U.S. Environmental Protection Agency
The Use of Race in Environmental Health Research: What Does/Could it Mean?
Pre-Symposium Webinar for the Strengthening Environmental Justice Research and Decision Making: A Symposium on the Science of Disproportionate Environmental Health Impacts

March 4, 2010 1:30PM-3:30PM
Moderator: **Devon Payne-Sturges**, PhD, Assistant Senate Director for Human Health Research with EPA National Center for Environmental Research
Speakers: **Gilbert C. Gee**, PhD, Associate Professor, UCLA School of Public Health
Charmaine D.M. Royal, PhD, Associate Research Professor, Institute for Genome Sciences & Policy, Duke University
Clarence C. Gravlee, PhD, Assistant Professor, Department of Anthropology, University of Florida
Hal Zenick, PhD, Director, US EPA National Health and Environmental Effects Research Laboratory
Next meeting: March 11, 2010 1:30PM-3:30PM

I. *Moderator:* **Devon Payne-Sturges**, PhD, Assistant Senate Director for Human Health Research with EPA National Center for Environmental Research

Alright, well good afternoon and thank you all for joining. My name is Devon Payne-Sturges and I'll be the moderator for you all today. Just a little bit by way of background I am the Assistant Senate Director for Human Health Research with EPA's National Center for Environmental Research. I'm also one of the co-chairs for the planning committee for the **Disproportionate Impact Symposium** that will take place in a couple of weeks March 17-19th here in DC. So welcome to this pre-symposium webinar. We are hosting two pre-symposium webinars as a way to facilitate common understanding among the symposium participants, who will be coming from diverse backgrounds. Our first webinar today, "The Use of Race in Environmental Health Research: What Does/Could it Mean?" will feature provocative presentations that will help us think about how to interpret racial differences in health and the implications for environmental health research. I just want to say that the second webinar will take place one week from today at the same time, that means March 11th at 1:30, and that particular webinar will focus on how environmental justice concerns arise in decision making and program implementation context at EPA, so if you're interested in that second webinar please register for that, and that information is up on our symposium website.

So, first I'd like to say a few words about the motivations for this particular webinar. As I hope most of you realize, the EPA has a very broad mission: to protect human health and the environment. EPA works to achieve this mission through a variety of actions and decisions. The Agency uses scientific evidence to support its policy and regulatory decision making. These decisions include activities to establish standards in the quality of our air and drinking water, permitting, which is limiting the emissions of pollution on say, industrial sources into the environment, the enforcement of standards and permits, and also involved in a lot of information and data collection, and issuing orders for waste-side cleanup. Often, the evidence that supports these kinds of actions includes information and data on environmental public health outcomes. Environmental public health outcomes of interest include: risk of health effects and disease outcomes, but also surrogate measures may be

used and they include: levels of pollution in the environment and levels of human exposure to pollution. Now, existing evidence, some of this information is collected by our sister federal agencies like HHS and CDC, but existing evidence shows that environmental public health outcomes are often socially-patterned; typically along racial, ethnic and income lines. For example, it's quite well known and well documented that in some cases, racial/ethnic minorities and lower income groups have higher rates of health outcomes that are known, or suspected to be environmentally mediated, such as: cardiovascular disease, cancer, autoimmune diseases like lupus and diabetes, and respiratory ailments like asthma. There are also known social disparities, exposures to environmental contaminants that are also associated with health effects. Such as: documented higher blood lead levels among African American children, higher levels of mercury in the blood of Asian American women in some cities, higher levels of pesticide metabolized measured in the urine of farm workers.

So, given that the focus of the symposium that's coming up in a couple of weeks is on the science to support consideration of different factors that may contribute to disproportionate impacts in EPA decision making. Data and research on racial disparities in health outcomes and environmental exposures will greatly inform discussions at this symposium. So, the question is, what does it really mean when racial differences are observed, meaning outcomes that are often subjects of analysis at EPA as I just described. And how can this inform environmental health policy and decision making? In order to answer these questions I think we need to step back a bit and educate ourselves on some fundamental issues about the historical context of race, the use and interpretation of race as related to health research, and how race is understood, as a biological and/or social construct.

Before we start the presentations, I'd also like to offer a definition of environmental health disparities for you all to consider, to ponder, as you all are listening to the presentations. Environmental health disparities are racial, ethnic and socioeconomic inequities in illness and exposure. These environmental health disparities are at least partially mediated by factors associated with the physical, social, and built environment. Now, definitions are really important because they can have policy implications and they have implications on what you measure. In particular, in this case, in offering definition to you, the focus here is that looking at health disparity and inequality as a particular type of difference in health or in the most important influences on health that, here's the main point here, that could *potentially* be shaped by policy.

The objectives of today's webinar are the following: to understand changes in the meaning of race over time and the challenges this presents for health disparities research and public health surveillance, to learn what the human genome tells us about race, particularly in the US context, and to learn how race is conceived cross-culturally and how that relates to health impacts.

So, I would like to introduce today's speakers. They are: Dr. Gilbert Gee, who is an associate professor at UCLA, School of Public Health, Dr. Charmaine Royal, associate research professor at the Institute for Genome Sciences & Policy at Duke University, we also have Dr. Clarence Gravelee who is an assistant professor at the Department of Anthropology at University of Florida, and then also a dear colleague of mine, Hal Zenick, who is the director of EPA National Health and Environmental Effects Research Laboratory. And he will be our discussant. So, to tell you a little bit about the order now. Each speaker will have about twenty minutes to give their talk, and

we will take 1 or maybe 2 clarifying questions after each presenter. As part of this webinar technology we have a way for people to submit their questions. There's a little question box. And what I'd like to ask is that those of you who would like to pose a question after each speaker, if you could kindly use that question box to submit your questions. If you could actually include what your affiliation is, I'll see your name, but it'd be nice to know from where you are coming and I will call on those questions. Then after the presentations, Dr. Zenick will give some remarks reflecting on what's was just presented and relate implications of the work he's involved in and that we're actually involved in at EPA. Then he will pose a couple of thought provoking questions to our panel of speakers to stimulate a dialogue among the speakers. Then the balance of the time we have, we will use to take questions from the audience. I think we'd still like to use the question and answer box for you all to submit your questions. And with that I can introduce the next speaker…… With that I'd like to call on Gill.

II.) **Gilbert C. Gee**, PhD, Associate Professor, UCLA School of Public Health
Scientific Challenges in the Study of Race and Ethnicity

Slide One:
Alright, Good morning everybody, I'm Gilbert Gee and today I'm going to talk about some scientific challenges related to the study of race and ethnicity.

Slide Two:
And what I'm going to do is review the use of race/ethnicity as a construct across several data systems and discuss implications of this for research and policy. And really, the main point I want to get across is how to use race and ethnicity with the same care that we use any other scientific **calculations/data**.

Slide Three:
I think it's helpful to begin with thinking first about how we actually measure and ascertain race.

Slide Four:
The slide you see here are some of the major ways that we collect racial information. One being looking at somebody for visual inspection, another is through their own self reports, another would be proxy reports, so for example, a parent could be reporting for their child. We also can look at "hard data" from birth and death certificates. Also, there is the possibility for genomic sequencing. As an example, I don't know if any of you have been watching the George Lopez show, recently he's had this series on whether Charles Barkley is blacker than Snoop Dogg and he actually has them go out and get their genes sequenced.

