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Welcome to Yale Cancer Answers with your host Doctor Anees Chagpar. Yale Cancer Answers features the latest information on cancer care by welcoming oncologists and specialists who are on the forefront of the battle to fight cancer. This week, it's a conversation about health disparities in cancer with doctor Kim Blenman. Dr. Blenman is an associate research scientist in medical oncology at the Yale School of Medicine where Doctor Chagpar is a professor of surgical oncology. Maybe we can start off by you telling us a little bit more about your research and what exactly it is that you’ve been doing.

I’m an immunologist and clinical chemists with expertise in drug discovery and clinical development and in aspects of pathology as you mentioned. I am in the Yale Department of internal medicine, section of medical oncology and Yale Cancer Center.
Briefly, I study the immune system of patients to try to understand how the immune system is involved in their disease and their responses to therapy treatments. I have done research in Melanoma and I am currently working in breast cancer as part of the breast medical oncology translational research group.

Tell us some of the studies that you’ve been doing in breast cancer looking at the immune system.

Our work is primarily conducted through clinical trials. As I mentioned, our goals are to really try to identify components or mechanisms of the immune system that will either help patients to respond or respond better to therapy or help them to reduce the therapy. The way that we do this is that we look at both genes and proteins of the immune system and of the tumor. To accomplish our goals we use many platforms, such as next generation sequencing to identify genes in RNA and DNA. And we also use Histology to identify proteins and different immune and tumor cell types. And with that being said,
my research is really interested in looking at many, mostly biological factors. As I said, they are responsible for the disparities that we have in disease and therapy, and I am currently working on triple negative breast cancer. You noted cancer accounts for approximately 10% of all breast cancers. This subtype of breast cancer is estrogen receptor negative, progesterone receptor negative, and HER 2 negative in regards to the biomarkers that we use to classify the type of breast cancer. It’s often more aggressive, meaning that it grows and spreads fast, so it tends to occur more often in younger women, and those were the BRCA gene mutations. So triple negative breast cancers have poorer prognosis than other subtypes, partially because treatment advances have lagged behind other breast cancers, but although treatment options are more limited than the other breast cancers, there are still several offices.
available to these patients. And these individuals are treated with some combinations of surgery, radiation therapy or chemotherapy. And right now I’m working on two clinical studies and one study is a retrospective evaluation of genes and proteins from Histology tissue. From the tumor page, two more patients with these triple negative breast cancers to try to identify immune components or mechanisms that may be responsible for the variations that we see in different racial and ethnic groups before the patients are treated. And then the other study is an ongoing clinical trial that is evaluating the benefit of giving our triple negative breast cancer patients anti PDL one immunotherapy with chemotherapy before they’re taken to surgery. Those both sound like really interesting studies and I want to talk about each one of them in turn. So the first one, the retrospective study where you’re looking at kind of the immune factors in these cancers retrospectively. So these are cancers that have already been taken out of patients and you’re looking at immune factors in these cancers.
Now I understand that triple negative cancers perhaps more than other breast cancers actually are immunogenic, they tend to have a lot of infiltrating cells in them.

Is that right?

Is that what you’re looking at? or are you looking at other factors as well?

That’s absolutely right.

And actually we’re looking at all the above and we’re doing as I said, looking at different populations of people within that particular space, and the reason is because the percentage of triple negative breast cancers among the total breast cancers diagnosed in non Hispanic whites, Hispanics, American Indians or Alaska Natives is between 10 and 20%.

I’m sorry 10 to 12% and non Hispanic Blacks is 21%.

We’re trying to understand why that difference exists and more of the biology, more of the biological questions and so we’re looking at the immune system to see if there are different immune players in terms of the amount of infiltration that we see between these different populations of people.
or the type of inflation.
What type of cells are being infiltrated in these patients?
And so we’re doing that by looking at the Histology.
Taking the samples of the tumor doing next generation sequencing on those,
look at the genes and then looking at different types of immune cells from the Histology tissue itself,
as well as just using our standard hematoxylin eosin to look at the actual global tumor infiltrating lymphocyte
into these populations sorry into these patients samples.
I want to make sure that I understood because I mean it sounds like such a cool project with so much there to unpack.
And maybe you’re looking at all of these questions.
But the first thing that it sounds like you’re doing is really looking at these cancers to see whether various immune pathways are turned on or turned off in the cancer themselves, whether the they have more or less infiltration with the immune system in these cells.
So do you find that there are biologic differences in triple negative breast cancer between African Americans,
and say, Caucasians?

