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00:00:00.076 --> 00:00:06.423 Announcer Funding for Yale Cancer answers is provided by Smilow Cancer Hospital.

00:00:06.500 --> 00:00:22.346 Announcer Welcome to Yale Cancer answers with the director of the Yale Cancer Center, Doctor Eric Winer. Yale Cancer Answers features conversations with oncologists and specialists who are on the forefront of the battle to fight cancer. Here's Doctor Winer.

00:00:22.423 --> 00:01:13.423 Eric Winer Tonight, I'm going to be speaking with our guest, Doctor Rachel Perry, who is an associate professor at Yale. Her lab at Yale examines the impact of obesity and metabolic dysfunction on cancer outcomes. And they recently completed a study on exercise and tumor growth. We've talked a lot in the recent weeks about the impact of lifestyle interventions on cancer and cancer recovery, but this is an opportunity to drill down on some of the science to understand why it is that exercise and changes in diet could affect the development of cancer, could affect how a person with cancer, does in terms of the outcomes after treatment.

00:01:13.500 --> 00:01:42.269 Eric Winer We're also going to talk a little bit about the general importance of science and scientific inquiry in both cancer medicine, but more broadly, in terms of how important science is in changing the health of Americans and people around the world. So without further ado, Rachel, it is a pleasure to have you with us tonight. Thanks so much for being here.

00:01:42.346 --> 00:01:45.461 Rachel Perry It's a pleasure to be here. Thank you, Eric, for having me.

00:01:45.538 --> 00:02:17.192 Eric Winer So maybe we could just start with, a little background on you. My recollection is that, you actually came to Yale to New Haven as a freshman in college, and, Yes, I actually haven't really left. What made you choose science as a career? And did you know when you were a freshman in college? Did you know that you wanted to ultimately have a lab and pursue science in the way you do?

00:02:17.269 --> 00:02:37.769 Rachel Perry My career has evolved over time. I have always been interested in science as early as middle school. I remember taking science classes and and learning, early in high school that it was an option to have a lab. And I thought, what a cool opportunity to be able to come to work every day and find out things that nobody knew before.

00:02:37.846 --> 00:03:00.538 Rachel Perry And I was really fortunate in high school to have a wonderful mentor, Doctor David Van Wagner at the Cleveland Clinic, who really gave me some great opportunities to come into the lab. As a high school student, I couldn't contribute meaningfully, let's face it. But he was very generous in allowing me to come in and, work with some histology samples, doing some quantification of something.

00:03:00.538 --> 00:03:24.000 Rachel Perry I can't even remember what we were looking at. In heart samples of patients with atrial fibrillation. And really, from then on, I was hooked. My my journey in science has been one really about people. It was that first mentor, who really got me hooked on it. And we've stayed in touch to this day. I went back, he invited me to come back to the Cleveland Clinic and speak 20 years later.

00:03:24.076 --> 00:03:52.153 Rachel Perry And that may have been my favorite speaker opportunity ever. So I, I knew from early on that I was potentially interested in science. When I was in college, I took a class in physiology called Physiological Systems, and I knew that I was interested in metabolism research. That is the study of how our body uses different nutrients and how different nutrients go to different places depending on the needs of parts of the body at the moment.

00:03:52.230 --> 00:04:16.346 Rachel Perry And I asked the professor, who had given this class on metabolic physiology for some recommendations for mentors, who I might be able to do research with. And as sometimes things work out, he gave me a list of five principal investigators I contacted all five. Only one wrote back, and then I was in his lab for the next 12 years, as an undergrad, PhD student and postdoc.

00:04:16.346 --> 00:04:41.038 Rachel Perry From that, I was I knew I was very interested in metabolism, but as my training continued, I realized metabolism is important not only for the sake of metabolism, but all the cells in our body use nutrients. And I knew that cancer metabolism was a really exciting field. And so when it came time to open my own lab, I knew that I wanted to study tumor metabolism.

