#### Mark (00:04)

It's almost summertime, and that means the risk of melanoma are increasing. Melanoma is the deadliest form of skin cancer. What's the latest research telling us about identifying and treating it?

## Marc Hurlbert (00:16)

I think we're at this, you know, moment in time with change. With the role of philanthropy, the role of nonprofits, like the Melanoma Research Alliance is gonna be even more critical. You know, nonprofits can move a little bit more nimbly than the government.

### Margaret (00:30)

Our guest is Marc Hurlbert, who earned a PhD in pharmacology from the University of Colorado. He served as the Melanoma Research Alliance's Chief Science Officer, and now is its CEO.

#### Dr. Hurlbert (00:42)

We've invested in some imaging techniques, some other techniques that, you know, aren't ready for primetime today, but I think in the near future, maybe. But we need tools for the individual at home, the primary care doctor and the dermatologist.

### Margaret (00:56)

This is Conversations on Healthcare.

#### Mark (01:09)

Well welcome Dr. Hurlbert to Conversations on Healthcare.

#### Dr. Hurlbert (01:13)

Thank you. Thank you so much, for having me on.

## Mark (01:15)

We're talking to you now. As, as you mentioned, also, may is Melanoma and Skin Cancer Awareness Month. And Melanoma Research Alliance is the world's largest private nonprofit funder of melanoma research. And you directly invested, and this is pretty impressive, 175 million towards scientific discoveries. I guess our audience would love to know, are we making progress?

#### Dr. Hurlbert (01:40)

Absolutely. So, making progress on the war on melanoma, since we were founded in 2007, as you noted, we've invested 175 million to 500 projects at the top cancer centers all over the world, top medical universities. And, the progress we've made, really in the last, a little over the last decade, there's been 17 new treatments approved for melanoma. If, if you have an early-stage melanoma on your skin, you know, that can be cut out by surgery and your, your monitor for a few years, and usually you're all good if it has spread throughout the body, which is quite common. If it gets a little too deep into the skin, that's when you need systemic treatments. And like I said, there's been 17 approved and, you know, and you, if you had a metastatic melanoma diagnosis, you know, 15 years ago it was quite deadly and, and, and urgent. And, today with these new treatments, we're able to cure about half of patients with metastatic melanoma. So a lot of good progress, but more work to be done.

## Margaret (02:42)

Well, we're really glad to bring, that optimism, to the show as well as of course, focusing on prevention. But we're also, so interested in the research, that is underway. So we know you recently announced funding to support 30 high impact research projects, around the country. I understand, I don't know if they were international, at various academic and medical institutions. Tell us about these investments. What's the range of the kind of research that's going on now through these high impact investments?

### Dr. Hurlbert (03:12)

Absolutely. We, we just launched, just announced another \$9 million investment to 30 projects. It's across the US a few countries in Europe and in Australia. So it is a global research portfolio. We are investing in some new ways to tackle melanoma detection, investments in some of these rare melanomas. There's a few rare melanoma subtypes I hope your viewers, have, learned about or have heard about uveal melanoma that starts in the eye. A rare subtype that starts on your hands and your feet called acro melanoma, and then one that starts on the internal mucus membranes. Essentially your, in your nasal cavity, oral cavity, and all the moist internal tissues. And so an investment on the rare melanomas. And then lastly, investing quite heavily in, in tackling brain metastasis. So when melanoma spreads from the skin or other, other sites to your brain or to your central

nervous system and spine, which is what we call leptomeningeal disease, it becomes very difficult to treat. And so much more research is needed there. So rare melanomas, brain metastasis and CNS disease and understanding treatment resistance. So really excited about this new group of projects.

#### Mark (04:24)

You know, I'd like to really explore a little more one area of funding, which is your supercharging anti-tumor immune responses and enhancing the body's ability to recognize and destroy cancer cells. What, how, how realistic is this looking, at this, at this time?

