The DNA Files: Unraveling the Mysteries of Genetics
The Human Genome Project: Mapping the Future
Transcript

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For further information about genetics and these programs, as well as the producers who
brought you this series, visit the project web site at www.dnafiles.org.

Send your questions about genetics and this project to feedback@dnafiles.org.
JOHN HOCKENBERRY: This is the DNA Files, I’m John Hockenberry. Some say we are about to undergo a global biological revolution.

FRANCIS COLLINS: It’s the book of life. It’s the instruction book for human biology. This sequence of DNA carries around all of our hereditary material. Three billion letters in length is basically responsible for our being able to do all the things biologically that we have to as human beings. The goal of the Genome Project is to read that script, to read our own instruction book.

JOHN HOCKENBERRY: The Human Genome Project is an international effort to map all the genes in the human body. With it we begin to look at ourselves at the chemical level to answer questions about our evolution: how we age, why we become ill, even what shapes our personalities. The project started in 1990 and won’t be done until the year 2003. But what have we learned so far? Coming up – The Human Genome Project: Mapping The Future. But first...

[pause]

The history of modern genetics began not with the description of DNA in 1953, but back in 1900. The rediscovery of Gregor Mendel’s work with pea plants allowed scientists to make great strides in deciphering the genetic code. But human genetics before World War Two was tainted by widely accepted theories of racial improvement called eugenics. A dark chapter it took some pioneering scientists to expunge, as John Rieger reports.

FEATURE STORY

JOHN RIEGER: We’re at a state fair in the mid 1920s watching in the warmth of the evening as a proud young family receives the Capper Medal. It shows a man and a woman beholding a radiant infant and the motto, “I have a goodly heritage.” The Capper Medal is a eugenics prize awarded by the judges to the fittest family.

DANIEL KEVLES: Competitions were usually held in what were called the “human stock” sections of these fairs.

JOHN RIEGER: Daniel Kevles is a professor of humanities at the California Institute of Technology. These fitter family competitions, he says, show the public’s enthusiasm for eugenics. Eugenicists believed that society’s ills could be traced to bad genes, and eliminated by selective breeding. They studied traits like prostitution, and poverty, shiftlessness, even something called thalassophilia, love of the sea.

DANIEL KEVLES: Since people who went out to the sea in ships were almost always male, and fathers who were ship captains gave birth to sons who were ship captains, and so on, this must be a sex-linked trait. That was ludicrous even on the face of it.

JOHN RIEGER: Eugenics was pervasive in the US, Britain and Germany before WWII. It was embraced by politicians, intellectuals and social reformers. But eugenics was a pseudo-science, rife with race and class biases. In America, so-called mental defectives were sterilized. In Germany it lead to the death camps. So entangled was the study of human heredity with eugenics
that serious geneticists shunned the study of humans. At Columbia, Thomas Hunt Morgan worked with fruit flies. In 1910 he discovered the principle of sex-linked traits. In 1913 his student Alfred Sturtevant drew the first gene map, three quarters of a century before the Human Genome Project. Their laboratory was filled with the scent of rotting bananas and colonies of fruit flies in milk bottles.

JAMES V. NEIL: Well, I washed those bottles.

JOHN RIEGER: James V. Neil, professor emeritus of human genetics at the University of Michigan crossed paths with the great Professor Morgan as a graduate student in 1937. By the end of WWII, Neil was convinced that the techniques of experimental genetics perfected on subjects like fruit flies could also be used to study humans.

JAMES V. NEIL: Coming out of this background of experimental genetics, I was absolutely determined to try to introduce into human genetics the kind of rigor that existed for experimental genetics. And this led me to studies of inherited traits of blood.

JOHN RIEGER: Neil turned his attention to a human disease called sickle cell anemia. It was known to be passed down in families, but just how was still a mystery. Blood could be easily sampled, Neil reasoned, and studied for a variety of well-defined physical traits.

DANIEL KEVLES: Most geneticists didn’t want to touch the area of human genetics.

JOHN RIEGER: Daniel Kevles.

DANIEL KEVLES: What Neil and others did in the beginning in the mid to late ‘40s and on through the ‘50s was to say we have to study traits that are objective. For example, we’ll look at the chemistry of blood or indisputable physical characteristics, and we’ll try to figure out the genetics of these characteristics.

JOHN RIEGER: In 1948, Neil showed that sickle cell was a recessive gene that followed normal laws of inheritance.

JAMES V. NEIL: At the very same time I was working on the genetics, Linus Pauling and some of his students were examining the hemoglobin of patients with sickle cell anemia. And they demonstrated very clearly that there was a hemoglobin abnormality.

JOHN RIEGER: Unlike the vague social concepts of the eugenicists, sickle cell was a clearly defined physical trait, a model for the objective study of human genetics. Since 1948, Neil has been involved in the largest human genetics study prior to the Human Genome Project, a study of the children of Japanese exposed to atomic radiation. But an important part of his legacy goes beyond his own research.

DANIEL KEVLES: Jim Neil was one of the few who said, hey, there’s no reason why the study of human heredity has to be perverted by racism. What we need to do is to try to emancipate the study of human heredity from class bias and racist bias. And he set out to do that and was a major figure in achieving that end.

JOHN RIEGER: For The DNA Files, I’m John Rieger.
JOHN HOCKENBERRY: This is The DNA Files. I’m John Hockenberry. The genetic structure of any living thing can be said to be like a symphony, each species composed of its own song. By this analogy, the symphony of the relatively primitive e coli bacterium might sound something like this:

[delicate music]

The symphony of frogs might sound like this:

[more enhanced music]

And the symphony of humans might sound like this:

[huge symphonic sound]

Humans, as we all know, love to blow their own horns. But go with me on this analogy – all humans will be this symphony with just a tiny variation in notes. But which notes bestow blue eyes? What musical phrases make us grow from infant to adult? What notes, played too sharp or too flat, create diabetes or Huntington’s disease or other conditions? The Human Genome Project is the scientific effort to write down the entire score of human composition note by note. Of course, the human genome is not comprised of actual musical notes, we’re composed of four chemicals organized in a precise sequence, much like a musical score, and we each have our own unique genome – except identical twins, who share the same genome.