00:04:41.038 --> 00:05:09.461 Rachel Perry How, tumors use different nutrients, that come in through diet and can be altered through things like physical activity. And, wanted to understand, you know, how we can parse out, how nutrients affect tumor growth? Because we know, based on a lot of prior epidemiologic literature, that metabolism is important to growing tumors, and we might be able to intervene and make prognosis better.

00:05:09.538 --> 00:05:15.307 Eric Winer Sure. And who was that mentor who you ended up staying with for 12 years?

00:05:15.384 --> 00:05:27.000 Rachel Perry Yes. My my longtime mentor is the cancer center member, a, professor of endocrinology and physiology doctor Jerry Shulman, really a trailblazer in the metabolic field.

00:05:27.076 --> 00:05:59.884 Eric Winer Right. And, and before we get to your science, maybe I can just ask you about being a woman in science. And while there are more and more women today than ever before, I think it's still a minority. Or women are in the minority. And certainly when you were in college, you know, 15, 20 years ago, looking ahead, you must have realized that there were a lot more men in science and who ran labs than women.

00:05:59.884 --> 00:06:03.500 Eric Winer And what's that been like?

00:06:03.576 --> 00:06:33.730 Rachel Perry That's a great question. And and certainly it has evolved over the years. We the role models that existed, certainly when I was in college were many more men than women. That's shifting over time. But I think, you know, we really have to be the change, and make some difference. I hope that, my presence may, make a difference for, for some maybe middle school girl right now, who's thinking about being a scientist.

00:06:33.730 --> 00:06:59.269 Rachel Perry And I think as, as we continue to, to do that, we can really change what the landscape, what the landscape looks like. I will say I've had really generous mentors and a really supportive environment. So I've, I've found it to be quite doable being a woman in science. But I think we we have to be conscious of valuing many different perspectives in particular in, in particular, many different leadership perspectives.

00:06:59.500 --> 00:07:16.307 Rachel Perry There is research that suggests that women may actually lead and practice medicine, if anything, more effectively than men, depending on, the, you know, depending on what exactly we're looking at. And so I think that highlights how important it is to embrace all perspectives.

00:07:16.384 --> 00:07:42.884 Eric Winer Well, I don't remotely question those data, about the effectiveness of, of women and their success. And in truth, all those years when women were excluded from science or largely excluded from science, we were depriving ourselves of half of the great brains, that that could contribute to science. Let's start talking about, some of your recent work.

00:07:42.884 --> 00:08:01.807 Eric Winer So in this recent study that you did, you looked at the impact of an exercise intervention on tumor growth in laboratory models. So this means you were looking at exercise in people, but, presumably in animals I would yes, yes.

00:08:01.807 --> 00:08:02.500 Rachel Perry In in mice.

00:08:02.576 --> 00:08:09.846 Eric Winer Tell us about, what you found and tell us how you how did you get those, those mice to exercise.

00:08:10.000 --> 00:08:31.730 Rachel Perry Absolutely. I I'd love to tell you about it. So our research I'll, I'll preface by saying our research was done in mice. But this is building on a lot of literature and research that's been done in humans as well. Some landmark studies here at Yale on my by Melinda Irwin and colleagues, showing that exercise is protective in people with cancer.

00:08:31.730 --> 00:09:06.884 Rachel Perry It reduces the risk, slows the prognosis, and reduces recurrence risk in individuals. So at all stages of their cancer journey, before, during and after exercise does seem to have protective effects, but we don't really understand how it is that it's working. And so because we don't understand exactly how it is that it's working, we have a hard time sometimes making specific recommendations to patients about how much they

should be exercising, what type of exercise they should do is a little enough, or do we need to be training for a marathon?

00:09:07.038 --> 00:09:32.076 Rachel Perry And so that's where mouse studies come in because we're able to, look at these mechanisms. The way that exercise may work in a different way than, than we can in people. And so what we did was to give animals with either breast cancer or melanoma, skin cancer, access to running wheels in their cages. So these are just like a hamster running wheels that you might have seen in in a pet.

