Suicide Prevention Across the Educational Continuum Series

Part 2: World Class Resources to Discover Genetic Risks for Suicide Death

Video Transcript:

>> Welcome to today's presentation, World Class resources, to discover genetic risk for suicide death.

>> As we have noted, the work of the Mountain Plains MHTTC and Mountain Plains PTTC is supported by SAMHSA and the HHF. We would like to know that today's presentation is provided free of charge and it's available in the public domain. Also, the information presented today, are the views and opinions of Dr. Hilary Coon and do not reflect the official position of the HHF or SAMHSA. Please, let us know if you have any questions about information in this disclaimer.

>> It is my pleasure to introduce our presenter, today. Dr. Hilary Coon receives her PhD. From the Institute of Behavioral Genetics of the University of Colorado Boulder. She moved to Salt Lake City in 1991, to start working at Department of Psychiatry at the University of Utah, on an NIH Post-Doctoral Grant that she receives -- Excuse me, that she was awarded for Schizophrenia and Bipolar Work. She found the University of Utah to be a fantastic place to work and has been there ever since. She is now a 10-year professor and her work focusses mainly on the development and applications of methods for gene discovery for complex disorders, including genetic risk and epidemiology of suicide. This work is made possible through a collection of over 7,000 DNA samples from complicated suicide -- Suicide, collected through a two-decade collaboration with the Utah State Office of the medical examiner. These cases have been linked to the Utah population database or UPDB, a statewide data resource that includes extensive genealogical record, demographics, environmental data and current medical data from over 11 million individuals. Dr. Coon's group pursues complimentary genome wide analysis for the discovery of common risk in our large sample and additional characterization of our resources from many psychiatric, medical and behavioral traits, using polygenetic risk scoring.

>> Now, I will turn the time over to Dr. Hilary Coon. Welcome.

>> Thank you so much and I appreciate all the people who are taking time out of their sort of crazy schedules in this unprecedented time to join us for this Webinar. And, I definitely thank that MHTTC and the PTTC for inviting me to present to you. It is a real honor, to be able to do this.

>> So, first off, I really do want to make sure that you're aware we're talking about suicide risk today and I know that this can be an uncomfortable topic for many people. And if this is at all triggering for you, I would encourage that you make sure that you

phone the hot line or hit the National Service Prevention website. I've included these resources here, partly because of wanting to make sure you're aware of them. There's certainly many more local resources that will be in your area and if you -- You want to reach out and understand some more of these resources, please, don't hesitate to do so. My contact information will be at the end of the presentation. So, there are also a lot of interesting research resources. These are national resources. Also, World Health Organization, which I didn't include here, gives you some global research resources. So, these are some resources that I've used in my own work, and they will also give you some information about your regional research recent findings.

>> So, just to put us all on the same page, I want to give you a little bit of background. As I'm sure all of you are aware, suicide is a major public health crisis now. Right now, it's the 10th leading cause of death in the United States. These are statistics from 2017. So, they're a little bit out of date, but close to 50,000 people in the U.S. die by suicide. Over 800,000 individuals worldwide. And the cause of death, this is a more leading cause of death in our younger population. This is definitely a public health crisis. It's also worth saying that there are a number of attempts. Suicide attempt is 25 to 30 times more common than death by suicide. So, over a million, close to a million and a half attempts in the U.S. in 2017.

>> And in spite of the fact that this is a major health burden in health crisis, the research funding for suicide is somewhat less than some of the other national health crisis that we're facing. This isn't to diminish in any way the burden of health crisis such as cancer. It's just to say that suicide has been a very underfunded area. Thankfully, this is starting to change. Suicide research is now a big focus for the National Institutes of Health and there is other funding, private funding foundations, that are trying to sure up this need as well.

>> The other particularly alarming aspect about suicide death is that this is actually an increasing problem. Suicide has increased 33 percent in U.S. since 1999. And, in Utah, which is sort of, you know, obviously where I live and where and I've been thinking about this, this has been particularly dramatic. Suicide has risen 46 percent, in Utah, and these increases have been particularly dramatic for women.

