#028 - Ally - They're made of meat?

Outline:

Introduction of "big ideas" so the audience can be thinking about the context of those as we get into the science stuff:

- Are we approaching a *real* cruelty free dietary option?
- Will see lab grown options become available for transplant waiting list patients?
- When necessity is met, will you then be able to purchase lab grown … "enhancements"? (ie. a Repo future and all that entails)
- IF YOU COULD (financial restrictions aside), would you purchase a lab grown genetic double for spare parts? (Be honest…) (ie. An Island future)
- Making synthetic animal products and growing organs: How will this affect the future??
- What's gonna happen to all the cows and stuff? DID NOT FIND ANYTHING ON THIS, which kind of worries me…

***** I'd like to discuss the real world applications that are available and happening now (and in the future based on these) and then get into the sci-fi future discussion of these about that that might change our world*****

We'll start with the medical side - there is so much more info available for this, and I feel like the food is going to be more of a high note to end on.

- In the future this could be a huge boon to transplant recipients - people won't have to depend on another life ending to ensure their survival. (not that I'm against organ transplants at all, it's just kind of a sad reality)
- Very exciting to see how these changes are going to affect areas of research that were previously much more difficult to access (development and neuroscience)
- With cosmetic implants already being a thing (everyone remembers that creepy Ken man right??), how long do we think it will be before 'made to order' items are approached by science? Or you you guys think that's too far fetched (please note that redonk situation above)?
- Overall, it seems to be very similar processes for creating each of these huge advancements: start with stem cells! That's why stem cell research is soooooooo important American.

MEDICAL SIDE:

11 Successful lab grown Body parts:

Note: organiod is a weird word that makes me uncomfortable for some reason lol

Fallopian tubes (2016) - cultivated from stem cells a small scale model was created that can actually e sustained in a lab environment (previous these cell could only be studied for day at a time), which allows for more long term testing an observation. The Max Planck Institute hopes that this will lead into understanding more about the effects and possible connections of bacterial infections and cancer.

Minibrain - (2015) Model about the size of a pencil eraser, cultivated from converting skin cells to pluripotent cells. Has functioning neurons with signal-carrying extensions like axons and dendrites (ie. has 99% of the genes present in the human fetal brain). Mainly this model is missing a vascular system but does contain a spinal cord, all major regions of the brain, multiple cell types, signaling circuitry and

even a retina. Even better still is this model has the potential to dramatically accelerate neuroscience research (for example, diseases like Alzheimer's & Parkinson's and development disorders such as autism can be created in these model sized brains and studied in greater detail than it's previous been possible.) (Ohio State University)

Miniheart (2015)- UC Berkeley in collaboration with Gladstone institutes have developed a template for growing beating cardiac tissue from stem cells. Benefits of the tech right now include synthetic models for development study and drug-screening for safer pregnancies. (ie. thalidomide test - most commonly reported birth defects involve the heart). This also has the potential to replace animal test subjects in the field of development study - typically performed by dissecting animals are different developmental stages.

Minikidney (2013-2015) - A team of Australian scientists grew a minikidney, differentiating stem cells to form an organ with the three distinct types of kidney cells for the first time. Prof. Melissa Little of Murdoch Childrens research Institute in collaboration with The University of Queensland have successfully created a mini kidney in a dish that has all of the cells types present within a human kidney and hope this will lead to drug-testing for effects on kidneys and possibly new treatments for patients with kidney failure.

Minilung (2015) - University of Michigan Medical School has created a 3-D model of a human lung that contains structures resembling both large airways (bronchi) and small lung sacs(alveoli). This model still lacks several components of the human lung (such as blood vessels), but the change from 2-D will provide more opportunities to turn basic scientific ideas into clinical innovations.

Ministomache (2014) - (Profs. Jim Wells, Cincinnati Children's Hospital Medical Center) Scientists hope could one day help researchers better understand how the stomach develops, as well as the diseases and disorders that can affect it (such as gastric disease and ulcers). Again, created with stem cells.

