Science AMA Series: We 3D-print self-assembling blood vessels and create human biological systems on a chip. Ask Us Anything!

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[1]Affiliation not available

April 17, 2023

Abstract

Hello Reddit! We're Monica Moya and Elizabeth Wheeler from Lawrence Livermore National Laboratory, and we're using 3D bioprinting techniques and special "bioink" to manufacture human-compatible tissues vascularized with self-assembling vessels and capillaries. We've engineered the printed tissue with human cells so that they grow toward nutrients, harvesting the ability of the human body to respond and develop complex vascular networks. This effort is part of a larger research project aimed at replicating the human body on a miniature scale, what we're calling iCHIP (in vitro Chip-based Human Investigational Platform). It includes research into recreating the central and peripheral nervous systems, the blood-brain barrier, and the heart. This is seriously a new frontier in biology. If we're successful, iCHIP could be used to develop new countermeasures against biological agents without having to use human subjects. But in order to get the various systems to work together properly, the "human on a chip" will need adequate plumbing. It's like a house with all these separate rooms, and we're the plumbers. We're really excited about the work, and we're here to talk about it. Ask us anything! We will be back at 1 pm EST (10 am PST, 6 pm UTC) to answer your questions. Update, 9:45am PST Hey we are just joining you now! Excited to see other geeking out with us about our science! We will start answering questions shortly! Thanks everyone! Update, 10:05am PST Here's an article about our work: https://www.llnl.gov/news/researchers-3d-print-living-blood-vessels. It includes an animation that shows how the bioprinted vessels self-assemble vascular networks. Update, 12:15pm PST Thanks everyone for the great questions! Wish we could have answered all 300+ questions but we have to get back to the lab and continue our exciting work! Thanks again! Super exciting that our AMA made it to the front page of Reddit! Monica Moya's biography: Monica L. Moya is a Research Engineer at Lawrence Livermore National Laboratory's Center for Micro and Nano Technology. She earned a Ph.D. in Biomedical Engineering from the Illinois Institute of Technology in 2009. Her current research centers around using 3D printing to print living vascular structures for neural systems and tissue engineering applications. Select publications: http://www.pubfacts.com/author/Monica+L+Moya. Elizabeth Wheeler's biography: Elizabeth Wheeler is a chemical engineer at Lawrence Livermore National Laboratory and a principal investigator for iCHIP, the In-vitro based Human Investigational Platform. She has expertise in medical engineering, microfluidics and bioinstrumentation. Select publications: http://www.pubfacts.com/author/Elizabeth+K+Wheeler.

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ABSTRACT

Hello Reddit! We're Monica Moya and Elizabeth Wheeler from Lawrence Livermore National Laboratory, and we're using 3D bioprinting techniques and special "bioink" to manufacture human-compatible tissues vascularized with self-assembling vessels and capillaries. We've engineered the printed tissue with human cells so that they grow toward nutrients, harvesting the ability of the human body to respond and develop complex vascular networks. This effort is part of a larger research project aimed at replicating the human body on a miniature scale, what we're calling iCHIP (in vitro Chip-based Human Investigational Platform). It includes research into recreating the central and peripheral nervous systems, the blood-brain barrier, and the heart. This is seriously a new frontier in biology. If we're successful, iCHIP could be used to develop new countermeasures against biological agents without having to use human subjects. But in order to get the various systems to work together properly, the "human on a chip" will need adequate plumbing. It's like a house with all these separate rooms, and we're the plumbers. We're really excited about the work, and we're here to talk about it. Ask us anything!

We will be back at 1 pm EST (10 am PST, 6 pm UTC) to answer your questions.

Update, 9:45am PST Hey we are just joining you now! Excited to see other geeking out with us about our science! We will start answering questions shortly! Thanks everyone!

Update, 10:05am PST Here's an article about our work: https://www.llnl.gov/news/researchers-3d-print-living-blood-vessels. It includes an animation that shows how the bioprinted vessels self-assemble vascular networks.

Update, 12:15pm PST Thanks everyone for the great questions! Wish we could have answered all 300+ questions but we have to get back to the lab and continue our exciting work! Thanks again! Super exciting that our AMA made it to the front page of Reddit!