>> So, it's important when we're thinking about studying suicide to kind of understand some of the basic epidemiology behind, what's going on here, and one fascinating aspect of this is difference in just very basic epidemiology, between those individuals who attempt suicide versus those who actually die by suicide. So, again, a suicide attempt is way more common, about 25 to 30 times more common. The sex ratio for suicide death is very male oriented. It is almost four to one, male to female, for those who die by suicide. For attempts, these are, of course, they're a lot more difficult to very accurately to determine, but attempts are about twice as common in females, especially in Utah. So, very different epidemiology of phenomena.

>> It's also the case that suicide death is quite familial. This has actually been known for quite a long time. I'm showing you a family diagram. So, in this diagram, the squares are male and the circles are female. And so, this is showing a genealogy, and this is from a study from the 1980s, that was done by Janice Egeland in the old order Amish,

Pennsylvania. She studied a number of families who had a high risk for psychopathology and what she noticed, even though there were dozens of these families, is that in the big extended family trees that she studied, only four of them had the aggregation of suicide deaths. So, even though, a lot of individuals who die by suicide do struggle with mental illness. It is the case that most of those who have mental illness don't actually die by suicide, unless she saw in her sample, not only among just the cases, but that it aggregated in this very familial way. So, this was an early indication that the familial risk of suicide death was potentially independent of psychopathology. And there have been a number of additional studies done by researchers in this country and other countries that suggest this same phenomenon that there really may be independent risk factors, they're unique to suicide.

>> Well, so, you are aware from the title of my talk that I'm interested in studying genetics of this phenomenon and I have to, of course, convince myself that it's truly something that has genetic ideology. So, the family studies tell us this in some degree, but families also share a lot of environmental exposures and risks. So, what we have to do is kind of look at different ways of convincing ourselves that there's a genetic contribution to suicide. So, one way to do this is kind of an interesting natural human experiment, which is to look at the comparison of twins. So, we know that identical twins share all of their genetics. Well, fraternal twins are likeful siblings. They share about half their genes, on average. So, people get the difference in the concordance between individuals who are identical twins versus those fraternal twins. This gives us a suggestion of the degree to which genetic contribution underlies any trait, let alone suicide death. So, you see here, this is a compendium of twin studies from the worldwide literature, looking at the concordance of suicide death among monozygotic twins. Again, these are the identical twins that share all of their genes. First, is fraternal twins who are the ones that are likeful siblings in half their genes, and you can see that the concordance is much more apparent in the monozygotic twins where there share all of their genetic material. The other nice thing about this particular design is that the twins are sharing sort of equivalent degrees of environmental factors. This will even go back to prenatal risks. So, you're controlling a little bit for the environmental risk that are shared. Another interesting design to look at whether or not there might be genetic underpinnings to suicide death is to look at adoption studies. So, with an adoption study, we can compare rates of any trait, again, among the adopted individual who is not being raised in this same family as their biological relatives. So, if we look at rates in the adopting relatives of an individual die by suicide versus the rates of suicide in their biological relatives. This will tell us a little bit more, again, about whether or not the genetics are actually contributing to this risk. And what you see is in the biological relatives of individuals who died by suicide. This is four, five times the population rate, which is about the same as what we see in the family studies, about what we would expect. In the adopting relatives it's not increased at all. So, this, again, gives us some evidence that there's some genetic predisposition to suicide risk and we can look at meta-analysis of all of the studies that had been done in the literature and come up with a number of that. It's about 50 percent of the genetic contribution is given to the risk of suicide death.