But why study the genome? That’s our question for this hour. Joining me to answer this and other questions are Francis Collins, National Institutes of Health Director of the Human Genome Project. Georgia Dunston is Professor and Chair of the Department of Microbiology at Howard University College of Medicine in Washington, D.C. Thomas Murray is a professor at Case Western Reserve University and a bioethicist on the National Bioethics Advisory Commission, and Vicki Whittemore is Vice President for Medical and Scientific Affairs of the National Tuberous Sclerosis Association. We also have questions from around the country, and we’ll be rolling all that tape and other surprises into the program as we go along.

Let me first say thank you all for joining us today.

ALL: Good morning, nice to be here, etc.

JOHN HOCKENBERRY: I’m going to begin with Francis Collins. What exactly is the Human Genome Project, and how important is it?

FRANCIS COLLINS: Well, your analogy of a musical score is an apt one, but for the non-musicians I’ll use a different analogy, and that is, it’s the book of life. It’s the instruction book for human biology. This sequence of DNA that carries around all of our hereditary material, three billion letters in length, is basically responsible for our being able to do all the things biologically that we have to as human beings. That genome, as we call all of the DNA, makes up about 80,000 genes, each one of which has a different instruction function. The goal of the Genome Project, which began in 1990 and aims to complete getting this sequence in a publicly available, electronic form by 2003, is to read that script, to read our own instruction book.
And why does that matter? Well, within that will be clues to diseases that we currently understand rather poorly, and from those clues, by much research done by many people all over the world, we will learn how to better predict who’s at risk for what, and most importantly, to be able to do something about that. So this is one of the most exciting developments in medicine in a long time.

JOHN HOCKENBERRY: Quickly, Francis, does mapping equal understanding something as complicated as the human genome?

FRANCIS COLLINS: No, not at all. This is sort of like building the Periodic Table of the Elements for biology. And the interesting part is once you have that periodic table, how do you figure out how all these genes work, and particularly, how they work together with each other?

JOHN HOCKENBERRY: Well, certainly, many of the questions we hear about in the popular media regarding the Human Genome Project, then biotech in general, regard disease. Vicki Whittemore, genetic diseases: how important is this project in beginning to help identify them, to begin to help treating them, and how personally are you involved in this particular quest?

VICKI WHITTEMORE: The Human Genome Project is very important in this quest, in understanding genetic diseases. Tuberous sclerosis is a genetic disease that affects about 50,000 Americans and a million people world-wide, and the Human Genome Project was key to finding one of the two genes responsible for this disease. Some of the individuals funded by the Human Genome Project played a key role in identifying one of the genes. My family is affected by this disease, and I oversee the research program that the National Tuberous Sclerosis Association funds on research on tuberous sclerosis, and much of this research is done in concert with the Human Genome Project.

JOHN HOCKENBERRY: Is this an exciting time to be doing what you’re doing?

VICKI WHITTEMORE: Oh, it’s a very exciting time. There’s new disease genes being identified every day, and maybe every week.

JOHN HOCKENBERRY: Maybe every hour. [laughter]

VICKI WHITTEMORE: Maybe every hour. It wouldn’t be possible without the techniques that are being developed and the mapping that’s being done by the Human Genome Project.

JOHN HOCKENBERRY: Georgia Dunston is an educator. You’re a professor who teaches genetics at Howard University, among other subjects. Do you tell your students: this is an important project, the Human Genome Project, for educational reasons. Or do you say, what you really need to do after you get out of my class is meet this Francis Collins guy, and he can get you the really good jobs in genetics?

[Muffled laughter]

GEORGIA DUNSTON: I tell them that it is very important for educational reasons as well as… I would like for them to be aware of the kinds of studies that are going on at the National Human Genome Research Institute that Dr. Collins is heading, for opportunities that will surely be available for them to become engaged in in the future. One of the things I do stress is the
significance of the Human Genome Project for how we view biology as well as how we do biology. It has been said that the Genome Project will be, will lead to information that will be, the source book for biomedical science in the twenty-first century. And I certainly subscribe to that statement. Therefore, it is absolutely imperative that they understand what the project is, what its goals are, how those goals will impact how they will understand biology, and what opportunities for careers will unfold as a consequence of this project.

JOHN HOCKENBERRY: Mmm. Georgia, quickly, is it fair to say that the Human Genome Project is finally putting to rest a lot of the mythologies that have plagued the twentieth century regarding genes and race and genetics and behavior and anthropology?

GEORGIA DUNSTON: [Little chuckle] I don’t know to what extent it has been successful yet in putting it to rest. I can certainly say that it has brought it out in the open for public discussion, and anthropologists have certainly been very clear with their statements regarding the realization that there is no genetic basis for the categorical groupings of races as we socially recognize them. So now the questions come: Then how do you account for the differences that we see in people, that are inherited, are transmitted? What do you mean? So I would say that now we have a chance to bring the knowledge that science provides to the table, to re-examine our understanding of race, and hopefully uncouple some of the erroneous associations that have been made, but certainly to take advantage of the opportunities that will lie before us as we better understand the biology.

JOHN HOCKENBERRY: Mm-mmm. Thomas Murray: certainly, the social implications of the Human Genome Project are part of your portfolio as an academic, as a consultant to the government. Is this the “Gutenberg Era” of biotechnology that heralds an exciting new millennium, or is the horizon perhaps a little more disturbing, from your perspective?