Slide Five:
If you look at this slide with the four people in front of you, the common denominator amongst all of them, beside the fact they make more money than I do, is the fact that they all have an Asian parent. And this may not be readily apparent if we only look at them and try to assign a racial classification. This is something people are apt to do and we do quite often. This is actually connected to some of our data systems.

Slide Six:

First and foremost being the US census. Now, of course the US census is a very important document. The collection of census data is mandated and written into the constitution. An important observation, race was recorded since the very first census in 1790. But up until 1950 the race for the census was based purely on visual inspection by whoever was the census taker and their assessment of whoever they were looking at. It wasn't until the 1980s that we started to collect census data by race using self-identification rather than visual inspection.

Slide Seven:
I think it's helpful to look at the history of the racial categories that was collected for the census. In 1970, there were basically two options: you were either white or black, and they differentiated between free and enslaved blacks. What's interesting is that you jump to 1860; new races emerge in the census, which are American Indian and Chinese. What's interested about that is that the Chinese "race" only existed if that person was in California. If he/she happened to step across to, let's say Nevada, they were no longer Chinese. In 1870, the Japanese were recognized. Jumping to the 1930s, Mexicans became a race. In 1940 we changed our mind and Mexicans were no longer a race. Jumping to the year 2000, we can see that there were Pacific Islanders were separated from Asians, and were considered two separate categories where as before they were considered the same. Also in the year 2000 people had the option for the first time to report multiple races. What this really says of course, is that racial categories really go with the times; the historical periods that we're in. And that they're always changing and they even very by educational status and geography.

Slide Eight:
Now this practice was mirrored in other kinds of data that we have, including NHANES. You can see in NHANES 1 and 2, race was ascertained by interviewer observation, but starting in NHANES III race was self reported.

Slide Nine:
We also see the kind of stuff happening in the National Vital Statistics Birth File. If you had for example, a person with race unknown in 1963, that person was assumed or imputed to be white. In 1964, that unknown person would have been imputed as the previous respondent on the data file. Up till 1979, if a child was born from parents of two different racial backgrounds the child was the race of the non-white parent. But in 1980 a major change occurred so that the race of the child was the race of the mother. So you can see on birth files that the classification of racial categories has changed.

Slide Ten:
Robert Hahn in 1992 published a really important paper in JAMA. He asked a very simple, but important question: is the race on a birth certificate concordant with the race on a death certificate. And here he looked at infants who died within one year of birth. And if you look at the cells you can basically see that 99% of the babies who were classified as white at birth were also white at death. 96% of the black babies stayed black at death. But if you look at the Filipino babies only 47% of them were classified as Filipino at death. And in fact 45% of them were reclassified as white. Now, what happened here? Was it that the Filipino babies suddenly have an existential crisis and decided they wanted to be white instead of Filipino? No, what probably what happened here was that the race on the death certificate was ascertained by the attending physician or corner who was basically looking at a dead body and checking off the box using their eyeballs. So you can see as something

that's "hard" of a birth or death certificate also has a fair degree of misclassification. I present Filipinos here but this misclassification can also exist for other Asian groups as well as Latino groups. I just shortened it to simplify the slide.

Slide Eleven:
We also know that self-reported rate is as much a political process as it is anything else. Here is some data from the National Longitudinal Study of Adolescent Health. I'm showing you just a little data of a study published in ASR. They asked children to classify their race and it mattered in what context the children were asked the question. When they asked the kids what is your race when the kids were at school 6.8% of the kids reported they were multi-racial. When those same kids were asked that same question at home it was only 3.6%, roughly half. If you reconstructed multi-racial using a different criterion looking at the whether parents' self-reported race was concordant, then the results were 4.6%.

Slide Twelve:
It's important to remember that the racial groups that we use, especially in the United States are very heterogeneous populations. I'm just going to scroll through these really quickly and stop at White. You know, if we even just consider the White category we lump together people from Saudi Arabia with people from France and England and Italy etc. So, it really raises some fundamental questions of what it is we're measuring when we're looking at these very diverse groups. Now, race is not only influenced by context, it's not only influenced by how we measure it in terms of our data systems and how we measure it terms of interviewers or whatever. Race is also constructed in our data systems themselves, as a function of computer programming, how we set up our databases, and things like that. So what we have here is data from the Veteran Administrations (VA) data files. If you were an alien from Mars and went into the mainframe at the VA you would conclude that there were only two racial groups across the world: white, black, and then other and unknown. Kressin did something very interesting where she asked veterans who were in that database to self-report and self-identify their own race. And now you suddenly see that there are 4,600 Asians are represented at the VA in those VA data files. And you can of course see that many of those Asians, 10% of whom were classified as white, many more were classified unknown or others. Also interesting to note of the veterans who self reported as being white only 61% of those veterans were classified as white and 1/3 were classified as unknown. So, racial groupings we have are also a function of our data systems, but they're also interestingly enough, a function of human subject protection.

Slide Thirteen:
So, I'm going to talk a little bit about the National Survey of Children's Health. That survey asked parents to report the race and ethnicity of their child. That report is reported verbatim. So somebody may say "my kid is Korean". Now, those verbatim responses were recoded into the typical racial and ethnic categories you see here. Those make sense from some perspectives, but those categories in yellow are further recoded. So American Indians, Asians and Native Hawaiians are recoded as "other race" in order to protect the confidentiality of people from those groups. So in other words, that makes sense, right? So you have a 14 year old Korean girl who lives in Boise, Idaho. If someone is looking at the data set they could say "Huh, I bet that might be Helen Kim", or something like that. Now, there is a little bit of an asterisk there. So, if you were Asian and you lived in a state where Asians were more than 5% of the population, then you were still Asian in the data set. In other words, if you were Asian in California, you were Asian. But if you were Asian in

Nevada, you were no longer Asian. I think there's a little bit of tension here, because the point of human subject protection goes to the ethical principle of the respect of person, right? But it also has attention with the ethical principle of justice, which basically states that the fruits of research will be equally shared by concerned populations. What this means is that the Korean parents who offered to join the study in Idaho, all of their data is essentially thrown away. Also, from a scientific perspective it is possible to calculate prevalence estimates of children in California for Asians in the data set. But those prevalence estimates would only be calculated for five out of the 45 states. So even though there is information on Asian in the other states, all that information is wasted and we would end up with essentially biased estimates. In addition, I fully support protecting human subject protection, but that's not applied equally. It's important to remember that African Americans are also not equally distributed across all US states. In some states such as New Hampshire and Montana, Black populations are pretty rare there. For those two states, as an example, Blacks are 0.7% of the population. If you look at the data set there are three African American respondents in Montana that you can probably identify if you really wanted to. So again, there is some slippage in the goal of protecting human subjects. And these policies are not equally applied.

Slide Fourteen:
Misclassification is consequential. So for example we find that misclassification by race for White overestimates the mortality by 1%, 5% for blacks and a pretty sizeable 11% for Asian Americans, and their mortality would be underestimated.

Slide Fifteen:
I want to pull this back and bring this back to issues related to environmental health. About a year or two ago Devon sent me an article asking what my opinion was about a study that basically wants to use a correction factor to create some estimates for **human excretions**. What they wanted to do was to create a mathematical algorithm to establish some references. Now, of course those references would be later applied possible for policy relevance. And I thought it was very interesting that they wanted to use a correction, a racial correction factor of 1.18 to essentially correct for differences in lean body mass between blacks and whites. And I thought that was very curious so I looked at that value of 1.18 came from a prior study.

