Dr Aviv Regev and Dr. Sarah Teichmann of the Human Cell Atlas

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Mark Masselli: This is Conversations on Healthcare, I am Mark Masselli.

Margaret Flinter: And I am Margaret Flinter.

Mark Masselli: Well Margaret the National Institute of Health has officially kicked off its much anticipated all of us precision medicine initiative it's an ambitious project that's seeks to advance medicine by enlisting the participation of a million citizens [inaudible 00:00:21] willing to offer up their medical and genomic data to advance the knowledge and understanding of health and disease in a way that has never been possible before.

Margaret Flinter: Well this is program that we're very proud to be part of at the official kick off NIH Director. Dr. Francis Collins called the All Of Us Precision Medicine Initiative one of the most ambitious research projects ever conducted in the United States and that's from the guy who oversaw the team that mapped the human genome, very exciting.

Mark Masselli: It really is, and he is absolutely right it's ambitious, it's ground breaking they're seeking a million volunteers citizen scientist offer up their genomic biological medical and behavioral information all to be coalesced in a massive database to allow researchers to get a more complete understanding of how disease happens and more importantly find ways to prevent it from happening in the first place.

Margaret Flinter: This Precision Medicine Initiative is going to provide so much vital information on so many aspects of population health across a diverse population of Americans. As we know health and disease are greatly impacted by people's racial and ethnic background, their economic status, their geography, their culture as well as their genes so this is incredibly exciting to me on the ground floor of this endeavor. I think we're all just very excited about where it's going to take us.

Mark Masselli: Speaking of exciting new frontiers in science and human biology that leads us to our guests today, Margaret, the mapping of the human genome a decade ago opened up the door to all kinds of new discoveries and there is a similar project just getting underway that could have huge implications for understanding the fundamental human biology more completely. Our guest courtiers of the Human Cell Atlas which seeks to map every cell in the human body.

Margaret Flinter: Dr. Aviv Regev and Dr. Sarah Teichmann will join us to talk about this massive project currently underway with trillions of cells in the human body. This is going to take some time but the implications for broadening or understanding of human biology and health are just astounding and we look forward to hearing more about the creation of the Human Cell Atlas.

Mark Masselli: Lori Robertson also stops by. She is the Managing Editor of factcheck.org. You can hear all of our shows by going to CHC Radio or you can also

find us on iTunes.

Margaret Flinter: And as always if you have comments please email us at CHCradio@CHC1.com or find us on Facebook or Twitter because we love hearing from you. We will get to our interview with Sarah Teichmann and Aviv Regev of the Human Cell Atlas project in just a moment.

Mark Masselli: But first here's our producer Marianne O'Hare with this week's Headline News.

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Marianne O'Hare: I am Marianne O'Hare with these Healthcare Headlines. Walmart weighing in on the Opioid crisis announcing its cracking down on initial Opioid prescriptions within the next 60 days saying they will limit prescriptions to just a seven-day supply. The CDC estimates 115 people die per day from some kind of Opioid overdose. Calorie counts – can we do a food counter near you the law requiring calorie counts on a number of restaurants food products is now officially in effect. It was part of the original Affordable Care Act in 2010 but was repeatedly blocked by lobbyists in the food industry claiming it was a hardship. Some evidence suggest posting calorie counts of foods leads consumers to pause before making unhealthy choices. Kids should not be consuming any nicotine products that's the word from FDA Commissioner Scott Gottlieb on this week's announced crack down on vaping products being marketed specifically to kids while teens are smoking fewer combustible cigarettes there has been an increase in vaping which can lead kids to becoming addicted to nicotine. Gottlieb says they will be stepping up enforcements of these stricter guidelines. I am Marianne O'Hare with these healthcare headlines.

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Mark Masselli: We are speaking today with Dr. Sarah Teichmann, the Head of Cellular Genetics at the Wellcome Sanger Institute at Cambridge a nonprofit British Genomics Research Institute and Dr. Aviv Regev, Chair of the Faculty and Co-director of the Cell Circuits program at the Broad Institute of MIT in Harvard. Both are Co-chairs of the Human Cell Atlas Organizing Committee a global collaborative of leading scientists dedicated to creating the first complete mapping of all human cells. Dr. Regev was awarded the NIH Director's Pioneer Award and the Overton Prize having earned a PhD in Computational Biology at the University of Tel Aviv and Dr. Teichmann has earned numerous awards as well including the Lister Prize and the Colworth medal. She earned her bachelors in biochemistry from Trinity College, Cambridge University and her PhD in Molecular Biology at Cambridge. Sarah and Aviv welcome to conversations on health care.

Sarah: Thank you.