### Dr. Hurlbert (04:42)

Well, it's, it's a, it's a proven treatment now. So in 2011, we had the first immune therapy approved called ipilimumab. And then in 2014, two new joined the class pembrolizumab and nivolumab and these immune therapies, those first three that I mentioned, they essentially take the breaks off the immune system and let the, let the immune system march forward into the tumor and have an effect. And like I said, this is curing about half of patients with metastatic melanoma. I think importantly for me, for these new immune therapies, they were approved first in melanoma, but now they're used in 24 different types of cancer. And so I think it's a, I consider immune therapy the fourth pillar of cancer treatment, right? So we have surgery, radiation, chemotherapy, and now the fourth pillar since these new treatments evolved is immune therapy. Our new investments are, trying to tackle that question, why doesn't every patient respond to immune therapy? These amazing drugs that have really saved lives and changed lives. And so we're looking at some of the cell-based therapies. You may have heard of CAR T and TIL therapies before. We're looking at some novel ways to stimulate the immune system. The, first group of immune therapy drugs sort of take the breaks off the immune system. They're, we're looking at a few research projects of how do we stimulate the immune system to go in and attack the cancer just like it would attack a virus or a bacterial infection.

### Margaret (06:05)

Well, you are, rightly so, very proud that MRA funded researchers have been part of every major melanoma breakthrough, that we've had. And certainly the patient community is deeply grateful to you, but we are always, I think, worried that the rates of melanoma are continuing to rise. And especially in younger people, I understand cases of melanoma, I think, have tripled in the last 30 years when we're fortunately seeing some diminishment, of other common cancers. I mean, I, when we ask ourselves, why is this happening? I don't know if we could all say too much sun exposure, but is something more than that going on? What, what is your answer to that question, which I'm sure you're asked all the time.

### Dr. Hurlbert (06:50)

Yeah, we don't know all the reasons. I mean, so melanoma cases did triple over the last 30 or so years. They have flattened out over the last five to seven years. So the incidents, the, the growth of incidents has slowed a little bit except for in those younger populations. And, you know, I don't know. I'm, I'm a child of the seventies and eighties, and we didn't practice sun safety as much when I was growing up. I think in the, the nineties and two thousands, hopefully we learned better, but I'm wondering if, if the next group of teens, if we need to do a, continuing the effort of education and practice on safety, and then there could be other factors around that we just don't know around climate change or other UV exposures. But, definitely need to continually practice sun safety. I like to tell, everyone, start your teens, your, your toddlers and teens, young practicing sun safety. And I also say it's never too late to get started if you're someone of an older generation and, and haven't practiced sun safety in the past. So wear sunscreen every day, year-round SPF 30 or higher on any sun exposed skin. And then, practice wearing long sleeves. There's amazing sun safety apparel. Now, if you do wanna spend a day out on the water, out at the beach, out at the pool, lots of sun safe ways you can do that, but still, we mean sun safe.

# Mark (08:04)

Well, that's great. That's a great public service announcement, right, right. For everybody, and hopefully they take key, the MRA, points out. Its funding and announcement is occurring at the same time. Unfortunately, the Federal cancer research funding is being reduced. I'm wondering what you can tell our listeners about the overall funding situation for melanoma research.

### Dr. Hurlbert (08:25)

Yeah, so melanoma research, at large is funded by the National Institutes of Health. NIH. The Department of Defense a few years ago launched a specific program called the Congressionally Directed Medical Research Program. And, you know, we're, we're still monitoring the situation and see what happens. Today the DOD funding is, appears secure, and we're monitoring what's happening with NIH. I think we're at this, you know, moment in time with change where the role of philanthropy, the role of nonprofits, like the Melanoma Research

Alliance is gonna be even more critical. You know, nonprofits can move a little bit more nimbly than the government, and we're able to fund innovation and maybe things that are a little bit more high risk, but might be high reward. And so I think, it's a changing environment. We're just monitoring to see what's happening and how best we can keep the momentum going. There's so much unmet need, but I think the role of philanthropy is gonna be critical. These next, you know, two to five years.

