Emily: 00:00 The Colorado Clinical and Translational Cciences Institute at the University of Colorado Anschutz Medical Campus builds the research teams of the future to speed the development of new treatments and improve human health. On today's President's Innovation Podcast, we're speaking with Dr. Ron Sokol, director of CCTSI, and professor of pediatrics at CU Anschutz about the life-changing, innovative work underway at the Institute. Thanks so much for joining us today, Ron, we're so happy to have you. To kick things off, I just wanted to ask for the benefit of our listeners. Can you give us an example of translational science or research? What is that exactly?

Ron: 00:41 Well, first of all, thank you for inviting me to speak with President Kennedy on this subject. Translational research: It now has a very broad definition. The concept is taking basic discoveries and translating them into interventions prevention, new therapies that benefit humans in a clinical setting, in a hospital benefit humans in a practice setting in the community, and finally benefit populations of people. So there's different steps that we talk about for translational research, the early steps going from basic research to a first in man type of research setting in a very structured environment in the hospital, we call that T-one research T-two research is taking that more into clinical trials. T-three research is taking the intervention into a community setting to see if it's effective in a real world setting. And then finally, T-four translation is taking this into a more global population, health population, health public policy setting. So that's how we view translational research these days in a very broad sense. And the CCTSI direction from NIH is to facilitate all aspects, all form translation from basic science to population health.

Mark: 02:19 It is a confusing word to many you've explained it very well, but each translation means an idea a discovery has more impact. When you go from step a to step B from animal to, to humans, to patients, to patients, to public health you're broadening and expanding the impact that an idea or a new discovery can do?

Ron: 02:44 Yes. And you're taking it closer and closer to the actual person from a basic discovery through the steps, but I think that's a nice way to put it. You're really broadening the impact.

Emily: 02:58 Can you give us a little bit of a background on CCTSI when it was established and how it came about?

Ron: 03:09 The CCTSI was established in 2008. It was in response to the National Institutes of Health transformation of some of their prior programs to support clinical and translational research into now forming research institutes and training programs at major biomedical research centers across the country. So we originally had smaller grants for call general clinical research center grants that were incorporated into this larger program, as well as some training and education programs that the NIH funded. All of these were integrated into one much larger expansive program, which now includes many partners, institutions that were not included before 2008. And these are funded by NIH in five-year cycles. So every five years, which is coming up next year for us, we have to resubmit a grant to maintain our funding.

So we are what's called disease agnostic, and this is by NIH mandate. So we are not a heart Institute. We're not a cancer Institute, we're not a pediatric Institute. We really have to support the best research and the best investigators, whatever field they're in.

But I did want to point out that the support for the CCTSI goes well beyond our NIH grant. And we have considerable in-kind as well as actual funding from our hospital partners are the university, our medical school, et cetera. So truly is a broad partnership of collaborative institutions, all with the same vision to bring cures and treatments closer to the patient faster.

Emily: 04:46 How did you get involved with the institute?

Ron: 04:51 I'm a pediatric gastroenterologist and hepatologist who had been involved in clinical research and childhood liver disease for many years. And I used to use the facilities of the general clinical research center to help facilitate my own research. In 1998, I was asked by them to become the director of the pediatric GCRC, it was called. And then in 2006, when the university decided to apply for one of these larger CTSA grants, I was chosen to lead this effort and I've been the director principle investigator since 2008.

Emily: 05:37 Well, one of the things that I was curious about is C CTSI promises to build the research teams of the future, in your opinion, what will distinguish research teams of the future versus those of the past, or even the present?

Ron: 05:52 That is something that we're constantly striving to and to support in all ways possible. Many would say the physician scientist, which is just one of the types of researchers that we promote, that the physician scientists may be a dying breed because of so many other pressures on physicians also to keep PhD and other scientists interested in biomedical research takes resources and training programs. So the translational scientists of the future is going to be a person who lives in team science, works collaborative with others, understands data science and how they integrate large data sets in order to answer scientific questions and the type of data that I'm speaking to our patient level data from electronic health records like we have in our hospitals imaging data, complex brain and other body imaging, data, genomics, gene testing and other technologies proteomics with a goal mix, et cetera, and environmental public databases which can geocode a patient's location and give us information about environmental exposures. And when you put all of those types of data sets together, it's going to take a new type of scientist that understands how to manage and analyze data in the future. That's not to say that basic science cellular work animal preclinical work is not just as important, but the translational steps in the future are really going to require more knowledge about analyzing large data.