THOMAS MURRAY: I think it’s both. The potential for very useful products made from the Genome Project is apparent, and lots and lots of people are scrambling to create these products and to make money on them. I mean, it’s quite common today to find geneticists, people in biology departments who also are partners or leading figures in biotech companies. To the credit of the people who created the Human Genome Project about ten years ago, they included from the beginning a commitment to try and to anticipate and deal with some of the ethical, legal and social issues. I’ve been focused more on them. Now, there are ethical, legal and social implications to biotechnology generally. But there are also some concerns that have been raised, concerns about things like genetic privacy and genetic discrimination, among others, and I suppose we ethicists tend to look more at the things that concern people than at the things that make them gleeful.

JOHN HOCKENBERRY: So ethicists are kind of like members of the media in that regard.

THOMAS MURRAY: [Chuckle] Oh, we’d never want to be compared to...

JOHN HOCKENBERRY: We’d never want to be associated with that gene pool.

THOMAS MURRAY: [Laughter]

JOHN HOCKENBERRY: I understand. We’re going to talk more about the Human Genome Project in a moment, but first, let’s glimpse into the life of one of the people coming up in our radio series.
BRENDAN HARRIGAN: My name is Brendan Harrigan. I’m eleven years old, and I like baseball, football and basketball.

[Sounds of a respiratory therapy session.]

REPORTER: What do you know about cystic fibrosis?

BRENDAN HARRIGAN: Well, it makes you have a lot of mucous in your lungs. And you have to take a lot of pills to digest your food.

JOHN HOCKENBERRY: We’re back. This is The DNA Files, I’m John Hockenberry. That was a clip from our program, “Prenatal Genetic Testing: Do You Really Want to Know Your Baby’s Future?” It’s one of the programs in our series. That young man, Brendan Harrigan, of course, has cystic fibrosis. Cystic fibrosis is a genetic disease.

Vicki Whittemore, you, as someone who has tuberous sclerosis and who found out that you had TS when your eight-month-old son was diagnosed with the disease, we understand there’s no genetic test for TS. But I’m wondering, if there was a genetic test for TS, how would that have affected your choices, any of the choices you’ve made in your family?

VICKI WHITTEMORE: That’s a very difficult question. In my family, my nephew was the first individual to be diagnosed with tuberous sclerosis when I was pregnant with my first son, and his mother and father, my sister and her husband, showed no clinical signs of tuberous sclerosis, so we thought he was the first case in the family, or a sporadic mutation. And it wasn’t until many years later when my son had seizures that he was diagnosed, and then I was diagnosed. And I probably would have had the genetic test, had it been available, after my nephew was diagnosed, and before my second son was born. I’m not sure what choices that would have left me with. I most likely would not have had additional children, knowing I could pass this on. Tuberous sclerosis is a difficult disease because you can have a very, very mild case of the disease and essentially not be affected by it, or, like my nephew, you can be very severely affected, and mentally retarded, have severe seizures. So, it’s a very difficult choice to make, and one that many of our families are having to make.

JOHN HOCKENBERRY: Forgive me, but I’m going to ask you straight out. Under any circumstances, if you had known, based on a genetic test, would you have considered aborting a pregnancy?

VICKI WHITTEMORE: No. I would not have. But that’s a personal choice, and I think one that each individual will have to make, but I would not have done that.

JOHN HOCKENBERRY: Thomas Murray, certainly, we’ve seen, and we’re going to see in our program, that the information that genetic testing gives us about our potential future is often terrifying to the individuals involved, and terrifying to their families, creating all these kinds of moral and social dilemmas. But who else is interested in that information, and what is at stake when someone is diagnosed with a genetic disease, besides simply their health?
THOMAS MURRAY: Well, if you’re diagnosed with a frank genetic disease, that’s of concern obviously to your doctor. We’re familiar with that kind of transfer of information. I suppose more interesting is if your – say a genetic predisposition to a disease has been identified in your family. There are others who might be interested, and certainly, insurers are interested. Health insurers, life insurers. Prospective employers might be interested, because they might want that information because they think that maybe it’ll tell them who’s likely to have more sick days, or who’s likely to end up boosting the company’s cost for health insurance. So there are actors out there who would be interested in genetic information.

JOHN HOCKENBERRY: Is there an ethical standard in regard to who gets access to genetic information? Is the insurance industry on record as supporting wide-scale genetic testing of large populations to come up with the kinds of actuarial data and pre-existing condition calculations that you talked about a moment ago?

THOMAS MURRAY: In 1991, the Ethical, Legal, Social Issues working group established a task force for genetic information and insurance. I chaired that, and we did a report on genetic information and health insurance. And we worked with insurers, we worked with people like Vicki Whittemore – who was not on our panel, but there were folks who were representing people with genetic diseases and genetic predispositions – to try to come up with some sensible recommendations about what to do with genetic information. And a few things became clear. One was that getting information about who was at risk of filing a claim – and that’s what it is to the insurer – is absolutely standard practice. And if genetic information were to be treated like all other kinds of information that insurers have access to, it would be used in those kinds of actuarial calculations to decide who gets insurance, at what rates, and what is covered. So it’s clear that the insurance industry would like to treat genetic information the same way they treat any other risk information.

But it’s also clear that, at least as of today, they’re not gathering heaps of genetic information. It’s just not useful enough yet, not readily available, and still too expensive. But in all likelihood, that will change.

JOHN HOCKENBERRY: Mmm. Well, the question of the usefulness of the – go ahead.

FRANCIS COLLINS: This is Francis Collins. I want to jump in on this.

JOHN HOCKENBERRY: Sure. Go ahead.

FRANCIS COLLINS: I think it’s a very important issue, and one that we need to address legislatively as soon as possible. There are some important issues. One is that we are all at risk for something, and so if we start down a path where that information is folded into whether or not you get health care or a job, the numbers of people who could have a very negative consequence are huge – potentially, all of us. It becomes both an unjust and an unworkable system rather quickly. And as Tom says, at the moment, insurance companies aren’t using much of this information ‘cause very few people have actually gone through the testing process. So we have an opportunity now to basically say, This is not on the table, and then stick to that, and avoid a real mess that otherwise sort of lurks in our future. If we don’t get to pick our DNA sequences, and I don’t think any of us have that opportunity, then to have that used against us, to deny us something as basic as health care, even though you’re currently healthy, is an unjust situation, and we should not stand for it. The Kassenbaum-Kennedy Bill which passed two years ago in fact outlaws the
use of that kind of information if you’re in a group health plan, but we need to plug the loopholes that still remain in individual policies. And there were draft pieces of legislation from both parties, in both Houses, and supported all the way to the point of the President, to do something about this, but they have not yet completely passed. They need to make that happen.