>> So, it's worth noting that, of course, suicide is very complex. We know that mental illness is a factor, but we also know that about 90 percent of individuals with a psychiatric diagnosis don't die by suicide. So, it's not deterministic. We also know that about 50 percent of individuals who died by suicide had no evidence of a psychiatric diagnosis. Now, this may mean that this is a missed clinical opportunity and they are struggling, but it is above interest that these risks don't seem to be completely overlapping. There are, of course, also medical risks including major illness, chronic pain, all kinds of exposures early life risks, emotional and physical trauma. Dramatic violence, drugs, alcohol, toxins. There's social factors, social isolation or social supports. Bereavement, poverty, financial losses and, you know, we have to say that, right now, we're living in sort of a perfect storm of suicide risk with folks meeting to do social isolation, potentially experiencing bereavement, experience extreme stress in these unprecedented times. And then, with a wave of potential financial stresses and poverty, about ready to break over us. So, we know that all of these stresses are extremely important and what we are doing in our studies is trying to find the biological risks that may tell us who is actually the most vulnerable to these particular environmental stressors. So, having a genetic risk factor certainly doesn't guarantee suicide risk. This is sort of like having maybe genetic risk for something like obesity. We know that some individuals struggle more with weight gain and this doesn't mean that they necessarily become obese, it simply means that they may have a biological predisposition to struggling with this particular aspect. So, this is what we're trying to do in looking for genetic risk factors is to try to identify those most at risk.

>> So, why Utah? Well, we know that in this map you can see on this particular slide, there's kind of a what we might call it suicide belt. The states that look bright red here have high rates of suicide and this particular diagram sort of changes a little bit year to year. We all get this sort of dubious distinction of being more or less on the top of the suicide risk rate. But you do notice that this also sort of interestingly maps on to the intermountain region. I do have a colleague who studies effects of altitude on suicide risk and it does is a very interesting hypothesis. I won't really get into that because that's a whole different area. It's fascinating, but the idea is that -- That individuals who are particularly at risk for oxygen processing in the brain, this may be a triggering mechanism. So, Utah is certainly is amongst the highest for suicide death rates in the country. And, in Utah, the suicide is leading cause of death for people under age 25 and our governor declared this an epidemic. A couple of logistical elements make this really attractive for research here. One of this is that we have a very centralized medical examiners' office. This is a statewide office, so this makes it just more logistically possible for us to get records from individuals who die from suicide and to have collection happen for samples for obtaining DNA, in order to do genetic studies. So, this collection was started by a very foresighted colleague of mine, about two decades ago, and we now have around 7,000 DNA from 7,000 individuals who died by suicide. This grows, unfortunately, at the rate of about 700 individuals a year. Again, this is statewide collection. So, this is a current resource and it's worth saying that most other worldwide studies think about looking at genetic resources don't really have this resource for studying suicide death. They need to study suicide attempt, because they just don't have the capacity to collect samples from individuals who have died by suicide. So,

have an opportunity to contribute to the worldwide knowledge of this really serious outcome. So, the other thing that I think was mentioned in the introduction that we have here in Utah, that's really quite amazing is the Utah population database. So, this is a State-wide data base, it includes a lot of stake holders and includes medical records data back to the year 2000. So, a couple of decades of medical records data. It includes a lot of demographic information. Includes some exposures and then, very importantly for us, includes genealogical records. So, these are records that go back to the 1800s, sometimes even 1700s from. That are from the LDS Church, this were donated to the University of Utah for medical research. And they are one of the reasons why the University of Utah has been a leader in finding some genetic predispositions for disease, such as the BRCA1 breast cancer gene and other genes. So, I'll talk a little bit about that in a minute. That is a unique feature of the Utah Population Database.

>> So, why do we need to study suicide death? We're very interested in doing this here and I think it's very important. One thing to note is that research has actually gotten quite a lot better at predicting who attempts suicide. So, there are models that have been developed now using electronic health records. These models actually are getting better and better at identifying people who attempt. But we know that about 50 percent of suicide deaths occur without any evidence of prior attempt and, actually, even among those who make attempts, only about seven percent of them go on to die by suicide. So, our capacity to actually predict who will die by suicide, needs some serious improvement. This is something that is very, very difficult. And we could try to focus our effect or efforts on looking at environmental risk factors. These are really difficult. So, we would need to be able to measure them accurately. We would need to be able to think about timing and intensity of environmental exposures and we think that, possibly, if we start with the genetic side of things, where we're looking at individuals who may be more at risk for exposures. That this will really help us in trying to focus our efforts better in looking at what we think is maybe much more complicated side of things in looking at environmental risks. So, again, what we have here is a resource that's really pretty unprecedented and came about through some of the forsighted individuals who started this collection. We'll probably have about 10,000 DNAs from individuals who die by suicide by the year 2024. And most of these do link to the Utah Population Database. So, it allows us some way of characterizing risk factors once we've tried to unravel some of the genetic underpinnings.