Mark Masselli: So much, Aviv let's start with you we will be getting to gain an

exponential understanding of human biology through the Human Genome Project, that ultimately led to the sequencing of the human genome often with such dramatic achievements these discoveries can unleash a whole set of new questions and answers and you are at the helm of an equally ambitious effort the Human Cell Atlas project and I'm wondering if you could tell our listeners about the goals and the mission of your endeavor and highlight some of the challenges and opportunities of this undertaking.

Sarah: Absolutely and it's wonderful that you started with the Human Genome Project because just like the Human Genome Project was a project to find the genes which are one part of the periodic table of elements of the human body the Human Cell Atlas aims to find all the cells which are another set of elements except that that there are 37.2 trillion of them. Just that shear number together with the huge size of the human body I think really underscores how difficult this can be. The other thing that's difficult is that the cells are different, different types of cells look different from each other. They express different genes in them and they have different molecules inside them and until recently we could only really analyze multiple cells at once maybe millions or tens of millions of them together but the average doesn't really tell you about the individual cells and if you don't know which cells are there you end up with something that can be very confusing.

Now we have new techniques that allow us to look at individual cells either after we separate them one from the other or when the cells are in the tissue but looking at all of their molecules at once. And with these new methods you can think of it as new microscopes that allow us to look at cells we can really take on this challenge of the trillions of cells that are different from each other and with this we hope that we can build the really comprehensive reference map or a periodic table of the elements of the cells that make up the human body. We can find both the cells that are there in health but also to use this information in order to better diagnose and monitor and treat human disease.

Margaret Flinter: I want to ask Sara this question you've assembled an international team of computational scientists and microbiologists and the whole panoply of experts from so many scientific disciplines just decree of framework that can support this kind of effort. Help our listeners to understand the complexities that are involved in scaling up the Human Cell Atlas project and how your team is navigating, some of these foundational logistics in order to actually bring this project to scale.

Sarah: Sure. The complexities are absolutely right. It is complex. It involves lots of different disciplines and as you can imagine where that complexity starts is with acquiring samples of human tissues. That really starts with our friends, the medical doctors, the surgeons also the biomedical specialists that focus on different tissues and the biopsies. Those samples are then analyzed using a variety of cutting edge genomic technologies. Single cell genomics is one of them. The excitement there is really the resolution revolution that's taken place in genomics where we can now study DNA and RNA nucleic acids in individual cells. That's an incredibly exciting. That resolution evolution is also going to the spatial level where we can study cells in their spatial

context. Then the output from that data generation of course has to be processed. The technologies are genome biologists I would say technology developers and the data processing is then carried out in a data coordination platform that we're happy to elaborate on later and that's a lot of software developers. People who specialize in database management of large data flows and organization of humongous data sets. Then the final sort of level the fourth level is the analysis of that data and the interpretation and the biological understanding through data mining and that's where computational biologists come in machine learning experts biologists who interact with these computational specialists it's a collaborative effort. It's really those four levels that have really catalyzed the whole Human Cell Atlas consortium. Those are very different types of people from all over the world that makes it a huge amount of fund, it's a global effort that's very disciplinary.

Mark Masselli: That sounds so exciting I don't know if there is an IRB and as I understand you are not only seeking to identify potential billions of cells in the human body the [inaudible 00:10:00] and so on but also to categorize each cell and how it fits in and how they behave you envision there will be terabytes, maybe zettabytes or maybe as you said humungous amount of data. Also it's going to be adaptable and accessible to many scientists and researchers who have been working with NIH and Dr. Collins on this whole of us initiative and sort of the curating of how scientists access data will be very important so maybe opine on some of those?

Sarah: So, you were right this is going to be a lot of data I already said 37.2 trillion cells in the human body and even if just some of them make it to the Human Cell Atlas that's still going to be as a big data as any of the big data endeavors that we're familiar with. One of the first activities to get going was our data coordination platform which is really a partnership across multiple institutions including the EBI in the UK UCSC in Santa Cruz, the Brode Institute where I am. Also engineers from the Chan Zuckerberg initiative who are buildings together a data coordination platform to house all of this data and make it first of all openly accessible to all you mentioned IRBs everything is with appropriate consent, but the data will be opened and accessible to all and the data platform itself is also a open source which means that anyone can use the same platform for many other applications. It's funny that you mentioned all of us in fact some of the team of engineers that participates in building all of us also participates in building the data coordination platform. There is also a connection to this more clinical view of the world. There has been such a explosion of abilities today in the world of software engineering and machine learning that has happened really in parallel to the explosion of our ability to collect these kinds of data. As a result we can bring to bear all of this wonderful engineering and machine learning skill on this kind of problem so that the data cannot only be housed and processed but to also it can be served with the right kind of visualization and query tools so that biologists and medical experts can actually use it.

Margaret Flinter: So, let's talk about governance of the Human Cell Atlas for you there is four pillars that you've identified on which this project is based share with us what those pillars are and some of the standards that the Human Cell Atlas will operate by?