JOHN HOCKENBERRY: Well certainly, ultimately at the bottom of all of this is the question of whether this genetic testing information is useful enough to make economic calculations about… certainly what we are seeing is the psychological impact it has on people who hear the… the idea that the disease, the notion of health is encoded into our genes in some sense, and that that’s going to affect the way we view health care, which raises a question that’s one of a number of questions we’ve gathered from around the country. This one is from a man named Eric Fixler, who’s a computer programmer in San Francisco:

ERIC FIXLER: One is, I keep hearing that they’re going to figure out which genes cause cancer and which genes cause X disease, and like that, and my feeling is that it leads people and scientists to ignore the environmental causes for cancer. I feel like, instead of cleaning up the environment and dealing with the quality of food products, these people think they’re going to go in and genetically fix cancer and other diseases.

JOHN HOCKENBERRY: Okay. We’re back. I want to address the question to Georgia Dunston. Do you see among your students this idea that “forget about the environment,” that “everything is determined by our genes,” and that you have to attempt to clue your students in that, in fact, it’s more complicated than all that?

GEORGIA DUNSTON: I definitely do not get a sense that it’s all in the genes. In fact, there is considerable concern about the extent to which attention will not be given to environmental, socioeconomic factors that clearly contribute to many of the common diseases of interest that we are currently attempting to map genes that predispose or increase susceptibility to, such as diabetes and cancer. We recognize that these are what we call complex diseases. They are multi-factoral. There are clearly biological or genetic factors as well as environmental, and often lifestyle factors, and they all interact. That’s complicated by the fact that the interaction can vary at different stages in life. So age is a factor in some cases, even hormonal influences which would make gender a factor. And all of these things have to be sorted out. So my position is, as a geneticist, it is important at this point in time that we understand the contribution that biology makes to the whole complex scene, but to recognize that, indeed, biology alone is not, in many of the diseases of interest, the single causative agent. And we must be as vigilant in identifying the other factors, and addressing how to improve or remove the contributors to disease here as we are with regard to the interplay with biology.

JOHN HOCKENBERRY: Francis Collins, based on what Mr. Fixler said in his little question there, it seems to me that eventually people are going come to you and say, Look, here is my gene. Tell me, according to my DNA structure, exactly how much dioxin I can take, how many cigars I can smoke, you know, how much alcohol I can drink before my body goes haywire. That’s all I really want to know. Is that information ever going to be available?

FRANCIS COLLINS: Not in those sorts of precise terms, no. Certainly, we are going to learn about individual differences as far as consequences of exposure to toxic agents. And in fact, to Mr. Fixler’s question, one response could be that studying environmental influences is very difficult, in part because we all are different, and something that may place you at risk for cancer
after a certain exposure may not have any effect on ninety-nine percent of the population, and therefore, it’s very hard to pin it down. Many would argue that the best way to really understand environmental influences is to do so in concert with understanding the genetic influences. But again, we should not make the mistake, as Georgia is pointing out, of moving into this mindset that genes are determining. They’re predisposing. They’re not predetermining. And you may have risks that are up or down for a particular outcome, based on your genetic endowment, but those will be blurry, and they will depend on a lot of other things.

THOMAS MURRAY: And that’s the way it should be.

JOHN HOCKENBERRY: All right. I’d like to take another question. This is from Tom Caregrate, who was a man who spoke with us outside the Museum of Natural History right here in New York. And this is his question:

TOM CAREGRATE: How are you addressing moral and ethical issues concerning genetic manipulation of fetuses?

JOHN HOCKENBERRY: Genetic manipulation of fetuses. Tom Murray. I’ll give that one to you.

THOMAS MURRAY: Well, thanks a lot, John, for giving me the easy one.

THOMAS MURRAY: Right now, in the United States the U. S. Government will not fund any research on fetuses, especially any research that might result in harm to the fetus or that would be intended to be done to a fetus who was not going to be born. The only research, I think, that would be regarded as ethically acceptable and legally acceptable, and fundable, would be research that would be directly intended to benefit a fetus. Say a new treatment for a disease that begins to manifest itself very early. I don’t see that changing in the near future.

JOHN HOCKENBERRY: Okay. We’re going to take a short break. We’ll be right back.

[Music break]

JOHN HOCKENBERRY: This is *The DNA Files*. I’m John Hockenberry, and we’re talking about the Human Genome Project and its implications for all of our lives. Francis, I want to begin with you, here. We’re mapping DNA, right?

FRANCIS COLLINS: Yes.

JOHN HOCKENBERRY: So presumably you’re getting some DNA from somewhere. It’s actually sequenced, right?

FRANCIS COLLINS: Right.

JOHN HOCKENBERRY: You didn’t get any from me, as far as I know.

FRANCIS COLLINS: Are you sure?
**JOHN HOCKENBERRY:** Whose DNA [chuckles], whose DNA is being sequenced? I’m pretty sure about that.

[Laughter]

**FRANCIS COLLINS:** Did you get your hair cut this week? No, that’s a joke, that’s a joke... Well, a very important question. It doesn’t make a lot of difference, actually, from the point of view of the scientific goals, because our DNA is 99.9% identical between all of us. And the goal of getting that first human sequence is to look at the part that’s all the same. We have a separate enterprise, to look at human variation, which is a new goal of the project, and which will use a different set of DNA samples that’s broadly representative of about 500 people with broadly different geographic origins. But for the sequencing part, where we’re trying to look primarily at the things that we all share, the donors are a series of volunteers who answered a newspaper ad, came forward, signed an informed consent, so they knew what they were getting into, gave a blood sample, and then that was turned into DNA, which is then being used from about four or five of these people, to generate the so-called reference sequence. The identity of those individuals is unknown, all of the identifiers were stripped off. Nobody knows who they are. Even they don’t know who they are, because a lot more people came forward and gave a blood sample than are actually being used.

