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00:00:00.076 --> 00:00:06.307 Announcer Funding for Yale Cancer answers is provided by Smilow Cancer Hospital.

00:00:06.346 --> 00:00:21.730 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.

00:00:21.807 --> 00:00:56.538 Eric Winer Today, we're going to be talking about brain tumors and specifically glioblastoma. About 20,000 Americans are diagnosed with gliomas every year, and about 13,000 have glioblastoma, which is a subtype of all brain tumors. It's a particularly difficult subtype with, five year survival that's unfortunately quite low. And this is a cancer where we really need more research.

00:00:56.615 --> 00:01:22.615 Eric Winer Tonight we're going to be talking to Doctor Ranjit Bindra, who is a professor of therapeutic radiology, a clinician and a scientist at the Cancer Center in the Yale School of Medicine. And we're also going to be joined by Doctor Seth Herzon who is a professor of chemistry. So not a clinical doctor, but a researcher

00:01:22.653 --> 00:01:39.000 Eric Winer in Yale's Faculty of Arts and Sciences. Ranjit, maybe you could say a little bit more about glioblastoma. As I mentioned that they occur in about 13,000 Americans. But these are Americans of what ages or all ages? Tell us a little more.

00:01:39.038 --> 00:02:01.384 Ranjit Bindra Yeah. Thanks so much for having us. Eric, these are very interesting tumors in that they are found in patients all the way from the infant stage to toddlers, all the way up into the elderly population. Unfortunately, there are really no boundaries for these tumors. They are incurable, despite, decades of research and clinical trials.

00:02:01.423 --> 00:02:03.269 Ranjit Bindra And so clearly a high unmet need.

00:02:03.346 --> 00:02:21.000 Eric Winer When one treats a patient with a glioblastoma. There are a number of different types of physicians that get involved. Their surgeons, their radiation oncologist, their medical oncologist, your ecologist, what have you. What's usually the first approach?

00:02:21.076 --> 00:02:47.192 Ranjit Bindra Yeah, most of the time, these patients, quite honestly, will end up in the emergency room. They'll be feeling quite fine until maybe they have a headache that doesn't go away or eventually, rather, will present with a seizure. And in the ER, often they'll do an imaging study, a CT scan or MRI, and they'll see something in the brain and that buys them a visit by the first part of our multidisciplinary team, which is a neurosurgeon.

00:02:47.269 --> 00:02:56.269 Eric Winer Can most of these tumors be removed neuro surgically? Are they able to remove the entire tumor or not?

00:02:56.307 --> 00:03:15.000 Ranjit Bindra I think that's been one of the most impressive, things over the last, you know, 30 some odd years, we'd have enormous evolution and progress in the way these tumors are handled surgically. Now, things that were unresectable many years ago now, with things like awake craniotomy and misguided, techniques, they're able to take a lot of tumors out.

00:03:15.000 --> 00:03:24.538 Ranjit Bindra But some, unfortunately, can only be biopsied because they're in two eloquent regions of the brain to take up, take out anything without reasonable, level of toxicity.

00:03:24.576 --> 00:03:32.653 Eric Winer So if in fact, they tried to do a total resection, the person would be left with just significant disabilities.

00:03:32.730 --> 00:03:34.807 Ranjit Bindra Exactly. And therein lies the problem. Yep.

00:03:34.807 --> 00:03:42.346 Eric Winer And I realize you're not a neurosurgeon, but what's the advantage of of doing these craniotomy with somebody awake?

00:03:42.384 --> 00:04:02.307 Ranjit Bindra It's very, very interesting. Recently, we now understand that you can wake up a patient in the middle of surgery. Obviously, you're under anesthesia, so they're not feeling pain. But then you can then begin to operate in certain areas, and ask that patient to speak, or if they're, you know, a musician, they could play the guitar and see if their function is disrupted in real time.

00:04:02.307 --> 00:04:08.730 Ranjit Bindra And that can tell the surgeon, hey, I'd like to take out tumor here, but it's gonna be too dangerous because they're going to lose function in that area.