Slide Sixteen:
So I went to the prior study. Table two here is from that prior study and you can see, I underlined that value of 1.18. Essentially, it comes from a regression equation and you can see the variables that went into the regression equation on the left hand side of the screen. So you can see what went into it: age, sex, ethnicity etc. Now what caught my eye as I was looking at this table was the sample size. The sample had 197 Blacks and 1300 Whites. And it occurred to me that what that suggested was that the study was not designed to measure racial differences. Because if it were, then you would expect the black sample to be larger than it is. I looked through the publication; I didn't see much reference how the race was captured and all that kind of stuff. As you saw from the preceding slide it is very important to think about how race was measured.

Slide Seventeen:
So, then I went to the reference that was referenced in that particular article to a Beck study in 1991, where they described the sampling criteria. What you see before you is the part of their table on eligibility criteria. What is remarkable is what's not

there. Race is not there. If you look at their exclusion criteria, a lot of it makes sense. You're excluding people with say, kidney transplant or those on dialysis. There's an interesting bullet on doubtful compliance as exclusion criteria. But there's again no mention about race or ethnicity.

Slide Eighteen:
It's really important to think about what else is going on. It's important to consider when we're thinking about race and ethnicity, is it really a good measure or good proxy for lean muscle mass. Are there other things importantly related to race. For example we can see from the 2000 Census that there are clear economic differences between racial and ethnic groups. You can see for African Americans the per capita income was about $14,000 and was about $23,000 for whites. What is important to note is that the wealth gap for Blacks and Whites is far greater than the income gap; it's almost ten fold greater when talking about net worth.

Slide Nineteen:
Another important thing to consider is spatiality. We know as a fact that segregation exists. So what you see here is a slide that shows a map that shows where African Americans and Whites live in Detroit, Michigan. And, potentially a darker green means a higher percentage of that particular group. If Detroit was not segregated essentially both of those maps would look pale green. You can see here that roughly 90% of Blacks or 90% of Whites would have to exchange residences to integrate Detroit as a whole.

Slide Twenty:
Racial segregation didn't happen by accident, but rather represents a continuing history of racial discrimination. It is certainly important to point out that residential segregation happens for all racial and ethnic groups in the US and it's also a contemporary process. In an important study done by Housing and Urban Development in the year 2000, found that about one in five African Americans, one in five Asians, and one in five Latinos were systematically discriminated when they were out to buy a house.

Slide Twenty-One:
So at a minimum, if were to come back to that racial correction factor of 1.18, if you look at the variables on the left hand side of what constitutes that regression equation, it's striking that SES is missing as a possible covariate, it's striking that maybe discrimination is missing as a covariate. I think this is not a matter of politics, but a fundamental matter of good science. Also, it strikes me that if you think that race is a correction factor for lean muscle mass, then maybe it would be more accurate to measure that rather than a proxy.

Slide Twenty-Two:
I'm just going to through out a definition of race. It's essentially "a group of people who are socially defined as given society as belonging together because of physical markers", and I think some of the other presenters will pick up on this so I won't dwell on it at the present moment, but hopefully we can talk about his in the Q and A. Here's a definition of ethnicity that might be more related to culture rather than physical features.
Slide Twenty-Three:
Now I want to give you a few recommendations to come out in a very useful publication in JAMA. In terms of thinking about race in our research we always need to provide a reason for using it. We need to describe how individuals were assigned

racial and ethnic designations and I think it's fundamentally important that race and ethnicity should not be a proxy for genetic variation. If you're really interested in that, then we should be using genomic sequencing rather than using the social proxy.

Slide Twenty-Four:
It's also really important to be clear about how we think about race and ethnicity. Is it a risk marker or a risk factor? Basically what that means is are we assuming race means something fundamental and inherent, or does it mean that race is a proxy for other kind of social exposure. I think point number five is critically important. When we're interpreting racial and ethnic differences, we should evaluate all hypotheses including racism. For me what strikes me is that the common denominator for all racial and ethnic groups, if we look historically, is the legacy of racism in the United States. It only strikes me as a matter of good science to evaluate whether the hypotheses of whether racism makes people sick should be evaluated. And again we should also look at SES and other things we think are important.

Slide Twenty-Five:
So I want to come back to a picture that I had on my opening slide of these two girls. Take a look at these twins, Kian and Remee Horder. The family exemplifies the complexity of our proceeding discussion. Will these two girls have the same life, opportunities, and outcomes? What is really important about them? Is it the race of the mother? Their self reported race? Or the race of how they are perceived? At the end of the day, the differences, if there are any, really come down to an empirical question. But the point here is to really consider all of these possibilities and to be clear about what we mean when we record for or provide one's race.

Question from Audience Member:
How do you quantify discrimination and the legacy of racism in a way as to include them in a mathematical equation?
Response from Speaker:
There are some ways to look at measures of discrimination. So, for example the index of dissimilarity is a number that can quantify racial segregation. There are some data sets such as the Home Mortgage Disclosure Act that capture, for example, bank loans and it's mandated that the banks or lending institutions report the racial characteristics of the applicants. So you can use that information to actually calculate disparities in terms of how people are treated in terms of bank loans and outcomes. There are also measures of self reported discrimination, there are measures of psychologists something called implicit attitudes and there's been some adaptation of those measures for research on discrimination. There's the fair testing method. Essentially what that does is you take two people who are identical in all characteristics except for their race, or gender, or other characteristic. You send them out into a housing market and you record the objective characteristics of what happened to them after they come back. So, what neighborhoods were they shown? Were they quoted in terms of pricing of the house and all those types of things? That's the method Housing and Urban Development and even Department of Justice have used for several decades. And there's several other ways to go about this, but I'll just stop there because that probably provides you with a nice highlight.

III.) **Dr. Charmaine D.M. Royal. "'Race' and Human Genetic Variation"**

Devon: I'd like to introduce Dr. Charmaine Royal.

Slide One: Race and human genetic variation. Now, I'm framing my talk in terms of starting out with talking about what genetics has taught us about race, and then I'm going to give some examples of traits and diseases that have been linked to race and genetics, and then the last part of the talk I'm going to talk a bit about where I think we need to go with all this information in terms of us thinking about health and the environment and how they all come together.

Slide Two: Now, the human genome project, which started in 1990 and ended in 2003, brought us a wealth of information, and this next slide just shows the two major publications of the Human Genome Project. Following the Human Genome Project there has been so much data on the genome and on genes that we've had and our knowledge of the genome has far exceeded what we imagined we would have and the information is so overwhelming and massive at this point that even thinking about how we use this information, how we analyze this information and how we understand this information and how we communicate this information has become a big part of human genetics and human genomics.

Slide Three: Out of the Human Genome Project we saw, and some of this information actually came prior to the Human Genome Project, but I think Human Genome Project has sort of confirmed some what we know or knew about the human population and genetics, and this concept of race. This slide shows a global map of movement of people from Africa. So, based on fossil evidence and genetic evidence we now know that humans originated in Africa and moved out of Africa 130,000 years ago. They moved from Africa and populated the rest of the world. This slide just shows movement of human population. Because of this common origin that we have in Africa, based on what our science shows us, the genetic variation that we see in populations is certainly not as vast as we have come to think about them in terms of these notions of race.