Mark: 07:49 I think it's important to point out as we're talking about using that data that we do take great care to make sure that any individual identifiable to a person aspects of that data is always protected. And we do take data privacy very seriously. But what you're saying is, if you look at the teams at tomorrow relative to yesterday, there's going to be a lot more bioinformatics in the mix than there was in the past and, and it's going to need both the scientists with the bioinformatics working together.

Ron: 08:24 Yeah. And as you said data privacy and data security in order to be able to have these data sets in a way that protects the individual patient or person is absolutely paramount. And obviously, is a big focus nowadays for all of us.

Mark: 08:43 And, and do we see this ultimately ending up in allowing for more individualized treatment of someone who comes into our doors based on the way it can tell us what's best for them as an individual?

Ron: 08:58 Absolutely. And precision medicine, personalized medicine really takes advantage of understanding a person's clinical makeup, their biologic makeup, their genetic makeup, their environmental exposures. And we don't quite have a handle on how to integrate all of this yet, but there's made many advances, particularly in certain diseases like cancer, where this information has driven a new way to look at treating cancers by their cancer, biology and genetics, rather than by a name given to the cancer. So it's already transformed many aspects of medicine, but there's much more to be done to really make individualized or personalized medicine the way we treat all diseases.

Emily: 09:52 The CTSI is a multi-institutional entity. Can you give us a sense of the breadth of institutions and specialties working together through the institute and the rate at which the CCTSI's continues to grow? I think it's pretty dramatic.

Ron: 10:12 Yes, I'd be happy to. The CCTSI is based at the CU Anschutz campus, but CU Boulder is a close partner institution in the CCTSI the downtown Denver campus of CU Denver is another close institutional partner and actually Colorado State University is our newest partner, we're going on about eight years of partnership CSU actually, and see, you have many partnerships in cancer research, nutrition research, the school of public health, et cetera. But since we're talking about biomedical research, our other partners that are extremely important are our hospital and health care organizations. So University of Colorado Children's Hospital, Colorado Denver Health, the Denver Rocky Mountain VA hospital system, and Kaiser Permanente, are our other partners in this endeavor. Finally we have many community organizations that we work with across the state, through research networks or through collaborations with faculty.

Ron: 11:33 And we usually say we have over 20 community organizations and these change each year. We also emphasize the health profession schools at the Anschutz campus. So this is not a School of Medicine Program. It's a program that involves the School of Medicine, nursing, dentistry, School of Public Health, pharmacy and pharmaceutical sciences and the graduate school, and many of the schools and colleges at Boulder and the downtown campus and CSU. So the way we can keep track of everything in this, a large collaborative organization is by asking all investigators, train the staff members, community members that others want to take advantage of the resources and training programs at the CCTSI. We asked them to become an online members. So we actually know who our constituents are. And we are now over 6,600 members registered with the CCTSI. I'll tell you what, our first grant, I estimated we'd have three or 400 individuals register with us. And now, again, by next year, we should be close to 7,000 individuals and we cleaned the database every year. This doesn't include people who are no longer in Colorado. So it's truly remarkable how much interest and need there is for translational research.

Mark: 13:09 Well, I think it also points there's, some government programs, you wonder if they're really effective, but this is a National Institute of Health program that was meant to spark collaboration. And just the idea that you have 6,000 people signed up electronically tells you that it seems to be achieving a team.

Emily: 13:28 As president Kennedy likes to say, we really are, collaborative partnerships and working together, it's, we're much more powerful working together. So that's pretty amazing. What are some of the biggest challenges or barriers to innovation and entrepreneurship at CU, and how does CCTSI help address these?

Ron: 13:48 So there are many challenges right now to innovation and entrepreneurship. And I won't even mention the pandemic, how this is thrown a wrench in a lot of the careers of individuals who had to put their research and innovation on hold for 15 months and all the stresses with caring for children at home, et cetera, et cetera, through the pandemic. And hopefully by the end of this calendar year, the greatest effect of the pandemic will be behind us. But other challenges that I see are the fact that most researchers are not trained in commercialization, product development innovations of their ideas, and it's a different culture and it's a different career path than most of us who've been brought up in the traditional medical research and clinical care pathway have been trained in.

Ron: 14:55 I was starting to imbue young trainees and young faculty in the excitement and benefits of thinking about commercializing and getting their products out there to help society. It's been an effort that the CCTSI is taking very seriously. So we have a few programs. One is called the iCore, Innovation Core, C O R

P S innovation core. That was originally funded by the National Science Foundation. And now a version is funded by the NIH and we have one of 10 sites at our institution and this trains investigators and trainee teams into how to assess market need for an idea they have, because lots of us have something we think is a great idea. But if you really look at the market, there's 10 competitors that are way ahead of you, and it doesn't make sense really to pursue that idea. So the iCorps program teaches them how to do a market analysis and needs assessment of their idea.