Vaginas (2005 -2014) - 4 Successful vagine transplants have tkane place place for 4 teens suffering from Mayer-Rokitansky-Küster-Hauser (MRKH) syndrome - these transplants were lab grown from the patient's own cell, and then transferred into the patient. Review on these trans plants advises that they are functioning and behaving just as expected. (Dr. Anthony Atala, director of Wake Forest Baptist Medical Center's Institute for Regenerative Medicine)

Penises - That same dr. is also working to create penises from patient cells that can also be transplanted. This would be treatment for traumatic injury, development disorders, etc. By making it out of the patient's own cells, they hope to bypass the possible host rejection. (both genital lab organs require a "scaffold base" - ladies get a biodegradable scaffold while men get a dead man boner. For real.)

Esophagus - (2014) Kuban State Medical University in Krasnodar, Russia, has grown a working esophagus that has successfully been transplanted into rats, and functions much the same way as the natural esophagus. Researchers led by Paolo Macchiarini of the Karolinska Institutet in Stockholm have also had success in this field, though they took the scaffold decellularization approach. Scientists & Dr. hope this tech can be used to help patients with esophageal cancer, congenital defects, or injuries after medical procedures or swallowing caustic materials.

Ear (2013) - Jason Spector,plastic surgeon at Weill Cornell Medical College in New York City. Scientists have 3D printed human ears, cultivating them by coating molded ear-forms with living cells that grew around the frame -- these are ten transferred to the *backs of rats* to grow for 1-3 months… Scientists hope to be able to treat things such as congenital deformities, and we could see human testing in as little of 3 years.

Liver Cells (2015) - (Prof. Yaakov Nahmias, director of the Alexander Grass Center for Bioengineering at The Hebrew University of Jerusalem) Up until now one of the biggest problems with attempting to create a lab grown liver is that the human hepatocytes cells lost their regenerative abilities once outside of the human body. Prof. Nahmais worked around this by building on existing research from the German Cancer institute involving HVP; by exposing the cells to proteins relating to HPV, the hepatocytes were released from cell-cycle arrest and allowed to proliferate in response to Oncostatin M (OSM, a member of the interleukin 6 (IL-6) superfamily that is involved in liver regeneration). Previous studies caused hepatocytes to proliferate without control, but turning hepatocytes into tumor cells with little metabolic function, the researchers were able to carefully select colonies of human hepatocytes that only proliferate in response to OSM. This OMS stimulation caused cell proliferation with doubling time of 33 to 49 hours. Removal of OSM caused growth arrest and hepatic differentiation within 4 days, generating highly functional cells. (This is called the upcyte© process and allows expanding human hepatocytes for 35 population doubling, resulting in 1015 cells (quadrillion) from each liver isolation. By comparison, only 109 cells (billion) can be isolated from a healthy organ.) Because researchers are able to use this method to create liver cells from multiple donors, they will now have greater insight of patient-to-patient variability and idiosyncratic toxicity. They also hope that this tech will advance a variety of liver-related research and applications, from studying drug toxicity to creating bio-artificial liver support for patients awaiting transplantations

Organ transplant tech - (2015)