>> So, what we've developed, me with lot of other collaborators, is absolutely a big effort on something that we call the Utah Suicide Genetic Risk Study and these are the overarching aims we want to try to identify some of the risk factors for suicide death. We know these are complicated and there will be many of them. We want to try to use this to characterize genetic subgroups. We want to understand what are the mechanisms that are implicated by these genetic findings. We, importantly, we want to recognize ELSI is ethical, legal and social impacts of this. We've already started some ethical studies trying to get information from individuals who've survived suicide attempts and the family members on how we think about this on about us attempting to identify genetic risk factors. So, we think this is also important. And I've put a bunch of puzzle pieces here, which are aspects of risk that are being studied by our group. I'll touch on a few of these and just know that we recognize these as a really big problem.

>> One of the things that we think is maybe the most unique about our resource is the extended genealogical data and just to give you a little bit more background on that and how we're using it. What happens is we get information from the medical examiner's office associated with an individual where we have a sample that we can use to extract DNA. This is given to the Utah Population Database and their staff is behind the computer firewall, they link then to genealogical records and health records. And then, de-identified that data. So, that us on the analysis side of things can look at the de-identified data set. And what we are doing with the extended family data is looking at these very large family clusters. So, with this clusters, we hope that within the family unit that we may be looking at a somewhat more contained, smaller problem, where the genetic predisposition within that family may be a little bit more homogeneous. That it's something that's passed down from those ancestors back in the 1800s. And then, by looking at the genetics of the individuals who are linked in these big families, we may be able to identify, at least, in that family, some genetic causes that are leading to the increase in risk for suicide.

>> Let me show you what one or two of these families look like. So, again, this is a diagram of the family, but we disguised the sex of the individuals. We don't really need it, at this point, and this just protects the privacy of the families. So, these are families that are really, really distantly related. And one aspect of this, that helps us when we're trying to isolate just the genetic risk factors is that most of these individuals really don't share much environment. We even tried to look at broad zip code data and we can show that within these families people aren't even living in the same region. So, they're really not sharing much in the way of environmental risks. So, what they share that has to do with their increase risk in these families, really, it has to do more with their common genetics. So, we've taken the individuals in these families and the ones that I've circled in red. So, anybody that’s jaded in black is a suicide death. We know that these suicide deaths from the medical examiner and actually from death certificates in the Utah Population Database, all the way back to 1904. So, when we look at these suicide deaths, we have the ones that circled in red there, we have their DNA. And we look at sharing of genetic, genomic regions among these families' members to tell us if they are sharing a region of the genome that has a gene that we could say that maybe this is something that is contributing to their increase in suicide risk.

>> And that was a relatively small family, here is a bigger family. These families, we have hundreds of them, because we have a very large data resource. Thousands of individuals who died by suicide. We have over 500 families that looked significantly high risk forces for suicide death, looking at these genealogical records. And one of the things that we did was pick about 45 or 43 of these really high risk families and look at their genotyping and looked what they shared.

>> When we did this, we came up with about 30 significant regions from these families where it looks like the individuals within the families are sharing a particular section of DNA.

>> When we look at these regions of DNA, we can go one step further and ask ourselves, ok, what are the genes in these regions? And these genes, then, are targets for us to look at, in more detail, as being genes that might be implicated in increase risk

at suicide death. So, you might think that 200 genes here is kind of lot, but it's way better than thinking about 18,000 genes across the genome. So, one of the things that the big families have done is they've allowed us to pair down to much smaller set of targeted genes to look at for potential important genetic risk factors that increase risk in suicide death.