And do you think that really explains why African Americans tend to have more triple negative breast cancers than other non African American races?

So this is one of the things that we actually are trying to tease out with this particular study and all the data is not back yet. And of course there are other factors as well that contributes to those differences, but as I said, we’re really trying to focus on these differences in the system that we have seen initially, and as we’re putting more patients on these studies and look at more things, we’re trying to see if that gives us any reason to believe that there are different immune cell populations that are being introduced that are different between those two groups and as well as other groups. But also if there’s maybe a difference in the amount of those immune cells that are being introduced, and so we’re still evaluating the data, but hopefully that’ll give us some
insight if that’s indeed true.
Because that would mean that we may need to think about how we treat the patients differently, right?
And it may give you some insight into potentially why certain people get triple negative breast cancers more than others.
Maybe some populations of people automatically have a more robust immune response to cancer cells as they are initially beginning such that they don’t develop into full blown tumors, and so you may be able to see differences.
Are you looking also at the immune factors versus stage at presentation?
Because that too might play into that whole story, right?
Correct, and so we’re looking at that as well.
That could definitely play a difference in what makeup looks like at the end of the day?
Because we want to make sure that we are comparing apples to apples.
And so for this part of the study, you’re actually looking at the tumors DNA, right?
You’re taking these tumor sections and doing next generation sequencing on the tumor and the microenvironment surrounding the tumor, has anybody really looked at the immune system of different racial groups to see whether there are differences in immune cell production between different races that might give you some insight into how people mount immune responses. Whether that’s the same for everybody, or whether there are nuances and so actually we have some evidence to that.

As you think about things like autoimmune diseases, autoimmune diseases tend to be more prevalent in certain populations, and they tend to have as you look at the immune system, the immune systems tends to be very overactive, and so these are things that can give us clues that maybe in different populations we may need to think differently about how we approach this, and so there are studies that have been done in different fields,
and I think that we can utilize that to try to understand how this is applicable to cancer as well, and this is actually one of the main goals of this particular study that we're doing is to try to tease that out as well, and hopefully we can expand on that in terms of digging a bit more deeper into them, these different patient populations. So what I'd like to look at, although this particular site is looking at, individuals of African descent, individuals of Caucasian descent, I would also like to expand that to individuals of Asian descent as well and other populations because I believe that that’s actually very important for us to be represented in order for us to understand exactly what’s going on with cancers globally. And the other thing that you had mentioned just in passing was looking at different types of immune cells,
So we often when we’ve been on this show, have talked about these tumor infiltrating lymphocytes. And we talk about T cells, but there are other immune factors and other immune cells as well. Do we have any sense of how these immune cells vary in terms of their response to tumors? Either different types of tumors or to the same tumor, but in different people? Actually that’s a really great question, and I’ve done some work in this in breast cancer itself, and so I’d like to share a little bit about a study that was recently published looking at breast cancers in predicting disease. Actually B cells in predicting disease free survival in breast cancer patients and just as a little bit of background, metastasis is a frequent early event in many cancers, and so in breast cancer, lymph node invasion is a key determinant in prognosis and treatment. So our previous studies have shown that T cells and injured cells in the
tumor draining lymph nodes may be altered in some breast cancer patients and can predict clinical outcome. But B cells are another major immune cell population for their role in solid cancers and is not well studied. So B cells isolated from tumor draining lymph nodes, specifically Sentinel lymph nodes, which are the first set of lymph nodes that the tumor drains into can recognize cancer associated antigens and are capable of producing antibodies against those antigens, and so in our study that we recently published we looked at the cells, and since all lymph nodes in breast cancer patients, we found that patients with higher numbers of these had longer disease free survival overall as well as in those patients with triple negative breast cancer that had actually good prognosis. Interestingly this can be seen in Melanoma patients and we recently also published this and we have found higher numbers correspond to longer progression free survival.
in patients with metastatic Melanoma treated with anti PDL1 immunotherapy. And so have we found a difference in terms of the number of B cells that are in tumors of people of African American descent versus Caucasians. So this is one of the things that we’re looking at and that data is still to be evaluated. Certainly, if it’s true that B cells do predict differences in survival, it sounds like it is a relatively simple prognostic factor. And it could give people an idea of how this biology is going to play out, particularly as it interfaces with the immune system. You’re absolutely right, and the other thing that I’d like to point out too is that the immune system is called a system for a very specific reason. It works as a system, so B cells do not work in isolation. T cells do not work in isolation, and so all these things require to be working together and so this is one of the things that we need to think about when we make these prognostics and predict.
the tools is to consider all these different immune systems and put them together to make choices that we move forward. We're going to pick up on that conversation right after we take a short break for medical minute. Please stay tuned to learn more about health disparities and cancer and the immune system with my guest doctor Kim Blenman. Support comes from AstraZeneca, working side by side with leading scientists to better understand how complex data can be converted into innovative treatments. More information at astrazeneca-us.com.