00:04:08.807 --> 00:04:14.730 Eric Winer And leave it literally. Which would you have somebody actually play a musical instrument during this?

00:04:14.884 --> 00:04:27.615 Ranjit Bindra Yeah, they're you know, there's some great videos online of, actually opera singers singing, people playing, all sorts of instruments. And it's, it's, it's pretty wild, but it's, shows you how far we've come, actually.

00:04:27.692 --> 00:04:50.115 Eric Winer Well, well, I mean, you know, all surgery has really advanced tremendously in terms of, being able to do more with comprising less damage to normal tissue. So this is just an another example of that. So I, I can imagine that taking care of kids with this problem might be particularly challenging.

00:04:50.307 --> 00:05:13.807 Ranjit Bindra It's a very difficult but meaningful part of what we do. And, really actually drives a lot of the research from the Bindra and Herzen Labs. When, folks see these kids, brain tumors, thankfully, are less common in kids. But as I always like to say, it takes one kid with a brain tumor that can disrupt an entire community entire school is in disbelief that a third grader has an und respectable, incurable tumor.

00:05:13.884 --> 00:05:17.307 Ranjit Bindra And it's definitely a difficult thing, but, something we need to do.

00:05:17.384 --> 00:05:34.730 Eric Winer And I mean it. Of course, cancer in in children is much less common than in adults. Acute leukemia is the most common type of cancer, but if I remember right, brain tumors are really high up. There is the second most common type of pediatric malignancy.

00:05:34.807 --> 00:05:39.846 Ranjit Bindra They are. And when we look at fatalities in terms of survival, they really rank up there.

00:05:40.115 --> 00:06:07.807 Eric Winer Now because we thankfully are able to to cure most of the children who have acute leukemia these days. It's really quite dramatic. You are a, physician and a scientist. You have a laboratory. You work with other people in the laboratory, like Seth Herzen, who's here with us, on the call. And, how did the the the two of you interact?

00:06:07.807 --> 00:06:14.576 Eric Winer So maybe I'll turn to Seth for that one. You know, Seth, what's it like working with Ranjeet?

00:06:14.653 --> 00:06:34.692 Seth Herzon It's great. You know, we I think we work. We work incredibly well together, you know, he covers the clinical side and the, sort of molecular, mechanistic side. And I work on the synthetic side. And so we now see, I think our expertise is just completely interlocked. And, you know, our, our time together goes back to about 2014.

00:06:34.692 --> 00:06:49.730 Seth Herzon We actually, first collaborated, to develop a screen to identify novel DNA repair inhibitors, and then we went, we went our separate, separate ways for several years, worked on several things, and then sort of re nucleated around this, glioblastoma project.

00:06:49.807 --> 00:07:14.807 Eric Winer Regimen to go back to you for a few minutes, and maybe you could just tell us about some of the different treatments that are presently available that are unfortunately somewhat inadequate, for people who have glioblastoma. So there's surgery, of course. And even if the tumor is completely removed, that's rarely enough by itself. Is that correct?

00:07:14.846 --> 00:07:36.000 Ranjit Bindra That's what's so mystifying about these tumors. We we call this extent of resection. And sometimes you can have a super total resection actually go beyond the margins. And we would think by first principles that that would get rid of the tumors. But but the problem is these tumors are highly infiltrated within the brain. So even though you think you got everything out, there's something often persisting.

00:07:36.076 --> 00:07:58.884 Ranjit Bindra And because of that local regional failure, as we like to call it, we radiation oncologist come in to give focused radiation therapy is essentially damaging the tumor, the tumor cell DNA. That's in those margins that we can't see. But that's not enough as well, because no matter what dose of radiation we give, we still see even more distant failures as well within the brain.

00:07:59.192 --> 00:08:19.269 Ranjit Bindra And that's where systemic therapy comes in. Traditionally, that's been chemotherapy. And we've tried, dozens and dozens of chemotherapies. We only really have one, maybe two, that are FDA approved and truly effective. But the future now is likely targeted therapy, which we'll get into later today in the work with the herbs on in vitro lab, but also immunotherapy as well.