## Margaret (09:25)

You know, I, I look at these figures, such as over a hundred thousand people in the US will be diagnosed with melanoma, sad they're diagnosed, good that they're diagnosed so they can get to treatment. One person every hour of every day, will die from melanoma. And there's, access to approved treatments. But I, I have to think about, and certainly from the, you know, the, the space that we're primarily engaged in around primary care Yeah. That all assumed they got to the point of diagnosis, which meant they either recognized a lesion and had somebody who could look at it and give them expert advice. They had access to care, you know, actually had, somebody doing a screening and that when they got screened, they could get to a dermatologist. Not such an easy thing. What's the role of your organization in, in tackling some of those issues? Because I gotta tell you, you know, people are not so accurate. Even people with some training are not so accurate at looking at a lesion and saying, yes, this is worrisome. It's not really takes somebody who knows what they're looking at.

#### Dr. Hurlbert (10:29)

No, absolutely. So detecting melanoma still is an area with where, with an unmet need for research, more research, more technology, and we've invested a fair amount in the past, but it's also one of our urgent, investment prior areas over the next five years. So, improving detection and, and you got it exactly right. Are there tools that we could empower people at home where they could, you know, on an app on their phone, look at, look at their moles and see if there's something, that that could help make it, make you aware if it's suspicious? Are there tools that we could help nurses and primary care doctors to really help cut down on what, which people are referred to dermatology, where there's something really of concern or not? And so we've invested in some imaging techniques, some other techniques that, you know, aren't ready for primetime today, but I think in the near future, maybe. But we need tools for the individual at home, the primary care doctor and the dermatologist. And we're investing in those areas and really believe that AI and imaging and imaging over time, will really help, you know, to, to help in this detection space. And so we're, we've invested a little bit in the past and, we'll be investing more over the next few years, but definitely dermatologists and primary physicians need more tools to help them.

#### Mark (11:44)

Well, Margaret, we've been very engaged in that, line of work as well. Our, con ConferMed, which, does eConsults with primary care providers. We've been working with a group out of Denmark, MELITEK, on a dermoscope that makes it much easier, for the primary care, practitioner to get a good image, which is oftentimes that, and there's a lack of dermatology. We, we cherish our dermatologists. They do such a good job and so important, but we also know getting to the frontline, and one would hope soon, as you suggested, maybe there's an opportunity for some home-based, access to this specialty care, right now. But I think there's a lot of interesting work, going on in this particular area. Do you have any of those types of, intervention models that you are looking at are best practices around the country?

#### Dr. Hurlbert (12:39)

Absolutely. The, the group you work with is fantastic. You know, one, one of the pilot projects, just as one example of about a dozen projects we recently funded was at New York University in New York City. And what they piloted was, the idea that at a CVS or a Walgreens or a Duane Reed, could you, have a place there where you could get, you know, three or four suspicious looking moles, examined with a dermatoscope, and then have it sent to a central dermatology lab where would be reviewed by expert dermatologists, and they would refer, you either get in quickly or nothing to con be concerned about, you know, keep monitoring for the next six months. And it proved to work out. And so they have piloted that at NYU and, you know, look, look at Covid, you know, when, when covid happened, you, you know, before that time you didn't always get immunizations at Walgreens and Walmart and CVS. And then we rapidly were able to do that, and could we do something similar for skin health? And that's, the, the dream and the vision, but I still think a little bit more research to be done.

### Margaret (13:42)

Well, we have, a lot of questions we'd like to ask. We may run outta time before we get them. I'll ask, but it does seem that, MRA is engaged at the, prevention, screening, early detection, and then treatment entire continuum.

And we probably have questions about all of them, but I wanna go to the, the genetics on this one. I understand there's a new gene-based blood test that has been shown to be, accurate in predicting whether some stage three melanoma patients are going to experience recurrences of the tumors or not. We're always interested in what is going on in the genetic, world around these things. Tell us about that.