Slide Four: This next slide is a slide by Sara Tishkoff and colleagues, and it shows variation in the CD4 haplotype, and CD4 involvement in immune response. And this slide really shows what we've see across a range conditions and haplotype in terms of variation. Here we see Africa, Europe and Asia, three of the major continents. The numbers just indicate variation in these continents. And we see Africa has the largest amount of variation in terms of 199 there. Europe next and then Asia has a smaller amount. The take home message from this slide really is the fact that most of the variation, as we look at how these circles overlap, most of the variation that we see in Europe, and in Asia, are also found in Africa. In fact there are geneticists that say this communicates a message, that this is more than just overlapping circles, or an overlapping Venn Diagram depiction of variation. The actual pattern of genetic variation when we look at Africa as a continent is really a nested pattern of variation. That really big circle that represents Africa fits the circle for Europe and the circle for Africa within that. So the variation that we see in other continents for the most are also present within Africa. So Africa has the largest amount of variation. We see that over and over again in studies that have been done.

Slide Five: So this whole concept of genetics variation, going back to the previous slide in terms of looking at how variation overlaps and is continuous across the continents really nullifies this whole notion of these discrete groups that we call

races. This slide talks about, really just gives three of the markers that justify, if I may use that word, the fact that humans don't divide into what we call races, biologically. Race is a biological term and there are some species of races, gray wolves have races, some type of deer, and buffalo have races. But humans don't have races, and these are some of the key factors that help us to understand why humans do not fit this criterion. There is this issue of geographic location, and the first bullet there says that biological variation of human species exhibits gradients of differentiation across geography, not subdivisions into these homogenous, discontinuous units, which is what I talked about in the earlier slide. That the variation is overlapping, it's continuous, you really can't' slice these continents the way we tend to think about that. The frequency of genes and variation is greater within these groups that we call "races". So, the amount of variation in any of these groups that we call "races" is greater than the variation between these groups. And that's what we've seen in our genetic studies, and in fact, that has been demonstrated consistently. So most of the variation within the human species is found between individuals and not these groups. The way we tend to think about genetics, and the way much of the studies that have been done in science tend to communicate this is that we tend to have this thinking that these genetic variants and polymorphisms in genes are found only in this population and not in another, that these populations have their own genes that are different from the genes in the other population. What we've come to realize is that the differences that we see in these genes and populations that we tend to extrapolate to race, these differences are greater within any of these groups than between them. The last point there is more broad, morphology, phenotype, how we look. And we have seen and known that combinations of physical traits, eye color, hair texture, skin color that we tend to use to define these groups are not linked to each other. So, someone with blue eyes doesn't necessarily have straight blond hair, or vice versa, or a straight nose. We see combination of these so they're not necessarily linked to each other whether by genes or anything else. Neither are they linked to health, disease or other traits, obligatorily linked. They can be linked, but we don't see them in terms of consistent pattern to be able to define groups as race. So there's a lot of evidence there that indicates that human groups do not meet the criteria that have been set for race.

Slide Six: As I've said race is really a biological term, it really originated in biology. We've made it social, and I will talk about that later. He's a quote from Stephen O'Brien, who's an oncologist, a cancer researcher really. He talks about race in terms of the "existence of one or more fixed genetic characters or genotypes that are present in all members of one subspecies, but not in any other". This quote came in 1996 when he talked about it. So basically what he's saying is if we're going to call someone a race, that entity has to be one in which the genetic characteristics, the genotype of that entity is present in all of that group and not in any of the other. We don't see that in humans. We see overlapping patterns of variation, where we see genes between this population and another population. But what we do tend to see in human populations, is that we tend to see variations in the frequency of these genes. So a gene, some variance, may more common in one population than another, but rarely do we see a gene present in one but completely absent in another, which is really what the notion of race is, what the biological definition of race is. So the previous quote by Stephen Bryan was 1996, this quote came from Darwin in 1871.

Slide Seven: And, it's pretty much saying the same thing. So as I said earlier the information we're getting from genomics is not new, the information to have been there, but certainly genomics has brought a new dimension to it in terms of helping

us to understand it more, we have new technologies to help us to study the genome in depth. But, Darwin talked about this when he said “it may be doubted whether any character (… whether physical, biological or anything else) that can be named which is distinctive of a race and is constant”. Which really again, just reinforces this truth that humans don’t subdivide into what we call “races”.

Slide Eight: So what does this all mean? So, in 2001 and this is just around the time that the first draft of the reference to the Human Genome was published. Here’s a quote from Robert Schwartz in 2001 in the New England Journal, so this was right after the information came out that humans don’t subdivide into races, that genetics has showed us that race is not real, because the science said so and science doesn’t validate this notion of human races. So, there was all this talk about race being social, and this quote by Robert Schwartz “race is a social construct, not a scientific classification…..Race is biologically meaningless”. A lot of people have raised these kinds of statements that race doesn’t mean anything biologically. But that begs a question whether that is really true. We say it a lot, but does race really not mean anything biologically, is race really not meaningless. There are lots of questions about what this concept of race has done to us biologically in terms of our health outcome.

Slide Nine: For the next few slides I’m going to talk a bit about, we’ve talked about race and what genetics has shown us in terms of humans not subdividing into these biologically entities, and that the notion that race is social versus biological, but we don’t use it on a biological basis. But, I think we all agree that race does have biological implications. We will talk about that a little bit later. But for these next few slides I’m going to show examples about how race and genetics come together in terms of health and traits. I’m going to talk about one trait, and that’s skin color. So here we have a map, a human pigmentation map that shows the range of skin color in humans. This is a map that was developed in 1940 or so, before 1940 actually. It’s data from native populations because we know that if we look if we just looked at populations today we’d see skin color all over the map. So these are native populations, because we know that if we look at populations today we’ll see these skin colors all over the map. So these are native populations in terms of people who were indigenous to these regions. What we tend to see, which many people already know, is that when you go below the equator pigmentation, or close to the equator, skin pigmentation tends to be a little darker. And above the equator it tends to be lighter. And just looking at this slide it’s obvious that the environment is what’s playing a major role here in terms of exposure to sunlight versus not. So we see darker pigmentation towards the equator and lighter on top.

Slide Ten: Now, so that slide really represents the environment piece in terms of skin color and the relationship to the equator and skin color, and where we are in location. This next slide, and I apologize for this, because I changed the slides and there’s not text there under dark skin and light skin. But this slide really shows… so what I have under the captions for light and dark skin are the genes that have been found to be associated with light and dark skin. There are several genes that have been found to be associated with, or that influenced skin color. Meaning there are some that have been shown to influence dark skin color and some that have been shown to influence light skin color. Now, on the left you see a cover of a journal, it’s a Science issue that was published in 2005. It’s about a polymorphism that was found to be associated with lighter skin color. It’s SLC2445, that’s the name of the gene. I remember just before the paper came out and people knew it was coming out, so this study showed this variance that is found in zebra fish, hence the fish on

the cover. It was also found in humans, and so the original, the ancestral gene, is linked to darker pigmentation, linked to populations in Africa and populations in some parts of Asia. Variance in this gene produce light pigmentation. So, the study showed variants in this gene lightened the color of the zebra fish and we also see that variance in this gene, polymorphism of this gene, is associated more with European populations. So when this paper was coming out I know there was a lot of buzz about what the implications of this are, and how people would interpret this information. My only message for showing this is really to only communicate that genes are associated with just about any biological trait you can find: skin color, eye color, hair texture. There are genes that are associated with that, but the genes are not the whole story. The genes are part of the picture but there are other aspects of the environment, and later we'll talk about health and behavior that need to be taken into consideration. So we can't throw the baby out with the bath water we can't say skin color is all environment and we can't say it's all genes, it's a combination. What we don't understand fully is how these interact, how genes and the environment interact.