This is a medical minute about colorectal cancer. When detected early, colorectal cancer is easily treated and highly curable and as a result, it's recommended that men and women over the age of 50 have regular colonoscopies to screen for the disease. Tumor gene analysis has helped improve management of colorectal cancer by identifying the patients most likely to benefit from chemotherapy and newer targeted agents, resulting in more patient...
specific treatments.

More information is available at yalecancercenter.org.

You’re listening to Connecticut public radio.

Welcome back to Yale Cancer Answers.

This is doctor Anees Chagpar and I’m joined tonight by my guest doctor Kim Blenman and we’re talking about health disparities in cancer and right before the break Kim, you were talking to us about some of the studies that you’re doing in breast cancer, specifically one study in triple negative breast cancers where you’re looking retrospectively at the various immune systems and immune responses that are mounted by patients with triple negative breast cancer and you kind of left us hanging in terms of the details of whether this is really different between African Americans and Caucasian patients.

We know, for example, that in triple negative breast cancer it seems to be more prevalent in African Americans than in Caucasian patients. Can you shed some more light on how different cancers affect different racial groups differently?

Yes, and as I mentioned,
my research interest is in the biological factors responsible for disparities and disease and their responses. So in that context, Melanoma is a great example. Melanoma is a skin cancer that occurs most commonly when the DNA in melanocytes is damaged by UV rays. That is sun exposure. Melanocytes are the cells that produce melanin, which gives skin its color. Eumelanin is a type of melanin that is responsible for darkening the skin and it has the ability to protect the skin from UV damage so when individuals tan as a result of exposure to the sun, youe melanin is responsible for the visible color that you see as the tan so individuals with naturally darker skin, have more eumelanin and are therefore at lower risk for developing UV induced skin cancer. So for decades, the messages that were shared in general and in communities of people of color with naturally darker skin was that people of color do not get Melanoma. However, today we know that the most common form of Melanoma found in individuals with
naturally darker skin is acral Melanoma, which is often found under nails.
On the palms of hands and the soles of feet, and disease of face.
The musician Bob Marley from Jamaica died of acral Melanoma.
And so this is a good example of why it’s important that we actually take into account these biological factors and try to find or look for things that may give us some clues as to why things are different that are not a part of social determinants of Health and so this is how we really got interested in looking into these different factors for these different cancers.
That makes sense in Melanoma, in breast cancer we were talking about before the break it’s a little bit more tricky in the sense that there doesn’t seem to be a particular factor. Something like eumelanin, which would be different between African Americans and Caucasian patients, which I guess is how you got into thinking about triple negative breast cancer is more common in
African American patients and could this have something to do with their immune system? Because certainly we know that triple negative breast cancers are immunogenic. Exactly, and actually, that's the link with acral Melanoma as well. So the thing about acral Melanoma is that it actually has a lot of infiltrating immune cells. and are a little bit less involved in individuals of Caucasian descent, you're thinking about, okay let's look at the immune cells. You know there's something different about the immune cells. and the types of cells also infiltrated that's making these differences that we see. And I suppose you did mention before the break about your study looking at B cells, and I believe you mentioned that you found that B cells were tied to prognosis in both Melanoma and in breast cancer, I guess that leads us to the next study that you had mentioned before the break, which is a prospective trial looking at immunotherapy because,
As we’ve talked about on the show previously, immunotherapy actually has really taken hold in Melanoma and is just starting to get evaluated in breast cancer and specifically in triple negative breast cancer, so maybe you can tell us a little bit more about your work there.