#### Dr. Hurlbert (14:21)

Yeah, no, absolutely. So it, it is really an exciting time in monitoring cancer through a blood draw, right? You know, essentially what we call liquid biopsy or blood-based biopsy. And yes, so now there's some new tools and new tests that can measure, whether you, have melanoma or not. If you have more advanced disease, stage three and stage four, you know, when you have thinner tumors like a stage one, it's harder to detect. And they, they might not even make it to the bloodstream. But, for more advanced melanomas, we can measure that just even the presence of that at the time of your diagnosis tells us something about your melanoma. The, we can actually measure in blood whether your melanoma has A-B-R-A-F mutation, which is the most common, mutation cause in skin melanoma. And then importantly, these blood-based tests can be used to monitor whether you're responding as you get treatment. And then, also help augment when you're doing imaging, CAT scans, PET scans, augmenting the imaging test to see if you're having a recurrence. And so I think it's really an exciting time I've been, involved in, in other organizations, before I joined melanoma funding, liquid biopsy, blood-based biopsy research for cancers since about 2008. And, for many, many years I was saying it's not ready for prime time. But today, I would say the message has changed. There are tests available, anyone diagnosed with melanoma or any type of cancer, you should ask your doctor if there's any blood-based monitoring tests that could help augment helping your, treatment decision making and monitoring for recurrence.

#### Mark (15:53)

You know, Margaret, one of the things that we keep a close eye on at the Weitzman Institute are clinical trials and the importance of clinical trials. And, you believe that a lack of enrollment in clinical trials is really a, a, a large obstacle to bringing new therapies to market. Right now, I believe there are around 400 melanoma faced focused clinical trials, testing new treatment areas that are currently recruiting patients. I'm wondering if you can, give us a high-level overview of the, of the, these trials, and also just a reminder of how important, for the general population, to consider enrolling, into these trials.

## Dr. Hurlbert (16:34)

Absolutely. Well, clinical trials in melanoma today, you know, we have so many new drugs that are the standard of care. And so the new trials are having to compare the new drug, the new agent, the new approach to an amazing standard of care. So, this idea that you might be a Guinea pig is no longer, you know, that's not valid. So that's a misconception. There are 400 trials. A lot of them are looking at novel immune therapies, novel targeted therapies. I'd say over the last five years, cancer researchers have found a lot of new targets within the cancer cell and also within the microenvironment around the cancer cell, how the cancer cell interacts with fibroblasts and other parts of, you know, the, the healthy tissues where it's growing. And, so how can they target the environment as well as the cancer cells. So these 400 trials are new immune therapies, new targeted therapies, combinations of agents. We're also looking at, questions, what we call neoadjuvant therapy. Do you give the, IV systemic therapy before surgery, before you cut out the melanoma? It's done in other cancers. So giving systemic therapy before you remove the tumor. And it's still, in the area of research, it's not, not yet FDA approved to do neoadjuvant treatment, but there's some suggestion from early clinical trials and from lab studies that giving these immune therapies I've been talking about before, the surgery might be more effective. There's, the, the hypothesis by scientists is that there's more tumor antigens around because you haven't cut it out, and that the immune system might be stimulated more to recognize it, then you could do the surgery and then continue these systemic therapies. So that's, that's what this, you know, current bunch of ongoing trials is doing. I will say, my, my message for everyone when I talk about clinical trials, you don't walk down to the Apple store today and say, Hey, I'd like an iPhone one or an iPhone two, right? You all want the, the 14, the 15, whatever generation we're on. So why would you go to your oncologist and say, give me, you know, medicine 1.0. You know, we want the most modern medicine. And that's what clinical trials are providing you today in melanoma.