>> I have a fantastic graduate student who is then working for a couple of years on a follow up of one particular gene in one of these regions. This gene is NRXN1 gene. It's a gene that is involved in synapsis. So, synapsis are how the neurons and the brain communicate with each other and this particular gene, NRXN1, is interesting. It controls synapse organization. And how is prior associations changes in this gene, a prior association with psychopathology, including schizophrenia, autism and bipolar disorder. So, what she did was look a lot at our data and find two specific NRXN1 genetic variants that show some statistical association in suicide death above and beyond the familial association that led her to this genome in the first place.

>> And then, she spent quite bit of time looking on the bench in a dish, looking at all these particular changes in NRXN1 could alter the aspects of synaptic binding. What she found was that the variants showed some increase in binding in post synaptic bindings. So, this just means that these particular variants when compared to the gene without any variants in it at all. So, these particular variant changes in the gene, they increase the synapse binding above and beyond what we would expect. So, there is some indication that these variants that she found might change the way that synapse are talking to each other in individuals who die by suicide. So, this is work that needs to be replicated that's in initial findings. And I should note that these variants are really rare. This is not explaining every single suicide death and it samples about one percent of our cases that might have one of the other of these variants. So, this is again, is an indication that this is a very complex problem and, even once, we might land on a gene that looks like it might be implicated in risk. The changes in that gene are really hard to find and studying them is going to be a long road.

>> So, to change directions a little bit, this is another strategy that our group is using. This is something called genome-wide association study. And what we do here is independent of our high-risk family studies. So, this is just taking all over suicide deaths and looking at every location that you have genotype information in across the genome and looking at the frequency, is in the changes in those locations across the genome, compared with really large publicly available data from controlled populations. So, this is UK biobank and another UK sample. And what we can see is that there are some locations in the genome where it looks like our suicide sample has a definitely different frequencies in these locations in the genome. And, again, this is kind of like the family study where this particular study design tells us some locations in the genome that really might be implicated in risk.

>> We can also look at those about 18,000 genes across the genome using this much broader, more complete, genotyping in all of our cases against these publicly available controls and just look at all the genes across the genome and we find additional about 10 genes that look like they might be implicated in this particular non-familial study design.

>> So, overall, these genome-wide studies gave us some 21 genes that look like they had some evidence that they might be implicated in suicide risk and we don't know exactly what the changes in these genes might be. This is going to involve additional study kind of like what we did with the NRXN1 gene in the family based studies.

>> So, one of the other things we can do here is also is to look at how can these genes sort of group together in regards to what are they doing in the body. So, we can, these are functional pathways. So, we notice that these genes are preferentially involved in neuronal development. Some of them are involved interestingly in metabolic function. We did actually find that also in our family based analysis and this might go back to the observation of my colleague that has to do with oxygen processing as being a trigger for some particular individuals who are at specific genetic risk. We also find that these genes look like they have prior evidence in schizophrenia, in Alzheimer's disease and in bipolar disease. And also that have differential brain expression in some psychopathologies: Schizophrenia, Autism, etc. So, these findings are showing us that we're starting to get a group of genes that look like they may be implicated in risk. And, again, we really think that this is a very complex problem and that there are probably hundreds of genes. That if we can start trying to define some of the genes that are implicated in risk and finding some of the actual changes in those genes, what are they doing that it will be able to help us identify individuals that are at much higher risk than other individuals.

>> One of the other things that we can do with the genome wide association data in our bigger sample is look at the polygenic risk scores. So, a polygenic risk score is a connotative score that reflects through the background genetics of a trait. And, what we can do is we can take genome-wide results from some external studies of other traits that we know might be implicated in suicide risk. For example, major depression, schizophrenia, bipolar disorder. And, we can apply those results from those external published studies to our data and look at the sum score across the genome for these other traits. So, this score really gives us more a potential sort of background. Polygenic risk of some associated psychopathology or behavioral trait. And there are hundreds of these polygenic risks that now can be computed from really, really large, very well powered published studies.