**JOHN HOCKENBERRY:** Except these people appear to be genetically-predisposed to reading newspapers and having a lot of free time. [Laughter] Right?

**FRANCIS COLLINS:** Well, we’re all predisposed to something, and I guess you could say that.

**JOHN HOCKENBERRY:** Georgia Dunston, you study variations in blood factors in African-American organ transplant patients. I’m wondering if these kinds of variations end up in that 0.1% variation part of the DNA sequences. And if so, how important is the Genome Project and mapping it in your work?

**GEORGIA DUNSTON:** Very important. Certainly one of the most challenging aspects of the Genome Project is the question of variation and its implications, both in terms of biology as well as the biomedical. There are a number of persons that are still concerned, in spite of the anonymity of the plan … are concerned about to what extent the first sequence will represent an anticipated norm, and not really at this point understanding fully how variation around that will be perceived. It becomes...

**JOHN HOCKENBERRY:** Well, I guess the example would be, you know, something we’re all familiar with, polling. In polling data, we get a sample that gives us some sense of the wider population that we’re studying, say, the electorate, or people who watch television, or whatever, in the various places that we use polling, and we know by the numbers that we choose how close we are to the actual expected variation in the whole population. Can you do the same thing when you sequence DNA?

**GEORGIA DUNSTON:** Well certainly you can get a sampling, and I certainly want to go on record as recognizing that we are more alike than we are different. But the reality is, those differences become very important in some types of biomedical interests. A single nucleotide
difference is known to cause changes that can have significant biomedical implications. So the concern is, while the Genome Project establishes a map as a resource for finding genes, and certainly the aspects of a map for all humans will be common enough, the question is now of the sequence of that map. We know that there’s tremendous variation among the entire human population, and it’s going to be very important for us to understand how much of that variation is biologically important, and how much of it is just a consequence of the nature of change in the genetic material, that is not, at this point at least, related to any of the biological problems...

JOHN HOCKENBERRY: Mmm.

GEORGIA DUNSTON: ...that we may be addressing.

JOHN HOCKENBERRY: Now, Francis Collins, you know, people who study evolution say that, in fact, there are wide differences in the variation factors in DNA, according to where you end up on the planet. And that in fact, if we accept the theory that human life began genetically and otherwise in Africa, the greatest amount of variation occurs among Africans, and so you’re better likely to get you know, a comprehensive DNA molecule from African-Americans, or from Africans, than you would be from Europeans. What do you say to that?

FRANCIS COLLINS: I agree with you completely. Again, the Genome Project has attempted to set up a new goal, which I think is going to answer many of these concerns, and that is to actually try to develop a catalogue of human variation. And you can think of this as an additional enterprise on top of getting that basic first sequence, which we’re trying to crank out by 2003. Again, that first sequence won’t tell you a thing about variation. If you want to study variation, you should study variation. So what we have done is to assemble a set of 500 DNA samples. They’re all collected from people in the United States because of the complexities of informed consent outside our borders. But they are people whose geographic origins are roughly evenly divided between Africa, Asia, Europe and the Americas prior to colonization – I’m talking about Native Americans. So in that set of samples, there is a pretty good representation, sort of a poll, as you were describing earlier, of the degree of variation that occurs within the human race…

JOHN HOCKENBERRY: Thomas Murray.

FRANCIS COLLINS: …and that will be a good starting point, I think.

JOHN HOCKENBERRY: Thomas Murray, is there a tradeoff though? If we begin to tag variations, we could slip down the road of, you know, racial identifications, behavioral identifications, and we can begin to make social judgements about people based on these conclusions we can draw about these various kinds of differences?

THOMAS MURRAY: That’s a good question, John. There’s no inevitability that that would happen, but there’s plenty of precedents in human history to be concerned about that. Clearly, that was part of the racial hygiene in the nineteen-twenties and thirties in Germany, a belief that first of all, biology determines destiny, that races were in fact biologically different, and that eventually, the conclusion was reached that some races are better than others. Georgia’s pointed out that the social category of race doesn’t correspond in any meaningful or consistent way with genetic differences among people. If folks will hear that message, that will help dispel some of the possible misuse. But there will be other efforts to try to explain – or explain away – all kinds of other group differences, and also to perhaps try to deal with social problems by reducing them to biology – by,
for example saying, Look, you know, maybe violence is really genetic at its roots, and if we could only identify those folks who are genetically predisposed and deal with them, then we could avoid that. That’s going to be a terribly simplistic, and, I think, ultimately dangerous way to deal with social problems.

JOHN HOCKENBERRY: All right, we’re going to talk more about the Human Genome Project in just a moment. But first, you know, what we discovered in assembling this radio series is if you take a few geneticists, and add a basketball, you’ll get some very interesting sideline conversations. Which is what we did.

[squeaking sneakers on wood floor, background voice, bouncing ball]

MAN 1: Most scientists that are working in the field don’t have the same concerns that much of the public does. I mean, particularly things about safety. Scientists feel that what we’re doing is very unlikely to be dangerous. We feel that most of these things are basically experiments that nature has probably tried already anyway.

MAN 2: The biggest fundamental difference is the speed at which you can make the change. And that, I think, scares a lot of people.

JOHN HOCKENBERRY: Some confident genetic scientists who work in the agricultural field, who wanted to assure us that their ability to play basketball has nothing to do with their scientific endeavors. That clip of tape is from our program, “Plants, Animals and Transgenics: a Tomato By Any Other Name.” And we’ll be exploring genetic engineering in that program and in the future.