Slide Eleven: Here we have a slide referring to sickle cell disease. I've talked about traits, and I'm going to talk now about monogenic diseases, which are diseases we tend to think of as being genetic, where/or single gene disorders where we know that the disease is caused by a single gene. Sickle Cell disease is an example I tend to use a lot. So we see a slide here that talk s about, here it has "incurable Negro disease strikes five in the family". Sickle cell disease we know, at least in the US is more common in African Americans. But we also find Sickle Cell Disease in other populations. It's found in Africa, in certain parts of Africa, west and central primarily, but it is also found in other countries like Greece and turkey. What we know about Sickle Cell Disease is the Sickle Cell gene that originated in areas where malaria was present, and seemed to have come about as a means of providing partial immunity to malaria. So the link that is often made to African Americans or black people in general to Sickle Cell Disease, yes it is more common in the US with African Americans, but it doesn't only affect African Americans. This piece here was done in 1966, when the information about the connection with malaria was just coming out and there still was not a whole lot of information coming out about Sickle Cell Disease and who get's it.

Slide Twelve: This next quote from a JAMA publication in 1947 really supports this whole thinking that Sickle Cell Disease just affects one group. "The most significant feather of sickle cell anemia is the fact that it is apparently the only known disease that is completely confined to a single race." So this thinking that the disease affects just this group, and when we see frequency of genes more common in one group, the general thinking is that it is only in this group, but we know that not to be true for just about all diseases.

Slide Thirteen: So these next diseases I'm going to talk about are the complex diseases, the complex common diseases which are the ones people tend to think about most when we talk about health disparities. We look at these diseases very much in terms of, at least in the US, of race and ethnicity, or the groups that we defined as races. This slide just shows a list of diseases and the common causes and the group that these conditions have been shown to be the most common in. Then, here we are going to talk about one example, hypertension, which is a common example. Here's a study that was done by Richard Cooper, and here what he tried to do was to look at international populations globally. In the US we talk about

hypertension and there's this thinking that, well not necessarily thinking because I think statistics also show that hypertension is more common in African Americans than in others. The fact that it is more common there tends to be a lot of focus on the disparity or the difference between African populations or populations of African origin as opposed to other populations, particularly Whites. The thinking, when we see these differences is that there is something genetic about this population that they are more susceptible to this particular disease. So, the quote here talks about the data that we've seen and how this has supported this lead to this strong hypothesis that there is a genetic predisposition to hypertension among blacks.

Slide Fourteen: This study here actually shows that when we look at populations globally we cannot say that African Americans are more predisposed than other groups globally. When we look globally we see here in this particular slide it shows that in Germany folks have an even higher rate of hypertension than US blacks. So when you look globally you realize there are other things going on that cause hypertension to be high. Now when we look at Nigeria, Jamaica, the first two blue bars and the US blacks, the next blue bar, we do see an increase in hypertension in those populations that we talk about as having the same ancestry, or similar ancestry, or more similar ancestry than other populations. So we do see an increase there, the question about that increase are questions that are raised based on questions related to why we see these increases as we move from Africa through the Caribbean to the US. Those questions have raised issues about the environment and how we have to think about the role of the environment. Another condition, another case that I am going to use in terms of thinking about race and health, not even so much genetics in this case, is the story of BiDil.

Slide Fifteen: Vital is a drug that was approved by the FDA and this is a quote from the FDA in 2005, just after the approval of the drug. "The FDA approved BiDil (bye-DILL), a drug for the treatment for heart failure in self-identified black patients, representing a step towards the promise of personalized medicine". So they approve this drug to treat heart failure in African Americans and it's the first that has been approved for a specific ethnic group. Here I just outlined a brief history of vital. It's a really truncated history. It's a combination of two generic drugs that has been found through some studies in the past that showed that African Americans, or seemed to indicate, that African Americans would benefit more from this drug. So researchers maintained patents for this drug. In 2002 they obtained the first patent NitroMed, which was the company that produced the drug, the first patent that indicated its use for blacks. So the patent they got in '89 was just a patent to treat heart failure. But in 2002 they got a patent specifically for blacks and then that patent was renewed in 2004. In 2005, it was approved. The approval of this drug circulated a lot of questions, hoopla, and concern about where were going in terms of using group membership to determine how health outcomes response to treatment.

Slide Sixteen: This statement for me really sums it up in terms of how the authors of this paper, and how researchers of this drug thought about this. They said: "our trial represents a departure from the recent approach to the design of cardiovascular traits. Rather than studying a large heterogeneous population, we examined a specific population in whom efficacy was more likely to be established. A heterogeneous population may have substantial variations in genetic and environmental factors that influence disease progression and the response to therapy." Which in essence what they're saying is this group is a homogenous group, so they don't have those differences to worry about. This kind of thinking is not unique to Taylor and colleagues, it's just how medicine operates, which is what

concerns many in the bioethics and genetics community in how we think about those things.

Slide Seventeen: Now moving more toward situations and examples that might be more relevant to the EPA in terms of thinking about health and exposures and the environment. This is a study that was done to look at **facultated** melanin that is melanin in skin color which is determined by genes as well as the environment, and tobacco use. There have been some studies that show that nicotine and carcinogenic substances accumulate in animal tissues containing melanin. So the more melanin the more that nicotine and carcinogens tend to accumulate in those cells. That's been shown in animal studies. So some researchers have hypothesized that the same probably happens in humans, so let's look and see if it does. What they found in a study of 147, which is not a huge sample, but they found that higher melanin levels, so people with darkest skin color essentially, used more tobacco, were more dependent on tobacco and they had higher nicotine exposure. The question about this is if we're saying that darker skin people, or African Americans, are more likely to be addicted to tobacco and to be exposed to it. In this study they actually looked at what other factors there might be, and they actually looked at stress and discrimination which have been shown to be associated with increased tobacco use, and they didn't find any relationships there. This study really even makes us think more about what factors there may result in these kinds of habits and behaviors and exposures. Diet is also something that has been shown in the literature to be associated with tobacco use, and they didn't look at that in this study. I mean you can't look at everything gin every study, but the take home message in terms of needing to expand our thinking in terms of the factors that might be associated with a particular outcome.