00:08:19.269 --> 00:08:22.884 Ranjit Bindra And there's a lot of new therapies on the horizon that are of great interest.

00:08:23.038 --> 00:08:30.653 Eric Winer And just for our audience, these tumors don't spread outside of the brain. Hardly ever.

00:08:30.730 --> 00:08:41.307 Ranjit Bindra Almost never. There is maybe 1 or 2 case reports of, what we call a drop ment into the blood. But almost never maybe seen 1 in 14 years as a practicing physician here.

00:08:41.384 --> 00:09:04.730 Eric Winer Yeah. No, it's it's it's really remarkable. It's, they, they stay in the brain, like many other cancers, which, of course, you know, a fundamental property of cancers is often that they have the ability to spread and spread to other organs. When these tumors spread to other parts of the brain, to what extent do they spread to very distant parts of the brain?

00:09:04.730 --> 00:09:19.000 Eric Winer So they might start, let's say a tumor would might start of, left hand side of the brain, towards the back of the head. Just as an example, credit spread to a totally different location in the brain.

00:09:19.192 --> 00:09:47.423 Ranjit Bindra I think it's interesting, when I first started out, you know, work as an attending, we we were sort of taught the mantra that it's local, regional, local, regional with time. I think with the absence of effective systemic therapies, these things will spread to distant parts of the brain. Surprising, but eventually they will make it. Now, that being said, if we can control it better earlier, they could prevent that distance spread a lot like breast cancer and things that you deal with as well.

00:09:47.500 --> 00:10:15.076 Eric Winer And what's the time course here. So somebody comes in, they have a headache. They've been maybe having headaches for a few days. They have this terrible diagnosis surgeries done. You then give them radiation, to the tumor bed and they let's say they go on some chemotherapy, which is, if I understand it correctly, oftentimes oral chemotherapy.

00:10:15.153 --> 00:10:16.346 Ranjit Bindra Correct? Correct.

00:10:16.346 --> 00:10:21.230 Eric Winer And, how long does it take before something else is showing up?

00:10:21.307 --> 00:10:38.653 Ranjit Bindra Unfortunately, within a year, in most cases, I'd say, the average, one year, sometimes only six months of durability, of control, sometimes maybe two years if you have special mutations that are very unique, maybe a little bit longer. But not not not that long.

00:10:38.653 --> 00:10:42.538 Eric Winer Unfortunately, when that happens, people have symptoms.

00:10:42.615 --> 00:11:03.576 Ranjit Bindra They often, have symptoms a little bit different from their first diagnosed, because now we're keeping a close, you know, every eight weeks for doing an MRI or having a visit with the doctor, so they can present with symptoms. But often now we see it because we're looking more closely before it becomes a problem. And then we try to enroll them in a clinical trial as quickly as we can.

00:11:03.653 --> 00:11:22.076 Eric Winer Yeah, I can imagine that having those scans every eight weeks is like living on a roller coaster. You know, you're you're having those scans. You have all this anxiety associated with the scan. Hopefully it looks okay. It does. You get a reprieve for another, oh, eight weeks.

00:11:22.153 --> 00:11:37.461 Ranjit Bindra They call it scans it for a reason. And a lot of my patients and patient advocates I work with talk about, you know, it's the week prior that they can't really focus. And those MRI's are no joke. You know, I've had been in one, you know, it's an hour inside a tube, the lots of loud noises, and it's very difficult.

00:11:37.461 --> 00:11:43.423 Ranjit Bindra Then you wait a few hours to even hopefully get a call from your doctor, about about the results of that scan.

00:11:43.500 --> 00:11:58.038 Eric Winer And then if someone has a recurrence and, and there isn't some investigational therapy, and we're going to get to investigational therapies in the second half of the show, but they would get additional radiation, they'd have more surgery. They get more drugs.