#### Margaret (18:42)

Well, I'm, I'm gonna keep bouncing around. You'll all have to forgive me from this prevention, early detection and, and treatment, continuum because I, I think melanoma may represent one of the best meta examples of how it all has to work, right? If we're gonna do a good job, we have to think about prevention, early detection, screening. Mm-hmm. And treatment. But, you know, I'm, I'm gonna start on the, the treatment end of this. Now, patient needs to get to a surgery site where they can have a MOS procedure or some, treatment if they're at a, an appropriate stage. But across the United States, we have huge sort shortages, right? Of the experts, the primary

care, the, the dermatologist, the specially trained dermatologist for melanoma. What's, what's your advocacy role as an organization, in that? Are you working with, schools and training programs, trying to develop new generations of, I'm sure physician assistants and nurse practitioners are also a big piece of that workforce. What are you doing to make sure that everybody can get access when they're diagnosed and that they have coverage to be treated as well? The insurance coverage?

## Dr. Hurlbert (19:52)

Yeah, that's a great question. And yeah, it's definitely an unmet need. We need more dermatologists, more surgeons, more oncologists and, and the staff, the nurse practitioners and physician's assistants that support them. We have a few programs, you know, for example, training new dermatologists interested in melanoma called our dermatology fellowship program. We have another program called the Young Investigator Award, which strips simulates new faculty within the first five years of their career. But absolutely more work needs to be done on training. Those we do encourage anyone diagnosed with, melanoma, especially if you have a more advanced stage, you know, stage 2, 3 4, that you really should do your best to get to an NCI designated Cancer Center, the National Cancer Institute, there's about 75 of them around the country. They're usually affiliated with top universities and medical schools in your cities and towns. And we do encourage people, at least to get a second opinion at one of the NCI designated Cancer centers. If it's a few hours drive away, go there for a second opinion, and then, you maybe could still get treatment locally back home once you sort of know what is the right treatment path for you. And so that's, that's where we encourage people. But absolutely there's a need for more physicians.

### Mark (21:06)

You know, Margaret, we talk so much on the show about machine learning, AI, MNRA technology, and CRISPR, wondering how all of those are playing a role in the work that you're doing as you look out on the horizon of new opportunities and new interventions that we may wanna keep an eye on?

### Dr. Hurlbert (21:25)

This is a great question. I think there absolutely will be a role for artificial intelligence machine learning, especially in melanoma detection and diagnosis. So if we have these imaging tools like a dermatoscope that the dermatologist uses or a primary care physician uses, there are other imaging tests I don't think we have time to get into today. But there are other imaging tools being developed, but any sort of imaging tests, anything that measures a change in your, mole or a change in your tumor over time is, perfectly ripe for being part of AI and machine learning. And so we've invested about \$10 million into this space so far, but more needs to be done. But absolutely, I think they will have a role in helping detect, changes in moles over time, helping detect when they, when a mole is melanoma and needs treatment. And then there will be a role, I think, in ai machine learning and monitoring patients with known cancer and as they, are treated over time. So I think it's an exciting area. AI machine learning can detect changes, potentially, you know, that someone with the human eyes can't detect, you know, if you can look at images, you know, microscopic changes over time. And so it's an exciting area that is worthy of more investments.

## Margaret (22:42)

All right. I'm gonna bounce back to prevention, prevention and research. We'll tie both of those, together. So, I had dinner with a friend not long ago who had been visiting her grandchildren in Australia, and she, showed me a photograph of the two, beautiful school age boys. And they were both where they had just come out from school and they were both wearing large kind of floppy hats. And I thought it was amusing 'cause little boys generally are not too keen on that kind of thing. And she said, it's not even a question in Australia. It's the number one, highest incidence of melanoma in the world. I don't know if that's accurate, but that was, her understanding, and that it is, it is the norm to see children wearing protective headgear and really everybody wearing it. So I wonder what your thoughts are, relative to research and human behavior, also in area that we're very interested in. Mm-hmm. And the Weitzman Institute, I don't see that happening around me in the United States. I don't see it happening at the beach, although maybe with the very, the babies, a little more attention to, covering. But what are you doing in terms of, research into how you really change behavior to move away from those numbers that we talked about earlier about the significant increase in younger people of melanoma that's gotta require behavioral change. What are you studying? What's effective? Does it have to come from the healthcare provider? Is it social norms? Tell us your thoughts on that.