Slide Eighteen: I'm going to talk just a minute or two about PON 1. And this is an enzyme paraoxonase 1 that has been in the news a lot. This is an enzyme that helps to detoxify the body of organophosphates, and organophosphates are typically found in herbicides and pesticides. So what the PON 1 polymorphism 1 gene helps to detoxify, but if you have a problem with your PON1, a problem with a polymorphism, you may not be able to detoxify and to rid your body of these insecticides, so you are more susceptible to poisoning from these insecticides. So there has been a lot of concern in the environmental justice community about what we need to do about these pesticides, but also about this link with the polymorphism. So here you see a list papers, of just a few of the papers that have been published on this, and as you can see most of them are in what we tend to call minority populations: Latinos, Mexicans and Southerners. And on all these paper, some of them show links to PON1 with these populations, and some of them don't show any connection, or any associations between the variants and outcomes. PON1 has also, in addition to being associated to these toxins; it's also been shown to be associated with cardiovascular disease. And so the question is about what did the variance actually mean, and when we've seen this in populations being more exposed to some these toxins, are they at greater risk. There was a study done by Gale Scharvic in 2002 that showed that increased activity of this enzyme is associated with intake of vitamin C and E. So, the links that have been made to the genetics about people that have a particular predisposition based on their PON1 status, it may not be an inherit genetic defect that they have, it may be their intake of vitamin E that which is reducing their intake of paraoxonase. So there are a lot of issues we need look at and think about when we think about when we start making links to genes and outcomes. It's not usually that straightforward and simple except for diseases I've talked about like Sickle Cell Disease, the monogenic, single gene disorders that where we know in order to have

the disease you have to have that genetic mutation. In these more complex conditions, and outcomes the genes are never the full story in terms of what causes it, or rarely I should say, there are other factors we need to look at.

Slide Nineteen: And so, winding down, moving from those examples of traits, and diseases, different types of diseases that have genetic links, but also raise questions about what else might be going on. There has been a lot of thinking about gene-environment interaction and a lot of talk. Here is a paper by genes from the CDC, about genome environment wide association studies that have been done looking at the genome, and looking at association between particular genes and variants and diseases. What he's proposing here is that we need add environment to that and start looking at the genome and the environment.

Slide Twenty: This is a list of variables put forth by Norm Anderson in 1999, in terms of the levels of analysis we need to look at. So when we talk about genetics we're talking about number 7, mainly, because genetics affect most of these others anyways. But we're looking at the basic molecular level. What Norman is saying here is that there are all these other levels we need to be thinking about when doing health research. We can't just be focusing on the genes and my position is that we can't just focus on the environment either. We need to see how they interact, and we social beings we're not just genes, or not just behavior, or not just environment.

Slide Twenty-one: This is a report, or just a cover of the report by the Institute of Medicine "Genes, Behavior and the Social Environment". Pretty much saying the same thing and looking at how all these things come together.

Slide Twenty-two: And when we talk about environment, we use the term environment very loosely. There are so many factors that come into play when we think about non-genetic factors. And we're talking about all of these here SES, psychological discrimination factors and questions about how we measure some of these is the big question in social science research. The answer is we do need to look at them the question is how do we better look at them

Slide Twenty-three: The next few slides are just some models that have been proposed by some. This is one that has been proposed by David William about how we think about health status, which you see he has on the end there, and the basic causes in biology. And moving through the social status and biological process you can see that the biology is there, the different status is there, cardiovascular, immune status is there, but also health, stress, medical care, access to care, culture, all these factors we need to bring to bear on how we think about this.

Slide Twenty-four: This is a similar construct by Cameron Jones in terms of looking at racial discrimination and health and all these factors that come together.

Slide Twenty-five: This is one that I worked on with Sharon Kardia at the University of Michigan with others. Again, genes are there, cells organs are there, but we also have smoking, we also have the different systems, so we have the genetic factors, we have access to information, food, advertising, diet, stress, all of these factors that need to be thought about.

Slide Twenty-six: This is one model that I worked on with colleagues at Howard that did the same thing again. So there's a lot of thinking about the complexity. We know it's complex and sometimes we avoid the complexity because we know it's so

complex. But we need to be bold and tackle the complexity, because in my view it's the only way we'll be able to define the environment.

Slide Twenty-seven: The environment broadly defined as the physical environment, our exposures as well as our social and behavioral environment, and how they influence health. This is a quote, or part of a quote by Bronfenbrenner, "…the principal main effects (of all these factors, the factors we're thinking about) are likely to be interactions". There are people who talk about genetic main effects, and environment main effects, and what he's saying here is that it's not very often we find either genes or the environment being the main effect. The principle main effects are probably in the interactions among those.

Slide Twenty-eight: And doing this kind of ecological research, trying to bring the genetics, which are biological aspects and biological effects together with the social effects, requires an ecological approach. It's not simple; it's not easy to do. There are sample size considerations, there are issues with costs, we need to bring big research teams together to start to tackle these things. The environment and genes, many people tend to think of genes and genetics is hard and complex, but there are many in genetics who feel that measuring the environment is harder than identifying genes. Which is probably why we're not doing enough of the environmental research that needs to be done, because it is challenging. How do we measure, how do we even determine what those variables need to be.

Slide Twenty-nine: Then how do we move these findings, when we start using these complex models to determine disease causality how do we translate that to improved health? When we find that it was actually some exposure in the environment that is interacting with a genetic predisposition, how do we get our society to change that environment? And that is the work; I know that is the work of the EPA, but a lot of it has to be done in collaboration with the geneticists and the others who are looking at these other personal biological factors that also influence health. And the beauty for me is how we try to bring it all together.

Slide Thirty: Again, thinking about looking at genes and the environment. Francis Collins who is at NIH, wrote this in 2004 for a case to look at genes and the environment, recognizing and acknowledging in this paper that the Human Genome Project has given us a lot of information, but we can't do it all just by looking at the genome, we need to study the environment as well.

Slide Thirty-one: And this is a phrase that Francis Collins and other had in a book they published in 1998, a textbook I used. And it really still captures the way he thinks about this in terms of "Paradoxically, one of the most important benefits of identifying genetic factors in disease susceptibility may not be the potential for gene therapy (as exciting a prospect as that may be), but rather the ability to treat or prevent clinical disease by manipulating the environment of individuals (not the genes, we can do that too, but our biggest bang for our buck might be in manipulating the environment, as I think EPA understands very well and that is the case they continue to make) identified to be at risk."

Slide Thirty-two: Here I'll make a close with this slide, which very much represents my whole thinking about where we need to move. Now this slide, is one that shows, you know, the second picture there shows where genetics, where we've come, in terms of science and medicine that the genome has changed the way we practice medicine in the ways we initially did or on the left, now we're able to manipulate the

genes and the genome. My message is that we need more than just the genome. We're not just a chromosome, we're whole people. For whom the chromosomes interact with other factors that are part of our lives, and we need to have a more holistic approach. Genomics is fantastic and wonderful and has brought us a lot of knowledge about biology, but it is not the full pictures, it is not going to give us optimal health. We need to look at these other factors and the sooner we can begin o do that in a really rigorous way, the better I think it will be in terms of us moving a health agenda for our nation. Thanks.

III.) Clarence C. Gravlee, **"How Race Becomes Biology; genes, environment, and health"**

Devon: And next we will have Dr. Clarance Gravlee who is Assistant Professor with the Department of Anthropology at the University of Florida.

Slide One: Good afternoon, and thank you Dr. Payne-Sturges for asking me to participate in this panel. I'd also like to thank my colleagues, Dr. Gee and Dr. Royal for your stimulating remarks, and for those of you in the audience for tuning into this discussion. We were asked to discuss two central questions today. First, what does it really mean when racial differences in health are observed? And second, how can the answer inform environmental health policy? Before we can answer either question though, we have to begin with a more basic one. Does race exist?