00:11:58.269 --> 00:12:18.115 Ranjit Bindra All of the above, you know, they could, again, surgeries become, so advanced that going back in and doing a re operation is quite possible. Radiation therapy, remarkable improvements in outcome, formality in our ability to rearrested and then novel therapeutics. There's an array of clinical trials that people can, can get enrolled onto.

00:12:18.115 --> 00:12:27.807 Eric Winer And when you say kind formality, that means how you're able to deliver the radiation, the sort of the shape of the field that you're getting.

00:12:28.115 --> 00:12:36.461 Ranjit Bindra Yes. And the precision, I would say down to like half a millimeter is the, the extent of our precision. Now, it's, it's really, really quite exciting.

00:12:36.538 --> 00:12:45.153 Eric Winer Yeah. No, that's, that's, that's pretty amazing. And you obviously need the patients to be very still when that happens.

00:12:45.230 --> 00:12:55.769 Ranjit Bindra Yes, yes. And we have really, really great techniques now to actually monitor them in real time. So even a hairline shift, the machine watch, we stop and we'll restart when they stop moving.

00:12:56.038 --> 00:13:09.307 Eric Winer I actually just heard yesterday, another center about people doing 3D printing to, develop these, these external devices that hold someone's head steady.

00:13:09.384 --> 00:13:17.730 Ranjit Bindra We were just talking about this. And there's something called the c rad that can actually map your surface anatomy and see any little change in milliseconds. And can adapt.

00:13:17.769 --> 00:13:43.230 Eric Winer And then they can actually, they were attaching the machine to this external device so that it would ensure the fact that just what they wanted to irradiate was getting irradiated. So these these things are amazing. Well, listen, we're going to have to take just a brief break. We'll be back in a minute. And then we're going to talk about how new drugs get made and how you think about all of that.

00:13:43.307 --> 00:13:44.615 Eric Winer Be right back.

00:13:44.692 --> 00:14:24.807 Announcer Funding for Yale Cancer Answers comes from Smilow Cancer Hospital, now providing care at 15 locations throughout Connecticut and Rhode Island to bring personalized treatment and world class expertise to patients closer to where they live. Learn more at SmilowCancerHospital.org. There are many obstacles to face when quitting smoking as smoking involves the potent drug nicotine. Quitting smoking is a very important lifestyle change, especially for patients undergoing cancer treatment, as it's been shown to positively impact response to treatment, decrease the likelihood that patients will develop second malignancies and increase rates of survival.

00:14:24.884 --> 00:14:53.846 Announcer Tobacco treatment programs are currently being offered at federally designated comprehensive cancer centers, such as Yale Cancer Center and at Smilow Cancer Hospital. All treatment components are evidence based, and patients are treated with FDA approved first line medications, as well as smoking cessation counseling that stresses appropriate coping skills. More information is available at YaleCancer Center.org. You're listening to Connecticut Public Radio.

00:14:54.000 --> 00:15:29.538 Eric Winer This is Eric Winer. I'm the director of the Yale Cancer Center. And here with you tonight on Yale Cancer Answers. I'm joined tonight by Doctor Ranjit Bindra, professor of therapeutic radiology, a clinician and a scientist here at the Yale Cancer Center and Yale School of Medicine, and by Doctor Seth Herzon, who is a researcher, and who works very closely with Doctor Bindra, in developing new treatments.

00:15:29.615 --> 00:15:37.153 Eric Winer So, Seth, let's let's open up with you. And, how did you decide you wanted to be a scientist?

00:15:37.230 --> 00:15:57.307 Seth Herzon How far back do you want to go? I, I was, I was actually, it was a bit of a, on a bit of a whim, you know, I went to sort of my undergraduate studies at Temple University without much of a, you know, internal compass. But I had read a book, entitled Life Itself, which is a popular science book about cell biology.

00:15:57.384 --> 00:16:15.807 Seth Herzon And I fell in love with it. And I met, when I was sitting with my advisor, she asked me, you know, what, field I wanted to focus on? And I said, I don't know, but I really found this book interesting. And so she signed me up for biochemistry and biochemistry. Then, of course, led me to organic chemistry.

