets handed out.
- Total social media following of more than 30k, used to promote Modern Meadow, Muufri, Clara Foods, Memphis Meats (in official collaboration), Mosa Meat, New Wave Foods, New Harvest and of course, Supermeat. This is addition to information on our site (English and Hebrew).
- 6. 30 educational videos on our YouTube channel on the subject of cultured meat, including videos specific to our cultured chicken project and our organization, general (translated to Hebrew) videos and videos from our "Rabbi Project". The latter is a set of interviews with Rabbis regarding the kosher standing of cultured meat, in efforts to connect with religious communities (kosher meat is also Halal).
- 7. Attending 2 environmental days at Israeli parliament and connecting personally with 10 MPs (out of 120 MPs).
- 8. Advising 20 students on their best course of action to join cultured meat research.
- 9. Co-founder Tom Ben Arye, initiated cultured meat (beef) research at the Technion as part of his PhD
- 10. Took part and helped organize and man a \$15k fundraising operation for New Harvest in 9/15 (which was then doubled).

Professor Nahmias's public statements regarding the technology

https://www.techinasia.com/supermeat-lab-grown-chicken-meat

(I)

Grab your fork and let's dig into the engineering of cultured meat.

First, nobody grows massive amounts of cells in plastic culture flasks in industry. The techniques you know from genetic research laboratories are for small batches, and require a lot of technical attention to replace medium, and keep cultures sterile. Industrial culture uses

suspension reactors, growing cells on carrier beads, in a much higher cell/volume ratio then you are used to. The process is continuous and quite sterile because technicians, too bored to keep things sterile, are not fiddling with the system. Try out eppendorf DASbox mini bioreactor in your lab; I think you will love it.

You obviously realize that without opening and closing the incubator door, a properly insulated suspension bioreactor requires very little energy to keep temperature constant. This isn't a major cost driver.

Second, we have stopped using fetal calf serum in my laboratory back in 2009 after we showed the predominantly negative effect it has on cell culture (Kidambi et al. PNAS 2009). In a recent paper we grew genetically modified human hepatocytes up to 10^16 cells (80 tons) in serum-free medium (Levy et al. Nature Biotechnology 2015). Your point about serum-free medium in general is simply wrong. Properly designed medium supports much higher replication rates than serum. Examples include FibroLife (LifeLine), TheraPEAK (Lonaza), etc'.

Third, I am also worried about growth hormones in milk that is consumed after flash pasteurization that is insufficient to denature the protein. But nobody should be worried about growth hormones in fully cooked meat. Growth hormone denatures at about 70 degrees.

You should be really worried about the fact that 70% of the chicken meat in the USA has unsafe levels of arsenic (e.g. roxarsone) and 20% of it is contaminated with antibiotic-resistant salmonella.

In any case, we are planning to use machine perfusion to grow the muscle (Uygun et al. Nature Medicine 2010), making it trivial to wash out any component of the perfused medium. The meat industry can't flush the plasma out of a living chicken 10-12 hours before it is slaughtered, we can easily flush medium through the growing muscle.

Anyway, you missed some of the important questions about cultured meat.

You didn't ask about the Hayflick limit that blocks cells growth to about 30 cell doublings (about 1 ton), requiring other groups to take thousands of biopsies each year (unless you are using our cells which are limitless).

You didn't ask about the cost of cell culture medium (\$50-500/liter), or the minimal volume needed to get to 200 million cells per gram (about 200 liters unless you are using our process).

(II) Q&A

Q 1. Your method for expanding cells to 10^15 relies on expressing papiloma virus proteins after infection with lenti virus. What are the safety guidelines of eating those cells? Is the public OK with eating with papiloma virus proteins given that people are afraid of much simpler GMO?

Q 2. You mentioned that since 2009, your lab relies on synthetic media and not FBS that involve cows slaughtering. Maybe I am confused but the same publication (Levi et al., NBT, 2015) clearly states that your group did use 10% Fetal Bovine Serum (FBS) for growing HeLa and HepG2 cells. Moreover, the Long term hepatocytes were cultured in the presence Bovine Serum Albumin (BSA). I am just a human geneticist but to the best of my knowledge, BSA needs cow blood :-). Please see screen shot of the Levi et al. Online Methods section.

Q 3. The SuperMeat movie claims that in the future we will be able to grow SuperMeat in our houses. Is this a realistic claim given that your process relies on industrial bioreactors?

Q 4. What is the actual cost of growing 1Kg of cells given that you need synthetic hormones, media, etc?

A (Nahmias):

A 1. Nobody in his right mind will use HPV to expand cells for human consumption. This work aimed to expand human hepatocytes for drug screening.

Your originals point was that cells don't grow in serum-free media that well (or at all). I consider it debunked. We don't need HPV to expand our chicken Mesenchymal cells, we won't use GMO

A 2.1. Yes. FBS is being used on my publications (mostly by collaborators). It is critical to compare our method to the standard. However, our primary protocols for stem cell derived hepatocytes, or expanding human primary cells don't use serum.

A 2.2 I didn't say I don't use BSA, I simply said I don't use serum. However, you can now buy Albumin made from rice (e.g. CellaSTIM) which we will use in SuperMeat <u>Albumin Human</u>

A 3. The creation of tiny vascularized tissue will be made using in a central processing plant with massive bioreactors. These tiny tissue (1-14 mg) will be encapsulated and send to consumers that will grow them in specialized machines using powdered growth medium and their own water

A 4. No idea. Prophecy is given to fools, but estimates are that ultimately around \$1-\$5 per pound (about 1/2 kg).

Q: Koby, can you please elaborate on the level of tissue development you looking to get? I ask because, if I'm getting this right, the tissues would need to be quite thin in order to allow cellular respiration to take place, if the transport of dissolved gases takes place by diffusion. I

saw your remark about vascularized tissue and it made me wonder if you have some way of providing a surrogate circulatory system or some other method to allow for thick tissues. Or in other words, should we be expecting steaks or minced meat?

A (Nahmias): Thinner than can you imagine, the diffusion limit for muscle is about 0.15 mm, so without blood vessels we are talking about slices 0.3 mm thick.

This is why our design includes endothelialized blood vessels the permit in vitro perfusion. It is slightly more complex than that....

I am aiming for a large muscle (something like beast muscle) but I don't know how far we will be able to get

<u>Sent 9/2/16</u>

To the points I sent last time I would just like to add a couple pertaining to Supermeat's crowdfunding campaign.

- The campaign, by the time everything is said and done will have raised roughly \$200k, placing it in the top percentile of crowdfunding campaigns.
- The entire campaign presence on social media consists of the foundation's volunteers. The campaign was featured on numerous animal rights related pages (including but not limited to Animals Australia, Mercy For Animals, The Best Video You Will Ever See) as well as "Now This".
- The foundation found Prof. Nahmias and got him interested in the project.
- The other two Supermeat co-founders are TMAF co-founders as well.
- The foundation was instrumental in getting the campaign publicity in the media, including in Yahoo Tech, Huffington Post, The Mirror. A full <u>list</u> is included.