- As of Oct 2015, 18,048 people received organ transplants. Another 122,586 people added their name to a waiting list and hoped for a donor. With the development of the CRISPER-Cas9 method, researchers have been been able to genetically modify pigs to make them more suitable for human transplants. So far doctors have been able to use some heart valves from pigs and cows to replace inferior ones within a human heart, but this new technology could lead to being able to use animal organs for replacements as well. Researchers stated we can expect primate trials within the next year possibly, and with luck, human trials following that shortly after.
- 3D Printing is also a promising alternative that might be a bit closer to being come reality; with a biopsy of the organ, researchers can isolate cells, grow them in a lab environment, then mix them in an oxygen-rich liquid with other nutrients to keep them alive. That mixture can then be printed into the appropriate shape for the individual patient, along with a biomaterial to provide structure. Currently, solid organs like kidneys and livers are proving difficult for 3D printers, but other less-complicated tissues are not. Flat structures like skin, tubular structures like veins, and hollow structures like the bladder have all successfully been grown in the lab, and can be used in applications like literally printing replacement skin for burn victims.
- Researchers in Germany reported that they have grown complete spinal cords from embryonic stem cells (2014) in a petri dish as well. This a huge break through b/c so far, most lab grown tissues/organs/etc require a “scaffold” that informs its genetic code and provides nutrients, however nervous tissue starts off as a flat sheet which then turns itself into a tub like shape that will attach to the brain at one end and the spinal cord at the other - the shapes are too intricate at this point to be replicated synthetically in a lab.
- Also in 2014, Anglo-Polish research team announced that they had performed a novel cell transplantation procedure on Darek Fidyka, a 38-year-old Polish man left paralyzed from the

waist down after a knife attack in 2010. Using cells taken from Fidyka's nose, doctors in England grew and implanted a "nerve bridge" in his damaged spinal column. After 19 months of treatment, Fidyka regained some movement and sensation in his legs. The long-term outcome of the procedure remains unclear, however, and its effectiveness has yet to be tested in randomised clinical trials.

RadioLab update episode on CRISPER stated that in the future this tech could possibly also be used on human embryos to treat genetic disorders prior to birth. China has done testing on this recently with mixed results.

Additional articles of interest:
https://www.theguardian.com/science/2015/jul/08/laboratory-grown-organs-transform-lives
http://www.smithsonianmag.com/40th-anniversary/organs-made-to-order-863675/

Discussing the food side, I'm really interested in what further development means for the commercial food industry. If we get to the point where this lab grown alternatives become more affordable and mainstream, how are they going to cope?
Also, if an animal free version of a product is available and it's close enough to the original that it does not make a difference, does that then mean if you don't choose that option, are you literally choosing to murder something for your enjoyment?
On a darker note, could labs create "human meat" or endangered species meat available for consumption on a creepy black market for creepers? To be honest, it would be the way to try cannibalism without having to murder someone, just saying….

THE FOOD SIDE:
Cultured Beef: Prof. Mark Post (University of Maastrich) created the first cultured beef hamburger in Aug 2013 -- this burger was cooked and tasted live in London. While it was given marks for a similar "mouth feel" it was not as flavorful or juicy as it's natural rival - probably due to the lower content of fat. With this development in the food industry, it's taken the concept of lab grown meat from a sci fiction idea to an engineering problem; How to produce this in large quantities for a reasonable price?
The start of the process:

- First gov funded research took place in the Netherlands
- Dutch agency SenterNovem funded cultured meat research from 2005-2009, partly because of talks between New Harvest founder Jason Matheny and the Dutch Minister of Agriculture in October of 2004.
- The original project was initiated by 86 year old Willem Van Eelen who had a long term fascination with cultured meat and even files a patent on the idea in 1997.
- Dr. Henk Haagsman, of Utrecht University was the principal grant writer for the project and it was split into 3 categories:
    - stem cell biology, conducted at Utrecht University by Dr. Henk Haagsman and Dr. Bernard Roelen;
    - tissue engineering, conducted at Eindhoven Technical University by Dr. Carlijn Bouten

    - culture media, conducted at the University of Amsterdam by Dr. Klaas Hellingwerf.
- In 2008, part way through the project, Dr. Carlijn Bouten had to pass on her project responsibilities. Dr. Mark Post of Eindhoven Technical University (at the time) took the reins of the tissue engineering project by supervising Dr. Bouten's PhD students. Motivated by the potential impact of cultured meat, Mark continued research even after the grant ended.

The process itself: The purpose of the cultured beef hamburger was to show the world that it was scientifically possible create an edible beef burger from cultured cells. The process of creating the burger used primarily tried and tested methods of muscle cell tissue culture.