00:16:15.807 --> 00:16:20.038 Seth Herzon And I think that's where I really found my, my central, you know, my, my passion.

00:16:20.115 --> 00:16:23.346 Eric Winer And your graduate work was in in what field.

00:16:23.423 --> 00:16:47.846 Seth Herzon Was in, synthetic. Synthetic organic chemistry? Specifically, what we call natural product synthesis. So, the objective is to try and, find molecules that are made in nature, typically by, bacteria or plants, and then find ways to recreate them, in the laboratory. And so that's I spent four years in graduate school working on one specific molecule trying to do that.

00:16:48.000 --> 00:16:53.153 Eric Winer So the idea is to develop new drugs essentially.

00:16:53.230 --> 00:17:13.615 Seth Herzon That is that is the long term vision for many of these projects. So I wouldn't say that's always the case. We have some projects where we're interested in molecules simply because their structures are, you know, intriguing from a fundamental perspective. But most of these, these natural compounds are produced, you know, for a reason. The cells need to expend ATP to make them.

00:17:13.615 --> 00:17:36.576 Seth Herzon So there's, there's, there's, there's, there's an activity that's often associated with them. And, they can frequently be repurposed as medicines for humans. There's a lot of work that often needs to occur, you know, from going from the natural structure to something that's a drug, but that that is, definitely a line of research that we pursue, you know, if the data supports it.

00:17:36.653 --> 00:17:55.269 Eric Winer You know, I think what you were just talking about speaks to the importance of fundamental research for what turns out to be very applied applications, in the long term, because without that fundamental research, we don't have a way of moving forward.

00:17:55.461 --> 00:18:17.346 Seth Herzon I agree 100%, Eric. That was that was sort of my entry point into this whole, glioblastoma space, you know, so when I, when I started at Yale, I was thinking very much just about basic science, but thinking about molecules that were bioactive. And I've always been intrigued with molecules that interact with DNA and studying their interactions with DNA.

00:18:17.346 --> 00:18:37.500 Seth Herzon And if they damage DNA, studying the mechanisms of DNA damage. But what I came to appreciate was that, you

know, in sort of the modern age in the 2020s or the 20 tens, if you're thinking about DNA damage, you really need to be thinking about DNA repair. That's sort of the other side of the equation. And they're all sort of interlocked.

00:18:37.576 --> 00:18:48.653 Seth Herzon And so that's led me to a lot of very fruitful collaborations, including, you know, this, this great collaboration that I've had with the Bindra lab over, you know, going on 12 years now, at Yale.

00:18:48.884 --> 00:18:52.230 Eric Winer So what what did the two of you do together?

00:18:52.307 --> 00:19:17.846 Seth Herzon The way this sort of evolved was that, you know, Ranjeet, so if, as I mentioned, we had we had worked together in 2015 on a drug discovery program and then gone our separate ways for a few years, and then he came to me in, I think, 2017 or 2018 and started sort of explaining this mechanism of acquired drug resistance in glioblastoma.

00:19:18.000 --> 00:19:34.538 Seth Herzon And if I'm being honest, it took me about a year or two to get my head around this mechanism. It's it's very complicated. But once I started to understand it, you know, then it was clear that there is an opportunity here to try and develop agents that could overcome that resistance mechanism.

00:19:34.615 --> 00:19:39.884 Eric Winer Can you in any simple way explain that resistance mechanism?

00:19:40.038 --> 00:20:10.730 Seth Herzon The chemotherapy that's used most commonly in the clinic for glioblastoma is a small molecule known as team ism. Eid which is marketed as timid, are timid, are is a DNA methylation agent. So it transfers a carbon unit to, to DNA. And most of those methylation are not significant. But there's a particular site within DNA, O6 guanine, which if it gets methylated, can be especially cytotoxic to the cells.