Ron: 16:04 Then we have a program that we work closely with CU Innovations on call the research education and commercialization hub funded by NHLBI (National Heart Lung and Blood Institute) that's into its third year, it's called reach SPARK. And the CCTSI and I've been involved in many ways in that program as well. And then finally ideas really take some funding to get to the next step, to see if it's something that's worthwhile to pursue. So one of our most popular research programs in the CCTSI are our pilot brand program. And we issue close to a million dollars a year of pilot grants anywhere from $25,000 to $60,000 each depending on the nature of the application. And so we usually administer 25 to 35 pilot grants, and this is across all of the institutions I mentioned to catalyze and spur new ideas into preliminary data and testing.

Ron: 17:14 And if the idea looks good, then we encourage other investigators to go on and apply for larger grant funding in order to support their research. And I guess one of the impacts and success stories is that our pilot grant program has achieved a 15-to-one return on investment. Every dollar of pilot grant funding that we issue ends up on average returning $15 of follow-on grant funding. And then that may lead to a venture capital funding, new startup company, et cetera, et cetera. So, so those are just some of the ways that the CCTSI, and again, in collaboration with CU Innovations and others also the Boulder innovation hub we try to facilitate and encourage a new commercialization of ideas.

Emily: 18:09 We actually recently spoke with Kimberly Mueller, executive director of CU Innovations at CU Anschutz. Can you just talk a little bit more about how CU Innovations and the CCTSI differ? You talked about how they collaborate, how are they kind of different entities?

Ron: 18:31 So the CCTTSI has about 17 different programs and 13 different training programs for faculty, students young investigators, senior investigators. We have a leadership training program. We have biostatistics resources, informatics resources. So we supply the necessary foundational ingredients in training, as well as facilitate the research projects themselves. And we supply mentoring expertise, et cetera, CU Innovations, takes it to the next level. Once there's a promising result from the research that could be transformed into a product digital drug biologic device, and they help investigators go through the steps of turning an idea into a product. And then business development, startup company development, FDA filing painting venture capital. That's really where CU Innovation takes over.

Emily: 19:46 So you guys kind of set up the ball and then they spike it over the middle. Well, in your opinion, what are the biggest opportunities for innovation and entrepreneurship at CU and across the CCTSI partners?

Ron: 20:04 Well, I, I think the opportunities lie in the amazing trainees and faculty that we have across all of the CU campuses, because it really takes curiosity and ingenuity and steadfastness among investigators to take an idea and develop it further and make real contributions. In biomedical research, we've made numerous contributions that have already reached patients and will reach patients in the future. So the opportunities are there. What we really want to do is encourage and support, particularly young faculty and fellows and postdocs students, et cetera, and even high school students to show them the excitement of a biomedical research career. And we do this through various programs with the GAM high school students, college students, et cetera. And by supporting their research, showing them how

to perform the research, facilitating it through our research units, we have what's called clinical translational research centers. These are research units where we supply nursing support, regulatory support. We have facilities, we do testing. So we supply, again, a lot of the infrastructure and training that is necessary to bring the next generation forward and to help current investigators as well.

Mark: 21:41 You were talking about the opportunity and earlier you talked about the big challenge being, how do we get more physician scientists to understand that they can go further than just the discovery, into the actual product or output that's going to impact people's lives? And that was one of the things when we talked with Stan Lapidus, who's one of the entrepreneurs that advises the SPARK program. He says, once we get him in the door of the spark program, we've got a pretty good track record. How do we get more to come into the SPARK program? How do we get more of our very smart, very innovative physician scientists, researchers to think beyond discovery and think to impact?

Ron: 22:33 Well, that is a topic that's actually undergoing a lot of national discussion because there's lots of pressures on physicians to account for the salaries, their clinical care responsibilities, their family responsibilities, and what we believe the single most important way to encourage physicians to stay in research is by having role models and mentors. And I know that Stan also believes particularly in the entrepreneurship space that having the right mentorship is absolutely critical to becoming successful. So through the CCTSI many of those pilot grants, for instance, that I mentioned are given to young, early stage investigators who have mentors. And we try to make sure that the mentorship given to the young investigators will be such that they will be successful in their research, get excited about their research. And if one who has transformed an idea into a product or an intervention works with a young investigator, you can help show them the way.