- Some of the problems encountered:
    - Price: The burger cost €250,000 to produce- this was due to the fact that it was created in a laboratory scale using expensive lab resources and equipment - and then the specialized techs that actually did the work had to get paid. (Well duh.)
    - One challenge in producing the burger was how to help the muscle fibers mature. Muscle fibers mature much better with contraction. Researchers in Mark's lab found that seeding muscle cells around a cylinder of gel allowed the cells to create a fiber in the shape of a ring, which then could contract on itself.
    - Another challenge was growing a large number of muscle cells. Because muscle grows only about 0.5mm in culture, the best way to mass produce the culture is by providing a lot of surface area for muscle cells to grow on.
    - Yet another challenge in producing the cell cultured beef burger was creating an animal-free system. The status quo for culturing tissue involves the use of fetal bovine serum, an unsustainable byproduct of the livestock industry collected from fetal cows. Like other animal products, there is a lot of variation from batch to batch, an inconsistent supply, and possibility of contamination. It is the status quo because it works very well, despite little understanding on why it works. It is also relatively inexpensive. HOWEVER, by the end of the burger project, the muscle strains grown for that beef were in fact make with ZERO animal serum, so it is truly an animal free product at that point.

As of early 2015, Mark post's lab was provided an additional $50,000 from New Harvest to fund additional research into animal free cultured beef - so hopefully we will see more interesting and delightfully sci-fi items from him in the future.

New Harvest has also funded research into lab grown, animal free Chicken & Turkey as well as Pork & Lobster - though they are not as far along as the beef tech (human tasting stage), so we're focusing as much on those. Of special note though, Jess Krieger at Kent State University is researching the prohibitive costs of production and finding cost-effective solutions - such as a bioreactor system for culturing meat. The bioreactor system that Jess is designing will improve nutrient and oxygen delivery to the meat cells by acting as an artificial heart that pumps artificial blood into the muscle. This system will also "exercise" the muscle to improve its development, the same way that muscle is exercised inside the body to increase its strength (Which should also result in muscle that has the taste and texture of meat harvested from livestock). The hope is that the meat cells grown in Jess' bioreactor system will produce a bigger and better output than current known methods are able to.

Companies of interest:
Prefect Day - dairy free milk, scheduled to release first consumer products this year (San Francisco). They basicly mix yeast with sugar and science to create the same proteins "real milk" has. They do state that they see their product as a compliment to the dairy farming industry (by elevating some of the pressure to produce) rather than a replacement, which I think is interesting.
Clara Foods - egg/chicken free egg whites. Also based in San Fancisco. (Gosh, they must be super crunchy there! :D) The second link at new harvest is better IMO. This company is creating basicly lab created " real egg whites" (still seem to be working on the yoke part?) - they use yeast again with sugar to create the same proteins found in "real eggs", and tests so far has resulted in lab made whites that behave very similarly to traditional hen eggs whites for cooking applications, such as meringues. (Ie. specialised egg whites for different applications. 636 gallons of water to make 12 eggs. Same technology used to make cheese and insulin.) Most info found so far is from 2015, so will keep looking…

Re-thinking the term"real" eggs and "real milk" -- the lad options *are* actually (or so far appear to be) the real deal, so that that feels a little disingenuous.

Labs of interest:
New Harvest - founded by Jason Matheny. Funds research in cellular agriculture. Helped kick start Perfect Day, Clara Foods, Mark Post's Cultured Beef, etc.

ADDITIONAL EPISODE LINKS
Surprisingly Awesome: Ep. 9 - Pigeons https://gimletmedia.com/episode/9-pigeons/

PS NOTE FOR EPISODE: Blake was wrong once again--the main villain of the new Power Rangers is totally Rita Repulsa--her costume design is just kind of similar and she uses Scorpina's rock monsters a bit. That didn't make it in so no problem.