Aviv: Sure so in terms of a basic pillar and this is something we share in common with the Human Genome Project is we want this data to be opened and accessible for the scientific community the medical community and everyone who has an interest in human cells and tissues and genomic data. Now this is such a big vision and ambition that we realize that we have to work together internationally to achieve this so coordination with each other is something that we're striving towards and we have been from the very beginning we have an organizing committee and Aviv and co-chair that there are working groups that are responsible for the data coordination platform the metadata. Then really this links also to the way we work and that is that we have the data coordination platform but also an analysis group where there is a rich eco system of computational methods and algorithms that are developed by the Human Cell Atlas working group and indeed any [Inaudible 00:13:29] group that can then share their methods across the community. On the biological side, we have collaborative biological networks that focus on specific systems and organs, so you know there's one for lung, cardiovascular system and brain and these bring together a scientific experts from the community who want to work together and share their expertise and their progress and coordinate to map these particular tissues and organs and systems of cells and so on. And then also we want to catalyze technology development and the Human Cell Atlas, I think has played a role in this very rapid resolution revolution I would say in genomics, where a single cell genomics technologies have just become extremely scalable and robust and affordable, so single cells cannot be sequenced but we can actually measure molecules in the content, their spatial context in the tissue within their tissue context.

Mark Masselli: We're speaking today with Dr Sarah Teichmann, Head of Cellular Genetics at The Wellcome Sanger Institute at Cambridge, the nonprofit British Genomic Research Institute and Dr Aviv Regev, Chair of the Faculty and Co Director of the Cells Circuit Program at the Broad institute of MIT in Harvard. Co-chairs of the Human Cell Atlas Organizing Committee, a global collaborative of leading scientists dedicated to creating the first mapping of all human cells. Aviv, I'm really struck by the fundamental idea here that we've been looking at cells with 150-year-old technology. Now we have the dramatic potential for CRISPR technology and I knew that Broad Institute has been front and center in that with the CRISPR9 and big analytics are accelerating our ability to collect, interpret data. What could you share with our listeners about these recent technological developments? How they're making this ambitious project possible?

Aviv: You should think about it as though you're trying to build a map, like a google map. We like to say Google maps for the human body and a map has to have coordinates. The coordinates in our case are going to be the expression level of every individual gene and really the transformational step that has happened is that we can measure the expression level of every individual genes. For every individual cell is a very massive scale. At first, we could do one cell and then a handful of cells and now it can be tens of thousands, hundreds of thousands and millions are completely within reach in a single experiment and similarly to that as Sarah described we can do it for cells when they are separated from each other and we can do it for the cells when we

see not only their coordinates in terms of the expression level of each genome, but we can see also the real physical coordinates. We can see where they are in three dimensions in a piece of tissue. That's like getting a new pair of eyeglasses, right? When you get your glasses and you put them on, all of a sudden everything comes into [inaudible 00:16:24]. That's how cells got discovered in the first place due to a new technology, the microscope and that's how we get to rediscover I mean their full richness using these new approaches, but once we discover that we have the cells, the immediate next question that we want to ask, what controls them? What makes them, them in their special way and this is where the ability to genetically manipulate cells become so useful and that's what CRISPR allows us to do, not inside humans, but outside people, in organoids, in cell culture, in model organisms. You can now start manipulating the different genes that are highlighted by this reference map and the map together with algorithms might predict what would happen if I take this gene out, is a question that becomes very easy to answer with the help of CRISPR. So these two were really made for each other and in fact, we can take a large number of cells, use CRISPR to remove one or more genes from every cell. Then use these single cell approaches to really measure what was the effect of CRISPR in each cell.

Margaret Flinter: Very exciting and a complex scientific research requires a lot of intellect and determination, but it also requires resources and I know the Human Cell Atlas is getting help from a number of sectors, including the teams at The Broad Institute at MIT in Harvard as well as your research facility, at The Wellcome Sanger Institute at Cambridge. I also understand there's some significant philanthropic input from The Chan Zuckerberg initiative, which has a mission of ending preventable disease by the end of this century. Talk with us, how their support is really essential to supporting this undertaking?

Aviv: Sure. The Human Cell Atlas relies on the support of many funders, government funders, many private foundations and large institutional ones, and that's what's really enabled us to hold the community, get together, start the data coordination platform, start producing the data that will go into the Atlas from the early days. The Wellcome foundation, also the The Chan Zuckerberg initiative, The Kavli Foundation and now more recently the NIH HuBMAP for the National Institute of Health and the NIH Cancer Moonshot. The Chan Zuckerberg initiative had provided support very specifically for the data coordination platform and that's where the data that's created by the HTA projects will be stored and organized. They are also supporting pilot projects on technology development that will all hopefully help the Human Cell Atlas effort.