Slide Two: As this recent cover of Scientific American suggests debate over whether race exists and specifically over the magnitude and significance of genetic differences between racially defined groups, has once again captured the attention of scientific and popular media outlets. In my presentation however, I would like to point out that much of the debate falters on Scientific American's framing of the question, because it can be interpreted in different ways. The implicit question on the cover and the focus of our new debate is whether race exists as a natural biological division of human kind. But we should also ask: in what ways does race exist as a social and cultural phenomenon that how force in people's lives? Indeed, one that has biological consequences.

Slide Three: These questions are often propelled in part by the face pace of discoveries in human genetics. Often with a focus on implications for medicine and public health, as in the article you see here from the New York Times. The debate also responds to a simple, epidemiological reality. That for nearly every major cause for sickness and death, there is evidence of racial differences in health across the life course. From birth weight, to blood pressure, to body mass, body composition, heart disease, diabetes, stroke, prostate cancer, breast cancer, colon cancer, kidney disease, Alzheimer's disease, HIV/AIDS and more.

Slide Four: These differences are often reported not just in academic journals, but also in mainstream news outlets. And here's where we return to the question of what it really means to observe racial differences in health. Scientific reports, and media portrayals, like this one, serve to enforce the conventional wisdom that race reflects genetic differences and that racial inequalities in health are ultimately genetic in origin. But this view deserves closer scrutiny. In particular, we need to consider more carefully what we mean by the concept of race.

Slide Five: And how well the data we collect measures what we think we're measuring. One basic problem here is that researchers often use the term race to mean different things.

Slide Six: And the failure to specify what we mean is a major barrier to explaining and eliminating racial inequalities in health. In particular, when some researchers talk about race, they mean genetic ancestry. Social scientists on the other hand understand race as a form of social classification based on the culturally defined meaning of race as an aspect of social status. One of our challenges is that geneticists have developed rigorous though imperfect methods for estimating individual genetic ancestry. Technically, obviating the need to use race as a proxy for what can now be measured more directly (genetic ancestry). There's not the same degree of consensus among social scientists about how to measure race as a form of social classification. And that's' one of the key challenges I want to talk about today. I'd like to take up the argument in the context of what some have referred to as the "puzzle of hypertension in African-Americans".

Slide Six: The first piece of the puzzle is that people in the African Diaspora tend to have higher average blood pressures and higher rates of hypertension than do others in the same societies. This pattern is best documented in the United States. The most recent data from the National Health and Nutrition Examination Survey, or NHANES, show that hypertension is almost 50% more common among Black Americans than it is among Whites, affecting four out of every ten African Americans. This pattern is significant, first of all for its devastating impact as cause of heart disease, kidney failure and stroke.

Slide Seven: High blood pressure is to blame for at least 15% of the premature mortality experienced by African Americans. That's more than from any other cause of death including: diabetes, cancer, HIV/AIDS or homicide. But the puzzle is also significant for what it reveals of the meaning of race in biomedical research. Because many researchers assume that some intrinsic racial difference is at the root of the problem.

Slide Eight: This assumption is reflected in the language of many of the reports in the biomedical literature. So take for example Langford's 1981 paper in the Postgraduate medical Journal: Is Blood Pressure Different in Black People? Or, Seedat's paper in the Journal of Human Hypertension: Is the pathogenesis of hypertension different in black patients? Or, Brewster and colleagues' paper in the Journal of Hypertension, which implies that the only open question is which genetic factor is responsible for hypertension in people of African dissent, not whether it is a genetic factor. These ideas persist despite the fact there remains no genetic evidence that people of African ancestry are uniquely predisposed to develop high blood pressures.

Slide Nine: So this dispute over the relative importance over genetic and environmental factors converges on the relationship between skin color and blood pressure, which is one focus of my own work. Within populations of African ancestry, people with darker skin tend to have higher average blood pressures than do their lighter skinned counterparts. This pattern has been observed in the US, Brazil, Bolivia, Cuba, Puerto Rico, and Egypt, although the magnitude of the relationship varies cross culturally. Some studies report that the relationship between skin color and blood pressure disappears after controlling for known risk factors such as: social class, diet and obesity. But other studies reveal a persistent association independent

of these risk factors. There've been two broad hypotheses to explain that residual relationship between skin color and blood pressure.

Slide Ten: The first is that skin color, as a marker of African genetic admixture, is linked to a genetic predisposition to hypertension in African derived populations. The second is that dark skin color, as a marker of social status in color conscious societies increases exposure to racism and other social stressors related to blood pressure. For the time being we can set aside questions about whether skin color is a valid marker of genetic differences related to blood pressure. Instead, I want to emphasize that these two hypotheses aren't talking about the same thing when they talk about skin color.

Slide Eleven: The conflation of biology and culture plagues most of the debate over racial inequalities in health. In particular, the hypothesis that skin color is linked to a genetic predisposition to high blood pressure refers to the phenotype of skin pigmentation. This variable can be measured in a relatively straightforward way using reflectant spectrophotometry, an objective method for measuring pigmentation in one's skin. By contrast the hypothesis that skin color is a marker of social status in exposure to racism refers to the cultural significance of skin color as a criterion of social classification. And, we can further distinguish between two dimensions of social classification: what you think you are and what others think you are. Measuring either one of these variables requires an understanding of what skin color means in any given cultural context.

Slide Twelve: I tend to measures these isolated variables based on research in southeastern Puerto Rico. The choice of Puerto Rico was important because the research of other social scientists had suggested that the perception of color was shaped not only by skin color and other physical features, but also by markers of social status like: wealth, residential area and family background. This fact means that for a give phenotype of skin pigmentation there should be variability in social classification, how people are defined, making it possible to differentiate between the social and biological dimensions of skin color.

Slide Thirteen: The take home message from this work is that in my Puerto Rican sample, blood pressure is associated both with how people perceive themselves and with how they are defined according to the local cultural model of color. By contrast there is no evidence that darker skin pigmentation is associated with higher blood pressure (in my sample).

Slide Fourteen: To get to this punch line I integrated a range of qualitative and quantitative ethnographic methods with epidemiologic techniques. On the slide here you see one relevant finding from the ethnographic phase. This figure is based on systematic ethnographic interviews with a diverse sample using a set of standardized facial portraits that vary in terms of skin tone, hair texture, and facial features. Among other things, I asked people to sort these faces into piles that they thought belonged together. And the graph you see here shows multi-dimensional scaling of the results. We can read this graph as you would a map. The closer any two faces appear to one another the more similar they were perceived to be in the aggregate. What's striking about this map is first of all, that there are five major categories of color, or color, that correspond to the way that people talk in everyday life. The second is that the distinction among these categories is a function not only of skin color but also of hair form. So you see there're two dimensions on this graph. One from top to bottom and varied in terms of skin tone and the other is hair form

ranging from straight or wavy on the left to kinky hair on the right. And you can see that for a given level of skin pigmentation, for dark skinned individuals for example, placement into one of these locally meaningful categories, of color varies based on other attributes such as hair tone. This is important because it confirms that expectation that in a given level of skin pigmentation there would be variability of how people are perceived and defined and treated by others.

Slide Fifteen: I then used the results from that phase of the work to understand whether skin pigmentation, or whether the social definition of color better helped us understand blood pressure variation. And here's one result from that phase of the work. You can see here that blood pressure is a function of the interaction between culturally defined color and socioeconomic status. So that in particular for Puerto Ricans who were defined by others as Blanco or Trigueño, White, or this intermediate category, blood pressure decreases along with higher socioeconomic status. But, for Puerto Ricans defined by others as Negro, or Black, blood pressure increases along with higher socioeconomic status increase. This may be puzzling at first, but in fact it's consistent with what we know about social scientific research in Puerto Rico about the experience of racism, in particular that racism becomes a more meaningful part of one's everyday experience as we move into social context of higher socioeconomic status.