00:09:32.153 --> 00:09:51.615 Rachel Perry And so they would run as much or as little as they wanted to do. And I think this is a really important point, because we did not have to force the mice to run. Mice actually love to run, a mouse will run 6 to 8km a day despite its tiny little legs. They they just love to run.

00:09:51.692 --> 00:10:12.500 Rachel Perry And so one could look at that and say, well, that that's a ton of exercise. I don't want to do 6 to 8km a day. And frankly, I don't want to run 6 to 8km a day either. But the flip side, the other way of looking at that is these mice simply moved as much as they wanted to, as much as they were motivated to and felt like.

00:10:12.576 --> 00:10:54.076 Rachel Perry And that exercise intervention slowed tumor growth by about 50% in female mice with breast cancer. So it had a really substantial effect to slow tumor growth in melanoma. The results were a little bit different. Simply having the exercise wheels did not really seem to slow tumor growth. However, baseline fitness. So so how fit the animals were at before we injected the melanoma cells that did predict slower tumor growth and so this suggests that the biology of the interaction between exercise and tumor growth may be different in different tumor types.

00:10:54.076 --> 00:11:13.153 Rachel Perry And so it'll be really important to study, people with cancer across different tumor types, and ideally develop biomarkers to allow us to predict who may respond better to an exercise intervention and perhaps be able to develop those interventions in a precision medicine type of way.

00:11:13.192 --> 00:11:32.346 Eric Winer Could you tell at all whether the intensity of the exercise made a difference? It's one thing to run 6 to 8km. It's another thing to run 6 to 8km super fast. Is there a way of of of of trying to answer that question in the laboratory?

00:11:32.423 --> 00:11:57.307 Rachel Perry So in our studies, the mice were all pretty much jogging. They typically don't sprint, when, when they're turning the running wheels around, the distance over the course of the day is more a matter of how how long, how many hours they spend, turning those wheels around. But what our data did show was that even a little bit of exercise did seem to make a difference in the mice with breast cancer.

00:11:57.384 --> 00:12:19.769 Rachel Perry And so I think one of the key messages of this study is we're looking at something akin to parking far away in the parking lot, taking the stairs regularly instead of taking the elevator, rather than training for a marathon in terms of what generated a beneficial effect. Now, more did seem to have more exercise did seem to have a greater effect.

00:12:19.846 --> 00:12:28.576 Rachel Perry But the message one of the key messages of the study is that even a small amount of exercise that the mice wanted to do did seem to slow their tumor growth.

00:12:28.653 --> 00:12:40.153 Eric Winer And so what's the underlying physiology of this? What's causing this change in tumor growth? Is it related to insulin? Is it related to glucose? Is it?

00:12:40.192 --> 00:13:00.615 Rachel Perry That's a great question. And one of the main reasons we did this study was to understand what the mechanism of these effects was. And it appears to be related to redistribution of glucose or sugar away from where we don't want it to be and toward where we do want it to be. So tumors consume a lot of glucose or sugar.

00:13:00.653 --> 00:13:25.269 Rachel Perry They use it as building blocks for their rapidly dividing cells. And so if you can deprive a tumor of glucose, you would expect to have slower tumor growth. And that is what we saw with exercise. So exercise redistributed glucose away from the tumor and toward the muscle. Both leg muscle that was running and also the heart muscle and muscles like to use a lot of glucose.

00:13:25.269 --> 00:13:40.615 Rachel Perry They use it for efficient function. And so we believe that by redistributing glucose, stealing it away from the, from the tumor and toward the muscle that that underlies at least some of the beneficial effects of this exercise.

00:13:40.692 --> 00:14:00.423 Eric Winer Wow. That is, really interesting. And I'm just going to we have to wrap up in just one second for this first half. But let me just ask you, could the same thing be achieved by having someone, simply consume a lower sugar diet?

00:14:00.500 --> 00:14:26.538 Rachel Perry Yes, potentially, at least in part, consuming a lower sugar diet would deprive the whole system of glucose. It wouldn't have that effect to kind of preferentially shunt glucose into the muscle, where it's beneficial and and away from the tumor. But we do know, based on other people's work, that a low calorie, a low sugar diet does seem to have beneficial effects in in cancer patients and in those who are at risk.