Mark Masselli: Well, that's wonderful and Aviv you've identified more than a million cell so far, there's obviously a long way to go and your website suggests that when this project's completed, it's going to have a dramatic impact giving us a better understanding on the immune system, the brain, the cancer developmental cells just to name a few and as you look ahead, what excites you most about the potential of the Human Cell Atlas to yield new insights and what are the greatest potential for discovery in biomedical advancement that you think might come out of this?

Aviv: You can think of it sort of as an augmented reality of our body, right? That has impacts for both the most fundamental questions in biology. What are the cell types that are there and how do they behave in physiology? And, we're already getting answers like these. We discover new cell types, new cell types in the blood, new cell types in the lungs, that we didn't even know exist. Then we can ask questions and how do they behave when things are good. Also how things go awry. I think in the context of disease, some of the most basic tests that are done when we're sick are basically single cell assays. The blood draw, you count how many cells are there of maybe six different types, except that we know that there should be dozens of types, so you can imagine a complete blood count 2.0 tells us much more about the status of our body right now. Same is true when the biopsy is taken, and you take a slide, you stain it really with those hundred-year-old or more techniques to look at tissue sections except that you will now look at all of the molecules that are there and you will understand how the cells relate to each other and maybe find new avenues for therapeutic interventions. When we find genes from genetic studies that are associated with disease, we don't know where these genes act, but the Human Cell Atlas, would give us a reference map to really say this gene is actually important in that kind of cell. That's the next place to look at, both to understand disease mechanisms and to try and develop the new drugs. When we screen for drugs, we could screen them for giving the cells particular set of molecules that is desirable and when we treat patients, for example, in wanting to have much better for toxicity because we would know all of the other cells that might be impacted by the same drugs. Both were fundamental biology and for biomedical research and applications, we think that having a map is much better than having no map at all, but I think we will leave it at that.

Margaret Flinter: We've been speaking today was Dr. Sarah Teichmann, Head of Cellular Genetics at the Wellcome Sanger Institute at Cambridge and Dr. Aviv Regev, Chair of the Faculty and Co-Director of the Cells Circuit Program at the Broad Institute of MIT and Harvard, Co-Chairs of the Human Cell Atlas Organizing Committee. They are dedicated to creating the first complete mapping of human cells. You can learn more about their work by going to www.humancellatlas.org or follow their work on twitter at Human Cell Atlas or the Broad institute at Broad Institute and the Wellcome Sanger Institute at Sanger Institute. Sarah, Aviv, thank you so much for sharing your very exciting and groundbreaking work with us, and for joining us on Conversations on Healthcare today.

Dr. Aviv Regev: Thank you so much.

Dr. Sarah Teichmann: Thank you.

Margaret Flinter: Bye.

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Mark Masselli: At Conversations on Healthcare, we want our audience to be truly in the know when it comes to the facts about Healthcare reform and policy. Lori Robertson is

an award-winning journalist and managing editor of FactCheck.org, a nonpartisan, nonprofit consumer advocate for voters that aim to reduce the level of deception in U.S. politics. Lori, what have you got for us this week?

Lori Robertson: 20 percent of the children in the United States, it's go to bed hungry. That's what House Minority Leader Nancy Pelosi said, but we found that she misrepresented government data. Pelosi claimed that, “One in five children in America goes to sleep hungry at night.” There is no precise measurement for childhood hunger in the United States, but the census bureau’s most recent Household Food Security Survey found that about 6.5 million children or 8.8% “lived in households” in which one or more child with food insecure. Pelosi's office referred us to a U.S. Department of Agriculture 2017 report on food security. The USDA administers the Supplemental Nutrition Assistance Program and several child nutrition programs for low income families in an attempt to combat hunger. The USDAs report is based on the 2016 current population survey, food security supplement, and as Pelosi's office told us the report says 16.5% of U.S. households with children were food insecure at some point during 2016, but that doesn't mean that the children in those households go to bed hungry. The government differentiates student security by whether it affected adults only or also children. For children, 8.8% lived in households where at least one child with food insecure and in 0.8% of households with children, both children and adults had very low food security. The USDA said that food insecurity with severe enough in those households that children were hungry or skipped meals, and that’s my facts check for this week, I am Lori Robertson, Managing Editor of FactCheck.org.

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Margaret Flinter: FactCheck.org is committed to factual accuracy from the country’s major political players and is a project of the Annenberg Public Policy Center at the University of Pennsylvania. If you’ve a fact that you would like checked, e-mail us at www.chcradio.com, we’ll have FactCheck.org’s, Lori Robertson, check it out for you, here on Conversations on Healthcare.

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Margaret Flinter: This is Conversations on Healthcare, I am Margaret Flinter.

Mark Masselli: And I am Mark Masselli, peace and health.

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