Ron: 23:48 I think a lot of the challenges though, are the competing needs for physicians in the country. And research is tough business. You know, it's called research for a good reason and there's lots of failures but lots of successes. So you have to be able to roll with the punches but have a support system that continues to encourage you and give you the support you need to stick with research. I've seen many young investigators sometimes have to submit eight, nine grants before they got their first grant, but boy, once they got that first grant, their trajectory increased dramatically. And one thing led to another and now they're national leaders in their field. We really have to look at the early career trajectory of various individuals and support them at that time. And the university actually has done a great job with that. I'm the chair of the committee that reviews the Boettcher Web-Wearing grants, which help young investigators accelerate their career by getting these wonderful grants for a few years. And the success of that program is incredible. So I think there's a lot we should do, but we really need to focus on the young investigator early in their career.

Emily: 25:17 What are some of the breakthroughs the CCTSI has advanced that are already having a positive impact in our communities?

Ron: 25:25 CCTSI doesn't set the research agenda. We've facilitated it to happen, accelerate it and make it successful, but it's really the investigators' ideas that spur the innovations. So for instance, at our pediatric CTRC, we've been very involved in the clinical trials and development of drugs for cystic fibrosis and just recently the new triple therapy drug for cystic fibrosis. And, matter of fact, this week was approved for children down to, I think age 5 or 6.

Ron: 26:34 These drugs have completely transformed the lives of children with cystic fibrosis, where 50 years ago, they wouldn't even survive out of childhood. And now the average survival is well into the 50s, if not 60s. And again, our site was one of the major sites and one of our faculty was the lead author in the

New England Journal article up the first drug to transform CF. We've also been very involved in the artificial pancreas development of these closed-loop influence creating devices for children with type 1 diabetes. And those are now on the market changing, again, the lives of children with diabetes. Likewise we've been involved in much of the COVID drug development and testing in the state of Colorado. And now we're involved in all of the vaccine trials that are for the vaccines that are currently available in the us. We reallocated many of the CCTSI's resources back in March of 2020 to allow us to facilitate COVID research. And literally we've been involved in hundreds of studies. We initiated a new pilot grant program last year and in early April to help stimulate COVID research. And I think we should all be very proud that, that we really played our part in Colorado in stemming the tide of the pandemic.

Emily: 28:11 Absolutely. And speaking of COVID, you've already said that the pandemic grit vastly tremendously disrupted research operations at the CCTSI, are things returning to relative normalcy?

Ron: 28:28 I'm really happy to say that as of June 1 on our campus, all of our laboratories are open at full operation. All of our clinical research has been back online for at least a few months. And our data scientists, they were the ones who were able to continue with their research throughout the pandemic because they could do this remotely. Our university obtained tens of millions of dollars of new grants during the pandemic to help study COVID and various interventions, as I've mentioned. And many of those are either winding down now or are completed. However, there's some brand new COVID challenges that I think all of us have heard about called long haulers or long COVID. And we are now right on the verge of getting a massive NIH grant in collaboration with Utah and New Mexico to study long COVID in, in our three states. And the NHLBI is funding back. They're making the final protocol changes now. So although our own research facilities have opened, we're still looking down the line at doing everything we can to better understand consequences and long-term consequences of COVID. And we're very excited about this new funding stream.

Emily: 30:13 Great. That's so important. The CCTSI has also been working to foster a culture of diversity equity and inclusion. Can you talk a little bit about what steps are being taken to address those issues?

Ron: 30:29 And we really thank you for asking that question, because this has been an area that we have been involved in since the beginning. However, the last year I think has really brought it to the forefront of us. That there's much more we should be doing, and particularly to look within our own programs and see if we have systemic racism built into our structure that we need to define and then eradicate. So the CCTSI is first of all, putting out a statement on our website about our commitment to diversity, inclusion, anti-racism and we want to be held accountable to what we say we're going to do. So one of the first things we did was decide to put on our executive committee that oversees the CCTSI to add more diversity. And we actually just last month brought in two community members who are one is African American. one is Latino to be on our 20-person oversight committee for the whole CCTSI that we call our executive committee. We're also going to bring in community members from underserved communities, into many of our committees to get a community voice and input in our decision-making bodies. We are also looking at various funding opportunities from NIH to be able to fund diversity candidates that are researchers to give them a better opportunity to become successful. And we just received this week, a grant from NIH to fund a young investigator for the next three years, who is African American our community engagement and research program in the CCTSI, which has been with us from the beginning is all about research and implementation of new best practices in underserved communities throughout the state of Colorado. And finally this month, we received a grant from NIH called the Community Engagement Alliance to address COVID disparities, CEAL.