00:14:26.615 --> 00:14:37.307 Eric Winer We'll get back to that right after the break. I'll be back with my guest, Doctor Rachel Perry, associate professor, at Yale School of Medicine.

00:14:37.384 --> 00:15:05.615 Announcer Funding for Yale cancer answers comes from Smilow Cancer Hospital, where more than a dozen dedicated teams work

across scientific disciplines to prevent, diagnose and treat specific types of cancer, from melanoma to sarcoma. Learn more at Smilow CancerHospital.org. Over 230,000 Americans will be diagnosed with lung cancer this year, and in Connecticut alone, there will be over 2700 new cases.

00:15:05.692 --> 00:15:30.153 Announcer More than 85% of lung cancer diagnoses are related to smoking and quitting, even after decades of use, can significantly reduce your risk of developing lung cancer each day. Patients with lung cancer are surviving thanks to increased access to advanced therapies and specialized care. New treatment options and surgical techniques are giving lung cancer survivors more hope than they have ever had before.

00:15:30.230 --> 00:15:55.346 Announcer Clinical trials are currently underway at federally designated comprehensive cancer centers, such as the battle two trial at Yale Cancer Center and Smilow Cancer Hospital, to learn if a drug or combination of drugs based on personal biomarkers can help to control non-small cell lung cancer. More information is available at YaleCancerCenter.org. You're listening to Connecticut Public Radio.

00:15:55.423 --> 00:16:31.807 Eric Winer Welcome back to the second half of Yale Cancer Answers. This is Eric Winer. And I'm here with my guest, doctor Rachel Perry, associate professor of medicine. Rachel is a scientist who studies metabolism. And we've been talking about studies related to exercise. And I do want to say to people that, although there's good preclinical evidence, meaning not in people that lower sugar diets could make a difference in terms of cancer growth.

00:16:31.884 --> 00:17:14.884 Eric Winer At this time, we don't have that kind of evidence in people. And one of the concerns many oncologists have is that oftentimes when a patient has cancer, that, indeed people make fairly dramatic dietary changes, some of which, could be detrimental. And so, generally speaking, what we recommend is that people try to consume a healthful diet, paying attention to not the new food pyramid, but the old food pyramid, which emphasized, fruits and vegetables and grains and a little bit of protein and a limited amount of, fat.

00:17:15.038 --> 00:17:34.230 Eric Winer So, this may change in the future, but, for the moment, I think that's what people should be thinking about it. Now, let me ask you another question about your study. Did you have some mice that were totally sedentary? And in those mice, did you see more rapid tumor growth?

00:17:34.307 --> 00:17:57.000 Rachel Perry Yes, we did have some mice that were totally sedentary. They had the same type of running wheels, but the wheels were fixed so they couldn't actually move them forward and exercise on them. So in case that wheel itself influence tumor growth, which we don't expect, that would be a control experiment. And we found the sedentary mice had about two fold more rapid tumor growth.

00:17:57.000 --> 00:18:18.730 Rachel Perry So their tumors grow, grew about twice as quickly on average as the mice that had access to the running wheels. And within the mice that had access to the running wheels. It seemed that the amount that they ran tracked with tumor growth. So the amount that ran the mice that ran more had slower tumor growth even within the exercising group.

00:18:18.807 --> 00:18:57.807 Eric Winer Well, this is all really fascinating. And it's in keeping with, certainly what we know clinically, which is that remaining active seems to be a good thing. And of course, there was a recent study that has been mentioned on this show before, a randomized study in patients with colon cancer, where they compared an exercise intervention, a structure to exercise intervention versus just standard treatment, and found that that exercise intervention actually altered both the number of patients whose cancer recurred, as well as overall survival.

00:18:57.807 --> 00:19:25.576 Eric Winer Now, that's going to have to be replicated in other tumor types. In other settings. There's still much that we don't know. People shouldn't feel guilty if they don't exercise, but at least at the moment, we do have. I think the preliminary data suggests that being active when you have cancer remains important. Not that everyone can be. And that's something we we really have to remember.