As we just heard, the scientists are fairly blasé about, you know, all the changes that are taking place in the engineering experiments that they do. But that clashes significantly with the impressions of some members of the public. So, I want you to listen to the voice of Linda Rose, who spoke with us in New York City:

LINDA ROSE: I think it’s very exciting, the very interesting technologies that are emerging from the study of genetics. It’s a little scary sometimes.

JOHN HOCKENBERRY: That’s a woman named Linda Rose, who spoke with us outside the Natural History Museum in New York City. Vicki Whittemore, how would you reassure someone who expresses fears about this emerging science, based on your own experience?

VICKI WHITTEMORE: Well, the way I reassure our members when they talk to me about this in terms of tuberous sclerosis is that we would hope that genetic engineering, or genetic change, would be done to alleviate disease, alleviate some of the different manifestations of a disease, or perhaps, in the earliest phases, to prevent some of the disease aspect from happening. In terms of tuberous sclerosis, we know that that would have to be done at a very early stage, as we were talking about earlier, because some of the most drastic effects of this disease are in the formation of the brain, and there are actually abnormal parts of the brain in individuals with tuberous sclerosis that then go on to create seizures and many different behavioral outcomes.
JOHN HOCKENBERRY: OK, we’re going to take a short break. I’m John Hockenberry. You’re listening to The DNA Files, the Human Genome Project: Mapping the Future. We’ll be right back.

[music]

JOHN HOCKENBERRY: This is The DNA Files. I’m John Hockenberry and we’re talking about the Human Genome Project and its implications for all of our lives. With me is Georgia Dunston of Howard University, Francis Collins, co-director of the Human Genome Project, Thomas Murray, a bioethicist from Case Western Reserve University, and Vicki Whittemore of the National Tuberous Sclerosis Foundation.

Thomas Murray, you know, we understand both from the series and the prevailing science that exists right now, that germline therapy in genetic treatment of disease is extremely controversial. The idea that you alter a gene of a single individual, and that is going to be inherited, and therefore, potentially change every generation hence. It’s very controversial in humans. But it sounds like what these scientists just said is that we’ve been doing it for a long time with pigs. Can those sorts of conditions exist side-by-side without affecting humans?

THOMAS MURRAY: Do you mean can we do extensive germline gene therapy in, say, animals without ultimately being tempted to do it in persons?

JOHN HOCKENBERRY: Right.

THOMAS MURRAY: Probably not, John.

JOHN HOCKENBERRY: Well, that’s pretty scary.

THOMAS MURRAY: [chuckles] Well, I’ve been thinking quite a bit about germline gene therapy lately. First of all, I hope everyone understands who’s listening, that the kind of gene therapy that we’ve been experimenting with right now with humans is what’s called somatic. Basically, any change we make would die with the individual in whom it’s made.

JOHN HOCKENBERRY: Right. And then we actually have a whole program on that entire subject. I guess the general point is that if you do changes that will affect many, many generations hence, if you can already do it in animals, are you tempted to do it in humans?

THOMAS MURRAY: Well, are you tempted to do it? Surely.

JOHN HOCKENBERRY: Will you do it?

THOMAS MURRAY: Should we do it and will we do it? Well, I’m going to give two answers here. I’m going to sound like a traditional ethicist, right? I see two sides to the story. On the one hand, if you had the power right now, say you had Huntington’s disease in your family, which is a terrible disease that manifests in adulthood, mostly, and I could cure it in you, but I could also cure it in all of your offspring, so that you wouldn’t pass on the risk of Huntington’s disease to anybody else, it’s hard for me to see what the – and I could do it safely, without placing you at danger, say, by the techniques – what would be wrong with that? It’s hard for me to see.
JOHN HOCKENBERRY: All right. But let’s ask. Vicki Whittemore, would you sign up for a program like that?

VICKI WHITTEMORE: Yes, I would.

JOHN HOCKENBERRY: Okay. Continue, Tom.

THOMAS MURRAY: But then I see, suppose the technology becomes then widely established. We know it’s safe, that we can do it with some of the really terrible diseases out there. The ones that we’re quite confident where if we change the disease, that we’re not also making some bad changes in the long run for the people. I mean, you’re never absolutely certain, but we’re very confident, let’s say. On the other hand, if once we got the techniques available, we will use them to try to alter the genetic composition of our offspring in ways that are not so much preventing disease but to make them more desirable... I mean, I had the head of a program at a major university talk to me about a request that he had received for human growth hormone – not for gene therapy, for growth hormone. It was the parents of a girl who was 5’9. Her coach said, “Look, if she were four inches taller, we could get her a scholarship to any college volleyball program in the country. So, would you please give her growth hormone, ‘cause we’d like to make her four inches taller.”

JOHN HOCKENBERRY: Wow.

THOMAS MURRAY: Well, I did ask him what he did, by the way, and he said, We don’t...we don’t do that here. But suppose we could do it for somebody right at conception? We could do germline gene therapy so that the embryo that would grow into that person would in fact be several inches taller? Would some people be inclined to try to do that? And my answer is, probably, some people would.

JOHN HOCKENBERRY: So we’re there. We’re already there.

THOMAS MURRAY: Well, we’re not doing germline, but we have enhancement technologies that are currently at hand, or coming down the pike, that we’re going to have to deal with in, I think, pretty short order. I should note that growth hormone probably doesn’t make otherwise normal kids taller. We now are pretty confident we know that.

JOHN HOCKENBERRY: Right. That will help us with the mail here at the office…

[Laughter]

JOHN HOCKENBERRY: One very quick thing. I mean, isn’t it the case, shouldn’t we tell people that there isn’t a real one-to-one correspondence – and this is to you, Francis – one-to-one correspondence between factors and genes? I mean, it’s just as likely that the gene for the performance of your spleen also might involve, you know, how much you use dental floss.