>> So, just to show you what a few of these look like, pretty much what we would expect for a lot of these background effects in our suicide data, in our suicide resource. So, we see elevation for depressive symptoms and major depressive disorder. For traits like neuroticism, loneliness, we see an increase in other psychopathology including autism, ADHD and this is compared to two different comparison samples. I don't know exactly what's going on with subjective well-being. Difference maybe is slight differences in the way that the data are being processed or collected. I'm actually of Scottish background, so, I just love that subjective well-being that's really high for generation Scotland. That's awesome, maybe that gives me some protected factors.

>> So, the family studies and the genome-wide association studies gave us sort of a good handle on what genes could we target, that, again, it took a lot of work to go to the next step and there are NRXN1 studies that we did for the family based analysis. We'd be faced with the genes from our genome-wide association study, too. We have to

really look for exact variants that might be implicated and do a lot more work to understand what's going on to specific variants. So, one thing we decided to do with a really talented post-doctoral group was to use the genome-wide genotyping has some variants that actually do affect gene function. Most of the variants in these genome-wide studies don't do that. So, they're trying to give you a lot of information about variability among populations. And so, they're mainly looking at genomic variation that isn't inside genes, that's in the spaces in between genes and our genome, that sort of junk DNA, that we call it now although it may not be junk at all. That has a lot of variability. Within genes, there isn't a lot of variability, as some might imagine. If you had variability there, it's often damaging. So, the genome wide genotyping doesn't include a lot of varied variants that really affect you genome function, but it does include some. And so, what we thought is, gee, you know, why don't we take advantage of this and look at the variants that are in this genome-wide genotyping, that actually do something to genes? And do an association study on just those really functional genotypes. So, to do this we kept about 40,000 variants, and you might think, oh! Wow! Forty thousand? That's a lot. But actually, that's a tiny fraction of the genome. The genome has three billion base pairs in it. So, forty thousand is about .001 percent of that. It's not lot. So, obviously this isn't inclusive of every variant that is out there. But it's a nice efficient way to look at genomic variants that might actually do something and bypass that step that we need to then pursue in any other study designs. So, we compared these potentially functional variants between our suicides and publicly available resources it controls, again, match for ancestory. And we came up with five variants that looked really interesting. These are variants, again, that this isn't just a gene that we're looking at now. We are looking at a gene change that likely does something in this particular gene. So, the genes that were involved here, really, are interesting. Several of them have supporting post mortem evidence from other studies, looking like they're implicated in suicide death. Also supporting studies that show association to bipolar disorder, schizophrenia. Some evidence is really interesting, implicating immune system dysfunctions, circadian rhythm and then, also, signal transduction. So, these gene variants are actually of interest to us, looking at exactly what did they do, pursuing some studies that [inaudible] looking at these. And also, the genes, did they have other variants that are involved in risk, gene pathways that are implicated by these genes, what are they doing. So, it's opened some other doors for us.

>> We're also looking with some of our colleagues in human genetics at another way of looking at little chunks DNA that are deleted or duplicated in our genome. These are called structural variants and sometimes structural variants can have a dramatic effect on genes. So, it's worth looking at these. They tend to be rare. I'm showing you a picture or a visualization tool. This fantastic visualization to all this, developed by the -- My colleagues in human genetics. We can actually see the deletion in the genome, in this particular location. This happens to overlap with the gene RGL3 [phonetic], which is a noromal differentiation gene. It's only in nine of our cases, right? So, this is a small set of individuals who died by suicide, becomes this comes from, as you know, sequencing data and it's so expensive to generate. So, we only have 281 individuals with this whole genome sequencing data. So, about three percent of them have this particular deletion. This is rare in comparison data, but it's not completely absent. So, again, this isn't

something that if you had this deletion, you're absolutely known -- It's actually know that you would die by suicide. This is going to be a risk factor, but it's worth looking at these particular types of genetic events as another way of giving us some clues about what genes are involved.