Slide Sixteen: This idea was captured in one of the interviews I conducted when a woman explained to me about racism that "you don't see it much among the poor. But among those who are better off economically, you see a lot of racism (she said) because they often reject people beneath them". So unbalanced in the evidence is more consistent with the hypothesis that the relationship between skin color and blood pressure is mediated through social and cultural process associated with the meaning of skin color and the experience of racism. But if we go back to the beginning of the skin color blood pressure studies, you'll recall that the original hypothesis treated skin color as a proxy for genetic admixture.

Slide Seventeen: As Edwin Boyle wrote in the Journal of American Medical Association in 1970, "… in an attempt at greater precision in the genetic identification of Charleston Negroes, a photoelectric reflectance colorimeter was used to measure skin color". More recently, as the technology available to geneticists has advanced other researchers have followed up on this hypothesis by producing genetic based estimates of African ancestry directly.

Slide Eighteen: And so here's one recent example of a paper where researchers estimated individual genetic ancestry, individual African ancestry. And measured whether individual African ancestry was predictive of body mass index (BMI), or blood pressure in African Americans and Mexican Americans.

Slide Nineteen: And they argue in this paper that their results "are suggestive of genetic differences between Africans and non-Africans that influence blood pressure, but that such effects are likely to be modest compared to environmental ones". There are a couple of remarkable things about this conclusion. The first is that the paper itself does not report a statistically association between individual African ancestry and blood pressure. But beyond that there's a problem of interpretation.

Slide Twenty: Because the authors are suggesting that the relationship between genetic ancestry and blood pressure would be indicative of genetic differences in blood pressure regulation. So their hypothesis then is that genetic ancestry is linked

to susceptibility alleles related to blood pressure regulation, which in turn is related to differences in blood pressure. But an alternative hypothesis, which they cannot rule out, is that the relationship between genetic ancestry and blood pressure is mediated through experience. That is that people of African ancestry in color conscious societies like the United States, or Puerto Rico, or Brazil have different sets of experiences based on the meaning of African ancestry in a color conscious society. Those experiences and environmental exposures would explain differences in blood pressure. Here's where we get back to a point I began with earlier.

Slide Twenty-One: That is to test competing explanations for racial inequalities in health, we need to distinguish conceptually and in our measurement strategies between genetic ancestry and social classification, so that we're able to isolate the relative importance of genetic and environmental factors. So to follow up on this idea in the Puerco Rican study, I've collaborated with my colleague here at the University of Florida, Connie Mulligan, who is a geneticist in the department of Anthropology in the US Genetics Institute. And one of our first steps was to use the methods geneticists have developed for estimating individual genetic ancestry.

Slide Twenty-Two: Work in this area is focused on the use of so-called ancestry informative markers, or AIMs. These are genetic markers, or variants, that show substantial frequency differences across punitive ancestral populations, usually defined as: African, European, Asian, and sometimes Native Americans. My colleague, Connie Mulligan, also suggested that we move beyond AIMs to examine a set of candidate genes for hypertension and to test whether adding cultural data about socioeconomic status and culturally defined color alters our understanding of the risk associated with candidate genes.

Slide Twenty-Three: So we looked at six polymorphisms in three genes of the adrenergic receptor family that were ascertained by our colleagues in the Center for Genomics here at the University of Florida.

Slide Twenty-Four: And as we saw with the work in skin color, the bottom line here is that in our Puerto Rican sample, blood pressure again is associated with how people perceive themselves and with how they are defined by others. But there is no evidence of an association between genetic ancestry and blood pressure, once we take account of these social and cultural variables.

Slide Twenty-Five: So one of the first findings from this work looks at the association between individual genetic ancestry and how people are defined by others in terms of color. And this graph shows, as you would expect, as we move from Blanco (White), to Trigueño (this intermediate category), to Negro (Black), you see an increase in the percentage of individual African ancestry. But what is most striking for our purposes is the range of overlap across these categories. That indeed at some points of African ancestry, for a given level of African ancestry, an individual may fall into any one of these three social categories. That makes it possible for us then to ask the question whether it is genetic ancestry or how people are defined by society that better predicts blood pressure.

Slide Twenty-six: And what we find is that how people are defined by society, in terms of color, and socioeconomic status predicts high blood pressure, not genetic ancestry. Now, if we replicate the analysis that are common in human genetics and genetic epidemiology, and we look only at the association between African genetic ancestry and blood pressure, controlling for a subset of covariates, then it appears

that African genetic ancestry is associated with high blood pressure. But that pattern holds if and only if we ignore the social and cultural variables. Once we include a measure of how people are defined by society and a measure or socioeconomic status we can see that those variables explain variation in blood pressure. And that the relationship between ancestry and blood pressure disappears.

Slide Twenty-Seven: We also find that once we include the social and cultural variables we now have evidence for an association between one particular candidate gene polymorphism and blood pressure. This association was hidden when we only looked at the association between candidate genes and blood pressure controlling for African ancestry and other covariates. Once we include some measures of environmental exposures as proxied by social classification and socioeconomic status, we improve the ability to detect candidate gene association. This point is important because it gets us beyond the stale debates between nature or nurture and suggests that if we measure both the genetic and the environmental components of complex phenotypes that we may be in a better position to detect meaningful associations.

Slide Twenty-Eight: So let me conclude with just a couple of thoughts about what this particular case study means for our discussion today. The first implication of this work is that it reinforces a point you heard the other speakers make as well, which is that genetic inferences require genetic data and tests of competing hypotheses. One of the fundamental problems in much research in racial inequalities in health is that race is often used as a proxy for some unknown combination of genetic, behavioral and environmental factors. And this makes it impossible for us to understand exactly what we're measuring, exactly what drives racial inequalities in health. So the argument here is not that we should always avoid genetic inferences but that if there is a genetic hypothesis, it requires genetic data and tests of genetic hypotheses ought to be put head to head with tests of environmental ones.

Slide Twenty-Nine: A second and related implication is that researchers must consider the biological effects of institutional and interpersonal racism in a way that these experiences can shape human biology. This follows from the observation that in the Puerto Rican study, that genetic ancestry is not associated with blood pressure but socioeconomic status and how people are defined by society is predictive of blood pressure. There's a growing body of research in public health equality across the social sciences that is identifying specific ways that the experience of institutional and interpersonal racism changes the way our biology works and may help to explain in large part racial inequalities in health. With that I'll conclude and hope that we can follow-up in some of the question and answer afterwards. Thank you.

Question: Clarance?
Response: Yea?
Questioner: Hi, I had one question. In your research in Puerto Rico did you see any differences in that phenomenon between men and women?
Response: You know that's a really interesting and important question. In our study there is some limited, but suggestive evidence, that the interactions may be quite complex. In that it's not just a matter of color and socioeconomic status, but gender also matters. Because the meaning of being dark skinned differs not only by class but also by gender. In our study we don't have enough statistical power to be able to really confirm whether that more complex interaction is taking place. There are a few other studies that again, are suggestive. But certainly that's an important direction for future work.