FRANCIS COLLINS: Absolutely. It would be a mistake to imagine that complex human traits are simply determined by a single gene. It’s going to be a whole suite of genes, each one of which has a relatively modest effect, and of course then interacting with the environment, which is a major factor in many of the things that people talk about wanting to modify, including height, for
instance. The fact that we’ve all gotten taller in the West over the last several hundred years has nothing to do with the gene pool. It has to do with the environment.

JOHN HOCKENBERRY: All right, well, let’s take this all the way to the most extreme aspect of our human species. I mean, certainly what we look like defines us as humans, but the way we behave [chuckles] is really what characterizes us as human beings. And I’m wondering, can our genes tell us anything about our behaviors? About why we do the things we do? In fact, why this person seems to be having so much fun?

MAN 4: I’m a big jumper. I jump off cliffs, waterfalls, just – uh, it’s fun [laughter].

[sound of parachutist instructions and jumping]

JOHN HOCKENBERRY: Jumping off of waterfalls and out of planes. If you’re willing to jump out of a plane, does that mean – I address this to anyone on the panel – does that mean you have something called a novelty-seeking gene? Can behavior be traced to genes? That actual tape is from our program, “DNA and Behavior: Is Our Fate in Our Genes?” – which is a good question for the panel. Is it?

FRANCIS COLLINS: I’ll jump in here. Certainly there are features of human personality which you can measure on a standardized test that have heritable components, and novelty-seeking is one of those parameters that people measure. And I think any of us who have met identical twins recognize that they may share some behaviors, but they also, if you get to know them very well, are different in many significant ways, as far as the kind of human beings they are. And that, of course, is nature’s experiment to give us a clear window into what is DNA-based and what isn’t. Identical twins have the same DNA, but they are not the same human beings. And that should tell you right away that while there are heritable components to behaviors, it’s very complex. And if you are successful in identifying genetic contributors to things like novelty-seeking, they will be relatively weak, and people have already claimed some of that. They’re very difficult experiments to do and be sure you got the right answer.

JOHN HOCKENBERRY: Georgia Dunston, I’m wondering if your students come in to class prepared to hunt for genetic determinants of behavior, if they think that maybe some of their behaviors have a genetic component, and how controversial that issue is in class, especially if you’re dealing with issues like homosexuality, violence, shyness, addiction, problems that, you know, have very serious social consequences?

GEORGIA DUNSTON: Yes, the students are very interested in the potential to actually identify genes for complex characteristics such as violence. I take that one because that did raise quite a stir in the community. I think it’s very important when we start talking about behavior that we indeed recognize that behavior is also very much influenced by our perception of reality, of what we believe to be true. It’s very clear that we have education, we have environment, but we also have experience, and individuals’ experience in what they perceive to be reality. And how we behave is very much interwoven with that. And..

THOMAS MURRAY: John?

GEORGIA DUNSTON: …has been of some concern.
JOHN HOCKENBERRY: Tom, it sounds like you want to jump in there.

THOMAS MURRAY: Yeah. Sorry to have interrupted you, Georgia.

JOHN HOCKENBERRY: That’s okay.

THOMAS MURRAY: Um -

JOHN HOCKENBERRY: I do it all the time, so -

THOMAS MURRAY: Well, you’re allowed to.

JOHN HOCKENBERRY: Oh, thank you.

THOMAS MURRAY: There’s a kind of battle of metaphors out there about how important genetics is, and who we become. I liked your opening, by the way, the notion of a sort of performance of a piece of music. One metaphor that’s been suggested is that our genes are our future diary. I’m not a big fan of this metaphor. It implies that somehow genes sort of write the book that is our lives. A colleague of mine suggested a better metaphor is a weather report. I mean, it mostly tells you, Well, you know, it may rain a few days from now, but we’re not really sure of that. And there may be violent weather.

JOHN HOCKENBERRY: But let me ask you about that. I mean, certainly, if one – depending on where one lives – if you can, you know, toss another metaphor in here and think of the human genome as a map of the world, while you may not know the specific weather on a particular day, you certainly know, if you live in the Gulf, that you’re more likely to have hurricanes down there than if you live in the middle of the Sahara, where you’re never going to see rain, and even knowing that information would have significant social implications, yes?

THOMAS MURRAY: That’s right, John. If knowing that, for example, if a woman has a clinically important mutated form of the gene, the BRCA-1 gene, a gene linked to breast cancer, that that tells something about the risk of, lifetime risk of, breast cancer, that’s a bit maybe like living on the Gulf coast rather than living in Cleveland, and your risk of suffering damage from a hurricane. But it doesn’t prescribe exactly what kind of life you have. I’ve proposed a variation of the future diary metaphor. I think it’s useful for me, at least, to think about my genetic makeup, or anybody’s genetic makeup, as in some way making the physical book on which we will write. Some books are thicker than others, will have more pages to write upon. Other books, some of the pages are more difficult to write on. The paper may be coarser, more difficult. I mean those are days, months, years that are…through which we’re fighting against disease or disability. But that’s all it is. We have to write the book ourselves. It’s not written for us.

JOHN HOCKENBERRY: Francis, you know someone who probably hears these kinds of metaphors all the time, grammar, books, diaries, symphonies…

FRANCIS COLLINS: [chuckle]

JOHN HOCKENBERRY: …that sort of thing. Have you ever found anything, first of all, that, seems to be pegged to a behavior?
FRANCIS COLLINS: As a metaphor, I think we’re perhaps getting over our heads in these metaphors. I got a little lost in the Sahara Desert a minute ago.

JOHN HOCKENBERRY: That’s okay.

FRANCIS COLLINS: I would say that it’s important when we talk about behavior to recognize that we are already accommodated to the fact that genetics does influence that, and it has not destabilized us as a society. Two of your guests here on this panel are at twenty-fold increased risk of criminal behavior than the other two. That’s Tom and me, ’cause we have a Y chromosome, and that’s an observed fact. And yet I don’t think that has been used for anybody to deny responsibility for their actions, or be let off the hook if they robbed a Seven-Eleven. We’ve learned to deal with that.