Monica Moya's biography: Monica L. Moya is a Research Engineer at Lawrence Livermore National Laboratory's Center for Micro and Nano Technology. She earned a Ph.D. in Biomedical Engineering from the Illinois Institute of Technology in 2009. Her current research centers around using 3D printing to print living vascular structures for neural systems and tissue engineering applications. Select publications: http://www.pubfacts.com/author/Monica+L+Moya.

Elizabeth Wheeler's biography: Elizabeth Wheeler is a chemical engineer at Lawrence Livermore National Laboratory and a principal investigator for iCHIP, the In-vitro based Human Investigational Platform. She has expertise in medical engineering, microfluidics and bioinstrumentation. Select publications: http://www.pubfacts.com/author/Elizabeth+K+Wheeler.

CORRESPONDENCE:

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What are the biggest roadblocks to further development and practical/commercial use?

generalbumble

For bioprinting, I would say the biggest roadblock would be the cell sources. Getting well-characterized and reproducible source of cells is key. Scaling up to large tissues like organs will require a ton of cells!

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My biggest questions related to your work are: 1. How far are we from being able to use 3d printing to create replacement organs for people in need of transplants? 2. Can stem cells be used as a universal "ink" for creating these incredibly valuable human body parts?

captainhorgan

We are still a good way off (we need to figure out where or how to grow the millions, billions of cells in an organ) from 3D printing replacement organs but that doesn't mean that bioprinting is useless until then. Bioprinting small human tissues can be applied to toxicology studies, medical treatment testing and provide a bed for fundamental science.

As for stem cells being the source of cells, that is a possibility because of their expansion potential. Induced pluripotent stem cells, an adult stem cell (like a skin cell) that has been reprogramed to be a stem cell is an interesting option. One challenge with stem cells is that we are talking about a cell that is early in its development process. Even differentiated stem cells, cells that have already committed to being a certain cell type, may still take a while before they exhibit the same properties as an adult mature cell.

1) How closely do you think systems like this mimic what is actually going on in the body? Will it be able to actually replace in vivo systems for accurately learning about cell and tissue physiology in most cases?

2) What kind of cells do you typically use for the tissue engineering? Are they stem cells? can you use primary cells? or are they immortalized?

Thanks so much for taking the time to do this AMA!

not_a_cleaver_man

Thanks! Our goal is not to recreate everything that is going on in the body but recreate enough that allows it allows us to do meaningful science outside the body. Even animal studies, in vivo work, are limited since we humans are pretty different than rats or pigs. That is why so many drugs that have success in animal studies fail when they go into humans. These on-a-chip system have the ability to provide a link between the gap with in vitro, in vivo and human studies.

The cells we currently use are primary cells but potentially other cells sources could be use depending on what your end goal is.

What is the lifespan of these chips? Would it be possible to run a drug across one if them for long periods of time--like 5-10 years or more--to assess long-term health risks?

Wheeeler

The current lifespan is on the order of hundreds of days. We're working to extend the lifespan for the exact application you mentioned.

It seems like you are focused mostly on high-throughput (though extremely complex) platforms for laboratory testing. Why not personalized medicine? Relates to other questions on cancer, heart disease, etc. Also, where do you get most of your financial support?

Spooler2

Although, not our primary focus this technology can definitely be applied to personalized medicine. At the moment this work is internally funded.

How would you differentiate your approach from Don Ingber's group at the Wyss Institute at Harvard, who also build interconnected "organ-on-a-chip" systems?

KakoiKagakusha

Our approach differs in the tissue systems that we're focusing on. To date, we've been focusing on developing a brain-on-a-chip.

hi Drs. Moya and Wheeler,

your work looks very exciting! And thank you for doing this AMA.

I looked over the iCHIP project on the LLNL website (link - https://str.llnl.gov/march-2014/pannu). It seems to me that the different organ systems will be studied in isolation from each other - could you please comment on this? Because as we know, the human body is a homeostatic environment that requires interactions between every organ system. Also, I was wondering how you are planning on building these different organ systems? Are you going to be just using primary epithelial cells? How would you achieve proper interactions between different cell types in every organ system?

rambobilai

We are currently building the peripheral nervous system, central nervous system, blood brain barrier and a cardiac platform. Each platform is built and validated separately and then we integrate them together. You're correct studying the integrated systems is the best way to get physiologically relevant results. > most

After the vessels form, how do you load [pump] blood through them?