00:20:10.807 --> 00:20:40.423 Seth Herzon That mechanism of cytotoxicity, involves a separate DNA repair pathway known as mismatch repair. And in the absence of functional mismatch repair, those alkylation by Tamannaah are not cytotoxic. And so when one treats a tumor with Tamina, you know, you're essentially selecting for subsets of cells that have deficiencies in mismatch repair and therefore resistance.

00:20:40.500 --> 00:20:45.769 Eric Winer And so the cells that don't have mismatch repair are able to survive.

00:20:45.846 --> 00:21:12.384 Seth Herzon Exactly. It's completely counterintuitive. You know, that you would think that the cells that were dysfunctional in a repair pathway would be at, you know, at a deficiency. But in fact, these are the cells that end up making it past the chemotherapy. And so when Ranjeet and I started, you know, talking about this, you know, he was saying to me, you know, here's the mechanism and we just need to find a derivative of team is all my that can overcome this resistance mechanism.

00:21:12.384 --> 00:21:17.192 Seth Herzon And that was sort of the genesis of the project and how we got started together.

00:21:17.269 --> 00:21:24.730 Eric Winer So here I thought you were going to tell me that you're looking for a drug to induce mismatch repair in the rest of the cells.

00:21:24.807 --> 00:21:25.269 Seth Herzon Now.

00:21:25.500 --> 00:21:29.076 Eric Winer But that which I guess theoretically could work, maybe.

00:21:29.153 --> 00:21:41.000 Seth Herzon Theoretically would work. Yeah. That would re sensitize the cells. I think, you know, that's a challenging proposition, I think. But, it was easier to try and find a molecule that can deal with the cells that have already lost it.

00:21:41.076 --> 00:21:43.038 Eric Winer How did you all go about doing this?

00:21:43.115 --> 00:22:03.807 Seth Herzon So I think the first step was recruiting, a top notch student. So we recruited a student named Kingston Lynn. And, Kingston was an MDP PhD student that was admitted to the program here at Yale. He did his undergraduate work at, UPenn and worked in synthetic chemistry. But then was, you know, really laser focused on oncology and in clinical work.

00:22:03.807 --> 00:22:25.307 Seth Herzon And so Kingston, was mentored jointly by both of us. He had, sort of, laboratory skills to make, make molecules and characterize them in my group. And then could go to Ranjeet lab and look at them in a biological context. And I'd like to say it was all rational design, but it was probably equal parts.

00:22:25.307 --> 00:22:39.884 Seth Herzon You know, make what you can make and then also, you know, rational design. And one of the molecules that we made, which turned out to be to be the lead compound, was a simple, simple change to team is. All right.

00:22:40.000 --> 00:22:48.653 Eric Winer So, either of you, Ranjit or Seth, where does this stand now? I mean, are you developing this further?

00:22:48.692 --> 00:23:06.538 Ranjit Bindra This was a wonderful collaboration, a great example of cross-disciplinary, work, because when I came to set you know, my, my father was a chemist, but that gene was not transmitted to me. But Seth is probably one of the best, chemists in the world. And he was able to solve this problem and, you know, working together.

00:23:06.538 --> 00:23:27.038 Ranjit Bindra We brought in another, a radiation oncology resident, an MD, PhD who was more of a biologist because, these folks made these beautiful molecules. But we still didn't understand actually how they worked. So we spent a lot of time, and this is Susan Gabel, who's now an assistant professor here. She, you know, really teased out the mechanism.

00:23:27.038 --> 00:23:34.115 Ranjit Bindra And then we, Seth and I, came together and actually spun out a company. I'll pass it back to set to talk about that, that pathway as well.

00:23:34.153 --> 00:23:54.769 Eric Winer But what I'm what I'm struck by is the number of people involved. You know, this isn't, you know, something that some mad scientist goes home at night and comes up with you know, in the course of a few hours. This is a very methodical process with lots of people involved and repeated experiments.

00:23:55.076 --> 00:24:19.000 Seth Herzon Yeah. And I think at its apex, you know, we had, four PPIs, 4 or 5 PPIs at Yale, you know, working across 4 or 5 different labs in about 12 different, you know, coauthors on our sort of our larger paper that describe the mechanism and efficacy of the compound. So it as more data came in, we had to recruit people to sort of help to to push the project forward.