>> So, we did this with these rather small set of genome data and we've looked at what are the deletions and duplications. What kinds of genes they implicate and we're finding these preferentially in genes that'll have to do with neuronal function. Interesting, there's some overlap with genes and gene pathways that we found in our association's studies. So, we find that really fascinating. We've got a lot of work to do with these, trying to figure out, do they overlap with the parts of genes that actually are functioning and affecting how the gene works. And we're also looking at a much bigger dataset of sequencing data, we've got about 400 more cases that are in progress. These are really -- Prioritizes being cases that look like they have more familial risks. So, they should be ones that have higher degree of genetic risk.

>> Another interesting thing to note is that we're working with individuals in the international community who are really focused on suicide risk. So, there is a large consortium group, that's part of the psychiatric genomics consortium that's now very interested in studying genetic risk of suicide. You can see this slide here as individuals from studies from across the country. This is also worldwide. iPsych is a big consortium, that is European. deCode is in Iceland, and we now are looking at -- I think it's more like upwards of 30,000 cases. This slide is a little out of date. A couple 100,000 comparison individuals. Well, it's actually documented that there's no attempt. It's worth saying that Utah really has the only big dataset here that, again, that's is looking at suicide death. So, all of these are really more looking at suicide attempt, but then, looking at the genetics of suicide attempt and comparing suicide death is a very, very, very, very important for us.

>> Ok. So, just to summarize a little bit. We've got genome-wide association studies. We've got family studies. We're looking at different ways of characterizing genetic changes, including structural variants. Some of these pictures here are looking at post mortem brain tissue, we have a very small collection of that. Hopefully, partnering with the NIH neurobiobanks to wrap up that collection so that we can look at actual changes in post mortem brain of tissue of individuals who died by suicide. Looking at exposures, we're looking at exposure to air pollution that kind of matches again with the altitude hypothesis, is this oxygen processing metabolic processes inflammation and function.

>> We have a lot of studies that are just starting out. In progress, I told you a little bit about the fact that we're working on new genome data. We're looking at epigenetic studies, which is a different way of thinking about genetic changes. We have some new studies where we're trying to link to position notes in the medical records. So, these give us a much more accurate picture of suicide attempt, both within our individuals who died by suicide and then, also, to compare in the control individuals. We have one researcher in our group that's looking at the overlap between suicide risk and opioid epidemic. We are looking at toxicology in hair samples collected from individuals who died by suicide. These would be both from pharmacological exposures, air pollution exposure, other toxic, environmental exposures that you can measure in mass spec

analysis of hair. We're trying to make sure that we really pay attention to our ethics' studies. We're planning interviews. We use survivor groups. So, these are the individuals in rural communities, looking in minorities and refugees. We're also interested in getting opinions about our research among providers. And we have our local and regional, and international, collaborations. We're hoping that this work really continues to grow and that we continue to make the discoveries on genetic resources.

>> So, just a reminder. So, this is super is complex, right? There are likely hundreds of genetic variants leading to suicide risk and we're seriously in this probabilistic universe, right? No individual variant is determining suicide death, the risk factors are going to just be identifying individuals who are more susceptible, potentially, to environmental risk factors.

>> And, just to end here, there's a lot of collaborators. My goal is actually to have so many people on this slide that you can't read it. We have fantastic collaborators in our department, across departments at this university, across institutions. So, Intermountain Health and then the Utah health department. We have collaborators who are external, who are advisers and institutions across the country. We have a partnership with Janssen research, who provided us some of the funding for genotyping and sequencing data in this project. We have support from the NIH, from the American Foundation for suicide prevention, from several foundations. We have some new support from the Huntsman Mental Health Institute. Here, to look at the new sequencing data and it really takes a village. So, we appreciate our collaborators and our funders.

>> And, again, I want to make sure that you're aware of resources. There are many resources that are available for thinking about research, but then also these prevention and help crisis services. And I want to make sure that that is available to you.

>> Well, thank you. I provided my contact information and I'm absolutely delighted to hear from anybody who might want to contact me. I love geeking out about this stuff and speaking with people about their thoughts about the work. Thanks.

>> Hilary, thank you so much for your awesome presentation and for all the research that you're doing right now. We're going to find out more and more as time goes on. So, thank you.