KakoiKagakusha

After the vessels form we hook them up to a pump to simulate blood flow.

Mrs. Moya, As a Biomedical Engineer, how did you get started with research? I'm in the process of becoming a Biomedical Engineer myself and I would like to do research someday, but so far I haven't met a Biomedical Engineer other than my advisors who has done research. Also, which schools would you recommend for graduate studies in Biomedical engineering? Thank you for taking the time to answer these questions!

TuffGuy68

Great response by bme_phd_hste below! I started doing research right after my first year in undergrad. Professors love energetic students! There are so many opportunities out there! If you are an undergrad consider applying to LLNL to be a summer intern: http://science.energy.gov/wdts/suli/

Hi! I'm an engineer (mechanical, but with a concentration in biomedical sciences), and what you're doing sounds incredibly interesting. My question is, how does one get into that field? I'd love to do something along these lines, but have no idea if I have the skill set for it. Would I need to go to grad school for a masters or PhD in any specific subset? Thanks!

runaholic13

Hi. I'm actually a chemical engineer by training. There are many ways to get into the field. Getting internships or hands-on research experience is a great way. Whether you need a to go grad school would larger depend on what you want to ultimately do with your career. To lead projects, it certainly helps to have an advanced degree. If you do think about graduate school make sure you take advantage of all the different fields of study at the university. Multidisciplinary teams are becoming more important in this field of research.

Hi Monica and Elizabeth I'm a doing a MSc. in biomedical engineer and a thesis in angiogenisis so I have many questions in my mind but I'll just ask the ones coming to me now. First question: do you think we are at the stage where tissue engineering is more of an engineering challenge than a biology one. aren't the problems you face at this point mechanical or chemical and rarely a biological one?

Question 2: are you focusing on the ICHIP because it's easier to work with small scales, specially in the third dimension, or it has some advantages of it's own?

Third question: Do you have any PhD positions in your lab? even with no scholarship I'd love to work with you. I'm extremely invested in the topic and it would be really a dream come true!

youcefhd

Great questions!

Question 1: Its definitely both, an engineering challenge and a biology one! Its what as a biomedical engineer attracts me to these projects! I think tissue engineering is a bit of a feedback mechanism. We can't engineer what we don't fully understand. In engineering tissues or tissue platforms we end up learning things about biology that we didn't know before and that allows us to go back and redo some of our strategies.

Question 2. There are many advantages to small scales! We can use these small tissues to do fundamental science or to test things we couldn't test in humans.

Question 3: Check LLNL out at http://students.llnl.gov for opportunities to come work at the Lab!

Just want to say what an inspiration it is to see female BMEs doing great things in the tissue engineering/bio printing world. You guys are living my dream. Thanks so much for taking the time to do this.

What challenge(s) do you feel is (are) the most vital to beat in order to have success?

Do you think clinical trials could ever need only iCHIP and no human subjects?

claireashley31

Thanks. We definitely appreciate and enjoy the types of research we get to do. Assuming you're referring to personal challenges, I would say the most challenging thing is to keep persevering - research is tough. In the long term future, tissue on chip systems could replace human subjects once they've been fully validated, but it's a long ways off. Guess it's a good job we love what we do :)

Hello there! This question is probably too technical, but:

If you're going to be 3D-printing blood vessels and other organs, will there be a problem with transplant rejection? If so, how does one get around that? Is bioprinting usually done with the patient's cells, or is the immune system suppressed? Or is this not a problem with blood vessels?

Also, thanks for doing this AMA. :)

ClickRicket

Hi there! Going the route of printing tissues for implantation, the way to get around the rejection process is choosing the right biocompatible material and cell source. We currently print using human primary cells. If immune suppression can be avoided that is always preferred as that opens the door for other complications.