00:24:19.000 --> 00:24:20.576 Seth Herzon It was very exciting.

00:24:20.653 --> 00:24:29.192 Eric Winer So where does this stand? A company now has been created, has the drug and is testing it.

00:24:29.269 --> 00:25:04.730 Seth Herzon Ranjeet and I, along with Kingston and Kevin Rifkin, co-founded a company known as which we named Modify Biosciences in 2021. And, it was really exciting. It was my first, you know, experience in early stage biotech. And, we did quite well. I mean, the compound works very well. And so we were going through rounds of development and financing and, we were ultimately, positioned, through a lot of the hard work that Ranjeet did, raising, raising funds.

00:25:04.730 --> 00:25:27.038 Seth Herzon We were in, in a position where we could have run a clinical trial. But then Merck and company actually came in sort of at the 11th hour and expressed an interest in, in acquiring the company, outright. And so we went through the process with them. That took some time. But then in the fall of 2024, the the compounds were officially transferred to Merck.

00:25:27.076 --> 00:25:28.846 Eric Winer And what's going on with them now?

00:25:29.038 --> 00:25:38.692 Ranjit Bindra We're hoping to bring this in the clinic as early as next year, which is, fabulous. Do you think of an idea that, you know, you know, 5 or 6 years to possibly be in patients? It's very exciting.

00:25:38.846 --> 00:25:50.884 Eric Winer That's great. And, it must make you want to look for other potential targets and develop other agents. I mean, you know, nothing like success gives you motivation.

00:25:51.000 --> 00:26:19.307 Seth Herzon Yeah, absolutely. And, you know, so we have another project that's very exciting right now. We're we're looking, essentially trying to do the same thing except targeting, tumors that are deficient in, what's known as homologous recombination repair. And this is actually a

much bigger patient population. It's estimated depends on how you count it. But, you know, approximately 15% of all cancers are air deficient.

00:26:19.384 --> 00:26:48.884 Seth Herzon And it's it's been an awesome collaboration. Ranjeet identified a molecule in his laboratory that was highly selective, for these tumors. And by that, I mean, selectively killed these tumors while not being nontoxic to, to healthy tissue. And then over the last two years, we've done a bit of, quite a bit of medicinal chemistry around these compounds to improve their both their activity, their selectivity, and then also their, their sort of suitability as a potential drug.

00:26:49.038 --> 00:27:02.423 Seth Herzon And we very recently, completed our first in vivo efficacy study where we saw very good activity, without any toxicity. And so we expect that this will form sort of the basis of another company here in the next year or so.

00:27:02.500 --> 00:27:26.346 Eric Winer Wow. And you know, I think what this also speaks to, though, is the importance of academic institutions in driving drug discovery. It doesn't all happen just in the pharmaceutical industry. These you know, this is an example of something that started at Yale and then moved to, to a company.

00:27:26.423 --> 00:27:45.538 Seth Herzon Absolutely. And I say that statement is becoming more and more true every year. You know, I think that big Pharma is is leaning more towards running clinical trials. And, sort of the discovery aspect of drug development, is now on the shoulders of academics and clinicians and physician scientists. Yeah.

00:27:45.615 --> 00:28:15.038 Eric Winer Well, this has been great. And, you know, I think what we've heard about is the challenge of treating brain tumors and the difficult outcomes now. But really, good reason to be hopeful for the future. And, you know, what's going on in your laboratories is going on in other laboratories around the country and around the world as well, which is why we're really going to make progress in the years ahead.

00:28:15.115 --> 00:28:38.730 Eric Winer So, I want to thank both of you, again, I've been on tonight with Doctor Ranjit Bindra, professor of therapeutic radiology and Doctor Seth Herzon, who's in the, Faculty of Arts and Sciences, both at Yale University. This is Eric Winer, and I'll talk to you next week.

00:28:38.807 --> 00:28:57.576 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.