Ron: 32:53 We were one of the 10 states to receive this. That's a very large grant, again, whose purposes to help rid the communities of disinformation about COVID, its treatment, vaccines and to educate the communities using messaging that they've helped us determine will be effective. In particular around vaccine hasn't been seen and treatment hasn't been seen as well. And we've already in one month made great strides toward developing the messages to our communities in the state of Colorado. And that will start being implemented next month. So those are some of the activities that we're involved in to try to address the diversity health disparities and the systemic racism.

Emily: 33:49 Wonderful. What other initiatives or projects are underway that we can look forward to from the institute?

Ron: 34:05 We just started a program this year and we're going to expand it next year in teaching young investigators how to be team-science members. So we talk about team science. We all know it's really necessary, but how does one really understand what it takes to be a good team member and become successful? So it's called teaming and we're running it four times this year. It's actually a CSU professor in social sciences. Jenny Cross, who her research is on teaming and team development. She and her team are teaching our young investigators how to become effective team members and improve their team science. The other new aspect of our training programs is our desire to help investigators be able to communicate their science to the lay public.

Ron: 35:20 And no time in our history, was this more important than during the COVID pandemic where so much misinformation was out there. And it took people like Dr. Fauci and others to continue drive home the message of science and of a reality of what the pandemic was all about, how to prevent transmission, et cetera, et cetera. So we are starting a program in September, and we're going to run it three times this year with a person who is outstanding in communicating science. Her name's Comilla Sasson, and she is very big in social media. She's interviewed frequently on CNN and other national stations. She is, she is putting together a curriculum of how to communicate your science to the lay public for our faculty and training needs. And this is going to be a virtual program. We may continue with virtually in the future or decide to do it in person, but it's a new a program that we think is absolutely essential in order to educate the lay community about science. .

Mark: 36:41 You know, Dr. Sokol, as we hear your answers, we clearly can sense the enthusiasm you have for your work. And it's gotta be very rewarding to labor every day at efforts that will ultimately bring new treatments and cures to people, help young scientists move along their path towards achieving those ends. It's gotta be very satisfying work that you do.

Ron: 37:05 It is President Kennedy, and I must say that it is not my work. It is our team, and we have an amazing team of researchers and leaders. And again, not only on our campus at CU Boulder, downtown CSU, the hospitals and it, this has just been the most exciting thing in my career to be able to, to lead this group and watch the wonderful successes that they create. It is extremely rewarding and necessary.

Mark: 37:47 There are probably those that are listening to this podcast that would love to be a part of that team and help out in some way, shape or form. Would there be any advice or suggestions you have for listeners that say, 'this is very exciting to me. I'd like to help with a contribution with whatever other means,' what, what are the ways that people perhaps listening to this podcast could reach out and help the efforts that you and your team are achieving?

Ron: 38:14 Well, if you're a young scientist or researcher, please go to our website. You can just Google CCTSI, and we're one through 30 on Google. And you can look at our programs. You can contact us. We get lots of

questions about how do I get involved? And we're excited to get you involved in the CCTSI. However, you know, the reality of research is that it's expensive. It takes resources, it takes funding, and there's philanthropic individuals that might be interested in supporting programs, even attaching their names to those programs. We'd be excited for them to work through the CU Advancement office to see what opportunities might be available. Also community members. Our community engagement program is always looking for community members that are interested in collaborating with our researchers and our institutions to look and see how we can help with a problem identified by a community in the community, whether our research programs or our clinical programs can assist them. And then finally we have a public-private membership, and this is for members of the government, people at other public institutions and people in private companies. Some of them are startup companies. Some of them are larger pharma companies. I encourage those that are interested to look at our membership page and become a member and contact us. We'll be happy to get you involved.

Emily: 40:08 Well, thank you so much, Dr. Sokol and President Kennedy for being here with us today, and yes, for sharing your enthusiasm about this wonderful institute. We're so happy to have had you on the podcast. Thank you so much.

Ron: 40:22 Well, I, I thank both of you and this has been a wonderful opportunity.

Mark: 40:42 This work is very important because unlocking the discovery and making it meaningful and a treatment that will cure somebody that will help them live a healthier life is so vital. So this is the sort of the last mile in discovery. And I think that, yes, we need support for discovery, but when you already have it, it's just so sad to see it not come to fruition. This is the opportunity to help more and more of the wonderful ideas that come up from our fabulous scientists and physician scientists to make it a reality that will cure people's ills and better their lives.