Hi! Is the 3D printing process material extrusion or some form of material fusion? What is the cost associated with printing these "chips?" And how do you test the integrity of the chips? Thanks!

rczqpu2

We are currently using an extrusion process to print the cells in the bio-inks. The integrity of the chips is evaluated by comparing the functionality of the cells to the functionality of the cells both in traditional cell cultures and in vivo.

As scientists we all have hopes & dreams for our research and its implications somewhere in the back of our mind as we move forward with our work.

What are some of your hopes and dreams, even if completely lofty, for where you see these advances taking us?

Thanks for taking the time to be here!

tonusbonus

Love your summary of scientist! I couldn't agree more that its the potential for making an impact that drives us day and day out! As a biomedical engineer working to solve the "plumbing problem" of tissue engineering I would love to be able to figure that piece out because it would really help get more tissue engineering work out of the lab and into clinic.

Hi, first I would like to say amazing work, people like you are making the world a better place. I'm a junior in high school and heavily considering a career in biomedical engineering. Would you have any suggestions or tips for somebody pursuing this field? What kind of work would this field entail? Thank you so much in advance.

thelebronofrhyme

It's a great field. The only suggestion that comes to mind is to work and study hard :) I'd also suggest getting internships and hands-on experience as soon as possible. There's nothing like actually working in the field to confirm it's something you want to do and make yourself more valuable for your next job experience. Good luck.

Hello! This is some awesome research. I am currently a graduate student and worked on a 3D printed bone setting cast project. We designed it, analyzed pros and cons when comparing to current methods, identified the type of FDA regulatory process our device would need to accomplish, and then performed a market analysis. I'm looking at the LLNL website and the work you guys do is awesome. Do you guys offer summer internships by any chance?

Mrivy13

Sounds like a great project. Yes there are summer internships here. Check out the web page (http://careers-ext.llnl.gov/jobs/search) for postings.

How can I get a job at your company?

vicinadp

Check out many exciting career opportunities at LLNL: http://careers-ext.llnl.gov

What type of role can an individual with a computer science background play in your work? Are these individuals important to your work?

Cas9n

We routinely work with highly multidisciplinary teams. Computer science backgrounds are definitely important. As you can imagine we generate large amounts of data and the problem then becomes analyzing the data in the most effective way.

I'm a freshman undergraduate student currently double majoring in biology and chemical engineering, and this kind of work is exactly the stuff that I want to start a career in. Do you have any advice for me about what steps I should take to get involved in this field?

Kunafisch

Great, you are already majoring in great areas! I always say the best way to get started is to try doing research. Find out what research is being done at your school and approach those professor about working in their labs. I started doing research the end of my freshman year and I was hooked! Doing research gives you the opportunity to find out what excites you the most in science as well as gives you valuable and transferable skills. We have internship opportunities for undergrads as well that you can take a look at: http://students.llnl.gov/pages/apply-info

Can you go more into the types of inks you are using? Are you printing cells directly or seeding them them afterward? I'm curious because I worked on a 3D bioprinter in my undergrad and we were never successful in printing cells directly with our design.

bme_phd_hste

We are actually printing the cells directly! Even in the tubes, we print support cells as part of the tubes and then seed endothelial cells inside the tubes to create the endothelium that is normally found in cells.

It is definitely more challenging to have cells present during the print process. We spend a good amount characterizing how our materials gel as they are extruded because we need to understand what forces our cells feel and make sure we keep them alive.

Hiring at all? I'd love to find a project like this.

Sybertron

Yes! Check out: http://careers-ext.llnl.gov

Would there be any applications to cancer treatment?

Ldreamer

The tissue systems can definitely be applied to cancer treatment, evaluating whether a therapeutic would be effective.

So when you say "bio ink", is this stem cell based or synthetic? 3D printing organs immediately brings the question to mind, "How you create living plastic organs?" But, I'm assuming they are not plastic?

DeltaCypher0

The bio ink is made up of human primary cells and our materials are natural---either they come from nature or they come from the body. We chose this route because we want to create environments that still allow for biology to happen. In other words, we are co-engineering with nature. By avoiding being totally synthetic we increase our chances of creating something that will integrate seamlessly with our body. So we do want it to be "plastic" in the sense that we want our materials to allow for change but we don't actually want to print literal plastic. :)