In the last five to 10 years or so, we’ve started to really recognize that the immune system has a role in how cancer patients will respond to many of the therapies that we give, including chemotherapy. So to take advantage of that fact, we are, as you mentioned, starting to identify and use therapies that directly impact the immune system alone or in combination with chemotherapy. So, for example, we have an ongoing study that is evaluating the benefit of giving our triple negative breast cancer patients Anti PDL1 immunotherapy with chemotherapy before they’re taken to surgery and the advantage of that is that we’re trying to understand whether or not this particular regiment of giving that
immunotherapy could help boost the immune system’s ability to see the cancer or to break it down so that the chemotherapy itself can respond better to the cancer. And, as I said, the study is still ongoing, but we are starting to see some very interesting results that have some positive benefit for Anti PDL1.

Now how does that immunotherapy work, particularly for people who have PD L1 or PDL or PD one receptors or would it work for any triple negative? Actually this is kind of interesting because we’re actually finding that we are getting affected regardless of whether or not the individuals have PD L1 as part of their tumor, and so there are other things going on there that are mediating this response that we’re still trying to learn for this particular PD1 PD L1 Axis. So it’s certainly a really interesting and novel thing to think about, and I know many of our listeners are
always intrigued by immunotherapy. It seems to be a really hot topic, but when we think about immunotherapy, one of the things that we always caution patients about is the side effects, which tend to be side effects that are an exacerbation of the immune system because essentially you rev up your immune system or as you say, you can make tumor cells more susceptible to the immune system, now have you noticed a difference in terms of racial groups with regards to those side effects? Because you mentioned that there is a racial difference in terms of autoimmune diseases so one would imagine that there might be a difference in terms of the side effects with immunotherapy as well. Have you found that so? That’s a great question and something that we are actually evaluating now. And so as I said, the study is still ongoing, so we don’t have enough patients collected yet in the different groups to actually make any statements. But this is actually something that I am very interested in.
And is one of my major goals of this study is to try to tease out those potential differences that we see between different populations of people, but no, we don’t have that information yet, but I suspect that we will be able to see in these studies and other studies that others are doing.

Do we know whether different racial groups will respond differently to immunotherapy? For example, if patients have a similar tumor in terms of their PDL1 status. The size of the tumor, the B cells and the T cells that are in the micro environment and you give them immunotherapy. Do we know whether, just by fact of different racial groups, they will Mount a different immune response that will then result in differences in terms of the effect? So I think one of the first things that we need to think about is the individual and the health of the individuals is influenced by many interconnected factors such as their individual biology,
their behavior, environmental and physical influences. The type of medical care that they’re getting and the social determinants which are influenced by both the socio economic and political factors. And so we now know that each of these factors can lead to the health disparities that exist in cancer, and so these are the things that we actually need to consider when we talk about potentially, one population being different than the other, so I think the individual health is something that we should consider versus the entire population of that individual. So with that being said, it’s going to be determinant on what their biology is that individual biology and how they are going to respond to that individual therapy, and so I don’t want to generalize to an entire population on that perspective, but I think you know the more pressing question for me is, how can we overcome these disparities that I just mentioned and for me I think that we need to do more inclusive research.
We need to recognize that as human beings we are part of a collective that is made up of different populations. And then in order for us to move forward in science and medicine, we need to include all of our populations in all of our research endeavors. This level of diversity is not only required in the populations that we study, but it also needs to be equally represented in the faculty members that are performing and or involved in these studies. So again, representing the diversity of our global population. Giving us some concept of the individual as well.

Doctor Kim Blenman is an associate research scientist in medical oncology at the Yale School of Medicine. 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 week to learn more about the fight against cancer here on Connecticut public radio.