## Dr. Hurlbert (24:10)

Yeah, no, absolutely. We definitely need to do more to educate the public on it. And like I suggested earlier on, maybe we've made some progress in the nineties and early two thousands, and maybe we need to double down on efforts, right? On sun safe behaviors. Absolutely. We've funded a few projects that were piloting ideas,

piloting ideas on social media locally to see if they could, get, the public and people, you know, to improve their knowledge about sun safety, not just sunscreen, which is critical every day, year round, reapply if you're gonna be outdoors for more than two hours, but also some of these long sleeves, these hats, sunglasses, other things to prevent, directly exposing your skin to the sun. And we need absolutely to do more of that because it is a behavioral change across society and absolutely Australia, leads the way in some safe behavior because melanoma is so critical down there.

## Mark (25:05)

Dr. Hurlbert, I think our listeners would be interested if you could share how you got involved in melanoma research and advocacy and leading this effort.

#### Dr. Hurlbert (25:15)

Absolutely. Well, thank you for that question. I'm a scientist by training my background's in pharmacology or drug development for the lay listener. And I've worked in neuroscience for a decade and then diabetes for about five years. And then I moved into cancer research, just over 20 years ago. I spent most of that time in the breast cancer field, and I moved over to Melanoma Research Alliance seven years ago, quite honestly, because I was very excited by these new immune therapies. I think stimulating the immune system to attack cancer just like it goes after a virus or bacteria, has been a game changer in melanoma, and now more than two dozen other types of cancer. And I think balancing that immune therapy with abnormal cancer cells will be the way that we cure many, many types of cancer going forward.

### Margaret (26:04)

And, and perhaps one more que question on my end. You're a big advocate, obviously, to try and, find this early and treat people effectively. But also the message that melanoma does not discriminate anybody, no matter your age, no matter your ethnicity, no matter your racial background, can get this and that you in fact are seeing rare melanomas more often in patients with black, Hispanic or Asian, ancestry. What's the message that you wanna get out there to all people about screening?

### Dr. Hurlbert (26:34)

Yeah, so everyone should practice sun safety. All races, all ethnicities, anyone, any race, any ethnicity, can get skin. Melanoma can get melanoma and particular people with darker skin tones, black, Asian, Hispanic, they should be, cognizant of changes, moles or abnormal naive blisters on their hands and feet. They can get these rare melanomas, acral, melanoma on their hands and feet. And they just need to be aware that melanoma isn't always just a brown spot on your shoulder. You know, it could, could be on your hands or your feet or under your fingernail beds. And, but I think the key message is any race, any ethnicity is, susceptible to melanoma. And everyone needs to be aware about their own skin and changes in their body over time.

### Mark (27:17)

You know, I'm sure Margaret, a lot of people who are listening this wanna know more about MRA's work. Tell us how people will get in touch, of the work that you're doing. Is there a place that they can go on the web, to find out the latest research?

## Dr. Hurlbert (27:32)

Absolutely. I would encourage the listeners to, join us at curemelanoma.org, our website. You could subscribe to our e-newsletter. It goes out every month with usually four to five new features, new research, highlights, new breakthroughs. We're very excited, this springtime, springtime of year. There's a lot of cancer conferences. I'm sure many of you, you, both of the, both of you follow it and many of your listeners do. And so we'll be reporting, in a few weeks from now from the ASCO conference, but really, would welcome any of your listeners to join us@curemelanoma.org.

# Margaret (28:003)

Perfect. And thank you Marc, so much for joining us. And thank you to our audience for being here. Just a reminder, be sure to subscribe to our videos on YouTube, find us on Facebook, and also, please share your thoughts and your comments about this program. Take care, and be well.

#### (28:22)

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