JOHN HOCKENBERRY: So we should basically round up all the men and put them in jail, is what you’re saying.

FRANCIS COLLINS: Well, some people seem to think that’s what happening right now. But no, I’m saying actually just the reverse, that we have learned how to recognize the fact that there are biological contributors to human behavior. And that as we learn more about that in the coming years, as long as we keep in mind that these are elements but not the whole story, we should not encounter, I think, a circumstance where we’re suddenly all shook up.

JOHN HOCKENBERRY: Free will is alive and well.

FRANCIS COLLINS: Hallelujah.

JOHN HOCKENBERRY: Let me pose to the panel this final point that’s very much in the news. The FBI now has a national computer database that allows states to swap DNA evidence about unsolved cases. Now, much of this is sort of forensic data, but it has sparked the advocacy of a national DNA data bank for all of us, saying that genetic fingerprints should be useful in identifying missing persons, plane crash victims, medical research. What are the implications of such a national data bank? And let me begin with you, Tom, and we’ll go around the panel.

THOMAS MURRAY: Well, many years ago when the FBI was first thinking about this possibility, they faced a choice. Some folks were pushing a system of DNA identification that would actually be based on genes. That is, that it would not only be things that would make you uniquely different from somebody else, but might also give information. For example, suppose we had a DNA database, DNA fingerprint data for things like cancer-related genes? So then we’d not only have identifiers for you, but we’d know something about your cancer risk. At the urging of many people, they abandoned that possibility, and now they’re looking at markers which seem to vary randomly and have no other genetic meaning, so that they can be used to identify you, but don’t tell us anything about any behavioral or disease risk or propensity. So I think that was a wise choice that they made early on.

JOHN HOCKENBERRY: Georgia Dunston, what do you think about a DNA database?

GEORGIA DUNSTON: Again, my concern is the application of the information. Certainly, if the motive of the question is identification, DNA can be very useful in that type of definition. But the concern that I have is that we are all in agreement that the knowledge is unfolding very
quickly, and that technology is outpacing our capacity presently to integrate that knowledge or to understand it. A concern of many is the fear that new knowledge will be applied with old thinking. And that’s a real concern. To what extent will there be projections about identification, DNA information, that really are not justified? Certainly there’s no question when it comes to disease and understanding, identifying disease and correcting disease. But the Genome Project does raise us to the level of biology, as we’ve discussed, where more than disease is controlled by the genes. And the application of that information from a pathology kind of mindset of the disease is a concern of many, and areas that… programs like this, the education becomes very critical because the application of the information is what’s of concern.

JOHN HOCKENBERRY:  Mmm.

GEORGIA DUNSTON:  Not so much developing the information, but we’ve got to also improve in our understanding of how to best apply the information.

JOHN HOCKENBERRY:  Vicki Whittemore, some final thoughts on this issue?

VICKI WHITTEMORE:  Yeah, I agree with Georgia. I think the concern is, What would that information be used for, and how could it be used against me? And, you know, certainly with individuals with genetic diseases who have volunteered to be part of genetic research for that disease, trying to identify the gene, their DNA is in a database somewhere. But the thought of that being widely accessible and being… anyone – employer, insurance companies, the government – being able to use that against you, is a pretty frightening thing.

JOHN HOCKENBERRY:  Mmm.

VICKI WHITTEMORE:  And, you know, anyone who volunteers in these research studies, make sure that their DNA will not be shared, and that information is not shared with anyone. So I think what the FBI has done, to set it up in terms of identification, is okay, as long as that’s as far as that database goes.

JOHN HOCKENBERRY:  Francis Collins, I’m going to give you the last word. Do you think, in the future, when I get my hair cut, I should take a Ziploc® bag and maybe invest in a pair of rubber gloves to keep people from identifying me?

FRANCIS COLLINS:  Well, your DNA is located in all of the cells of your body, so it’s potentially possible people can collect that kind of information, and certainly Hollywood is having a good time with these various scenarios in some of the latest science fiction flicks. I think we do need to be vigilant about this, and I think the concerns that the others have expressed are right on. But I also think that we need not be fatalistic about these being unsolvable problems. We need, and we deserve, right now, effective federal legislation to prevent the use of genetic information to deny people health care and to deny them a job. And we can do that. It’s clear, with numerous policy discussions, exactly what needs to happen, what language ought to be in these bills. If we could just do it, and then reassure ourselves that those risks are greatly diminished, perhaps we could get a little beyond the current circumstance. And if we could set up privacy legislation, as well, that basically criminalizes an invasion of your privacy, to find out things that you did not give permission for regarding your DNA, that would also provide people reassurances. I think it’s time to act.
JOHN HOCKENBERRY: Interesting issues and tough challenges ahead. Thank you very much, Francis Collins, National Institute of Health Director of the Human Genome Project; Georgia Dunston is Professor and Chair of the Department of Microbiology at Howard University College of Medicine in Washington, D.C.; Thomas Murray is a bioethicist on the National Bioethics Advisory Commission, also a professor at Case Western Reserve University; and Vicki Whittemore is Vice President for Medical and Scientific Affairs of the National Tuberous Sclerosis Association. Thank you very much for a fascinating hour.

ALL: Thank you. Thanks, John.

[Theme Music]

Credits for The DNA Files:

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JOHN HOCKENBERRY: You’ve been listening to *The DNA Files*. I’m John Hockenberry.

For more information and for an interactive look at some of the issues behind this program, go to our website at [www.dnafiles.org](http://www.dnafiles.org). For tapes and transcripts of this program and this series, contact VisABILITy, Inc. at 303-823-8000. To contact *The DNA Files*, send your e-mail to feedback@dnafiles.org. *The DNA Files* Executive Producer is Bari Scott. The Project Director is Jude Thilman. Today’s program, “The Human Genome Project: Mapping The Future” was produced and edited by Loretta Williams. The engineer was Caryl Wheeler. Additional tape provided by Francesca Raymond and Ancel Martinez.

[music]

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