00:19:25.653 --> 00:19:53.076 Eric Winer Maybe we can talk a little bit about science in general. People sometimes forget how important very basic science is. Basic science that asks fundamental questions about how genes and molecules interact. Fundamental questions about the immune system. Maybe you can just comment on the critical nature of science.

00:19:53.153 --> 00:20:19.461 Rachel Perry Absolutely. That's a great question. And absolutely basic science is so important. And certainly that's not to knock the importance of clinical science. We need to be doing clinical trials as well. And really, our ultimate goal in our basic science lab is to generate, knowledge that will lead to improved outcomes for patients and better trials for patients. But if we don't have that basic research, we won't know how to do that.

00:20:19.692 --> 00:20:48.500 Rachel Perry So one example, is we're working on developing biomarkers for exercise response that can be measured in in people. So this is not in the published paper. It's in a follow up study that's going on in the lab. But we're looking at molecules that may change with exercise in mice with breast cancer and will then be exploring the possibility of measuring those biomarkers, biomarkers of fitness in individuals.

00:20:48.500 --> 00:21:09.076 Rachel Perry People who have cancer. And without the basic science study in dozens of mice, we wouldn't have any idea what to predict. Might be useful as a biomarker for for studies in people. So really, I believe the basic science studies in the lab lay the groundwork for the really important translational clinical studies that we can do.

00:21:09.153 --> 00:21:49.192 Eric Winer And the interesting thing is that it can

go both ways. So oftentimes basic science leads to the development of hypotheses that are then tested in people. In this case there was the observation that exercise might be beneficial. And we then took that. We very broadly speaking, meaning most of you and others in the lab took that back to the laboratory to try to understand it in a more comprehensive manner and try to understand the underlying mechanisms that could then inform how we develop interventions in patients.

00:21:49.269 --> 00:22:14.115 Rachel Perry Exactly. It needs to go both ways. Where we take observations in the clinic, physicians will come to PhDs like me and say, you know, a lot of my patients are reporting this to me. Is is there something we can study in the lab? You can study in the lab that might generate some some knowledge on that. And then we in the lab can come to our clinical colleagues and say, look, we found this really, potentially really important thing.

00:22:14.192 --> 00:22:24.038 Rachel Perry Is there some readout in patients that that we can test? And I think the scientific and clinical ecosystems work best when we're talking in both directions like that.

00:22:24.115 --> 00:22:58.461 Eric Winer Yeah. You know, I often say that, without the underlying basic science, we would never develop new, new drug therapies. And then, of course, without really very carefully done clinical trials, we would never have drugs on the shelf of pharmacies to be given to patients. You need all of these steps and they all have to work together and they all take funding, which is, of course, why many of us are very worried about the funding situation in the United States at the moment.

00:22:58.500 --> 00:23:06.038 Eric Winer Are you worried about what's going on in terms of, federal funding of cancer research at the moment?

00:23:06.115 --> 00:23:34.115 Rachel Perry I am, I think, at a very high level, most members of the public, and of the administration understand that science is important and therefore scientific funding is important. When I talk with people out in the community, I was just last week talking to a group of senior citizens, mostly non-scientists, about this particular work, and had a great discussion about the importance of science and sort of where everything's going.

00:23:34.115 --> 00:24:01.000 Rachel Perry I think in general, people do agree and understand that we need to have funding for research, but there can be many roadblocks, in that funding actually coming to fruition. And, you know, I do want to not miss the opportunity to say what a tremendous detriment it would be to research, to have pause in federal funding for any of the pre-clinical or clinical studies.

00:24:01.076 --> 00:24:13.461 Rachel Perry It's not just a one month pause, you know, a pause of of one month in funding, translates to a much bigger opportunity cost, to, to move those studies forward.

00:24:13.538 --> 00:24:41.307 Eric Winer And of course, the other worry is that when funding is limited, young people who might go into science start getting

word. And if people are turned off from going into scientific careers because they're worried about getting funding to do the research, then we will find ourselves five, ten years from now with, what is often referred to as a brain drain.

00:24:41.384 --> 00:25:00.653 Eric Winer And we need those young minds, we need people to go into science, we need people to go into medicine. And, you know, that's really how we're going to improve human health, whether we're talking about breast cancer or melanoma or diabetes or heart disease. It's just so very important.

00:25:00.730 --> 00:25:24.269 Rachel Perry Absolutely. And, you know, I think that's my favorite part of being a Pi is mentoring, more junior scientists in the lab. And I do see within my own trainees and other trainees with whom I interact a certain anxiety that is very understandable about the current, scientific world, in part because of these challenges with funding, and all that surrounds it.

00:25:24.269 --> 00:25:34.769 Rachel Perry So I really hope that we can continue to, to move science and move research forward, because 100%, as you say, we need those brains and their excitement and their energy in the field.

00:25:34.807 --> 00:25:45.346 Eric Winer Well, to take these, this room, our anxieties to the positive. Tell us about the next set of experiments you plan to conduct in the laboratory.

00:25:45.423 --> 00:26:16.884 Rachel Perry Yes. So we're looking to, piggyback off of these studies to the next set of studies, that will develop specific interventions based on the effectiveness of exercise. So in a follow up set of studies in Ghazi, a King, Bassel, who was a PhD student in my lab and a member of our cancer biology training program, as a PhD student here, she did exercise studies in female mice with breast cancer and looked at a broad spectrum of what changed.

00:26:16.884 --> 00:26:54.230 Rachel Perry So she did metabolomics and gene expression analysis and found some interesting targets that aren't published yet, but that we may be able to supplement, in our animals. That may not be exercising. So, so really, the dream is to recapitulate some of the effects of exercise by giving a pill. I think, you know, we would all agree that there are huge effects, beneficial effects of exercise, cardio, metabolic, cardiovascular, pulmonary, metabolic, mental health wise, there are many effects of exercise that may not all be able to be recapitulated in a pill.

00:26:54.307 --> 00:27:16.846 Rachel Perry But the reality is a lot of patients with cancer or with other conditions aren't able to exercise much for whatever reason. And so if we could, derive some of those beneficial effects with a supplement, that would really potentially be very beneficial for these patients. And so that's an area that we're very excited about moving next.

00:27:17.000 --> 00:27:40.038 Eric Winer So the first step would be to encourage people to exercise. But for those who couldn't exercise because they're too

fatigued, because they've never done that in their life, and it's just not something they can do that there might be some way around it. You know, we're we're coming to the end of our time. Just wondering if there any last comments you have.

00:27:40.115 --> 00:27:41.653 Eric Winer For our audience.

00:27:41.730 --> 00:28:04.038 Rachel Perry I just want to reiterate, the beneficial effects of exercise and their ability to be harnessed, by simply moving a little bit more, taking a walk around the block, stairs instead of the elevator occasionally. As much as we talked about the distance that the mice would move, we're not talking about running kilometers a day.

00:28:04.115 --> 00:28:16.769 Rachel Perry So I really do think this is an achievable intervention for those for whom it's achievable. And we're doing research now to really expand the number of people for whom it may be achievable down the road.

00:28:16.846 --> 00:28:36.461 Eric Winer I think we're at the end of our time. It has been a real pleasure talking to you, Rachel. I've been speaking with Rachel Perry, who's an associate professor of medicine at Yale School of Medicine. And it's just great to talk to you about, these these studies in the laboratory. Thank you so much for being here with us tonight.

00:28:36.576 --> 00:28:38.500 Rachel Perry Thank you. Eric, it's been a pleasure.

00:28:38.576 --> 00:28:57.346 Announcer If you have questions, the address is CancerAnswers@yale.edu. And past editions of the program are available in audio and written form at YaleCancerCenter.org. We hope you'll join us next time to learn more about the fight against cancer funding for Yale Cancer answers is provided by Smilow cancer Hospital.