



**National
Multiple Sclerosis
Society**

**MS Learn Online
Feature Presentation
MS: the Genetic Connection: Part 1**

Tracey

Welcome to MS Conversation, I'm Tracey Kimball

Tom

and I'm Tom Kimball. Tracey, have you ever wondered why you have MS and nobody else in your family does?

Tracey

Although I'm glad for that, I do wonder why that is... and so do many researchers.

Tom

True. In the first of our two part series, MS: The Genetic Connection, we'll meet several people with MS, hear the questions they have, about the genetic connection, and hear what researchers have found out about the role of genetics in MS.

Tracey

Let's listen in.

HOST

As members of the human species, we are wonderfully complex creatures. Each of us is a result of countless genetic and environmental characteristics that make us truly unique individuals. We all share millions of factors that make us similar ... and millions that make us different. Of the billions of people on this planet, millions are united by a potentially disabling and mysterious disease ... Multiple Sclerosis.

Karen DeJoe

I was diagnosed with MS approximately 11 years ago, and it came at a time when I was just beginning my residency so I was right out of medical school.

Vincent Buchanan

I was diagnosed in January of 2001. At that time my symptoms were very small. The problem with progressive MS is it starts with something very minor, and then it gets worse and worse and worse.

Debbie Hazlett

I was diagnosed 4 years ago and like most people had symptoms I think probably since my early twenties.

Joann D'Amico Stone

I've had MS for just over 11 years now.

Joann D'Amico Stone

I lost the use of my right leg so I couldn't drive with my feet anymore, I went and learned how to drive with hand controls because I'm not going to be a prisoner in my own house. So I have a van that now has hand controls on it.

Maryann Murray

I'm a volunteer coordinator at the National MS Society central New England chapter. I have had MS officially diagnosed 09/2000, I have had symptoms since 1997 but it took them awhile to figure out what it was.

Frederick McKoy

I'm the youngest of 4, and no one else has MS, thank God for that, they don't want it.

Frederick McKoy 07:15.14 ++

People look at me and they think, you look fine Freddy. It messes different things, not just my face. My face looks ok people see me and say ok you look fine you don't look like you have anything wrong with you because I'm walking straight. Fine but I have something going on up here too you know (*points to his head*) you don't know about.

HOST

These people are typical of the hundreds of thousands throughout the US and Canada who have MS. Like so many others, they wonder how it is that each is one in 750 people who have contracted MS. More importantly, they wonder when researchers will find effective ways to treat, and ultimately cure this disabling disease.

Unfortunately, understanding MS is as complex as understanding the millions of factors that make each of us unique.

The logical place to begin is with the DNA molecule, the basic building block of every human being ... encrypted in what is known as the genetic code. Unraveling this code was the awesome task of the Human Genome Project, which began about 10 years ago and involved scientists from around the world. The first task was to sequence ... or decipher ... the 3 billion letters, called nucleotides, which make up the DNA molecule. Scientists succeeded in deciphering more than 99% of the sequence for a few individuals.

Then scientists compared the DNA of hundreds of individuals to see how much variation there is from person to person.

They found that of the 3 billion nucleotides that make up the entire human genetic code, only about 10 million are actually different from person to person.

That means scientists can focus on about one-third of one percent of the entire genetic code to study the variations that exist between two people. By comparing the base pairs of people who have MS with those who don't, scientists hope to identify the genes that may be associated with MS.

To help us further explore the current state of MS genetic research, we have two guests joining us in the studio, Dr. Steve Hauser is the chair of the department of neurology at the University of California San Francisco and Dr. John Rickert is the National MS Society's Vice President for research and clinical programs and as a scientist has an interest in genes and multiple sclerosis.

Dr Hauser let me begin with you. Why are we studying genetics in connection with multiple sclerosis.

Dr Hauser

Our hope is that genetic studies will make MS a simpler disease for us to study. Currently, sometimes it seems as if we know too much about multiple sclerosis, we know that allergic cells are turned on in the blood stream of people with MS. These cells move into the nervous system, they are turned on again, they make chemicals and other molecules that injure myelin, injure myelin producing cells and ultimately injure nerve cells as well. What we don't know is what begins this entire cascade of inflammation. Hopefully genetic studies will get us to the root cause of what begins the inflammation in MS.

Host:

Dr Rickert, with all the research options that the um, or the direction that the multiple sclerosis society could take, why are you concentrating on genetic research?

Dr Rickert:

Most commonly when people think about genetic research in MS // they think that we're talking about the ultimate cause of the disease, and while genetics are certainly going to play a significant role in starting out the cause of the disease, the information we will learn from genetic research is much broader than that. For example, it's likely that genetics research will help us understand why different people have different forms of MS. We'll have some remitting forms versus more progressive forms of MS. Genetics research is also likely to identify new genes in the immune system that will identify new therapeutic targets that we can aim new treatments toward. And so it is very likely in the short term we will have some new therapeutic opportunities as a result of the genetics research. It's also likely that we will understand that there is a genetic basis for why some people respond to some medicines and not to others and so it's very possible for example, that we will within a few years be able to customize therapeutic options for individual people based on their genetic background.

Host

Two scientists who have been involved genetic research are Dr. David Hafler, the Breakstone Professor of Neurology at Harvard Medical School and Dr. Dessa Sadovnick, Professor in the department of medical genetics at the University of British Columbia.

Dessa Sadovnick

I think that there was a false concept that people were getting that as soon as the human genome project was finished we would have a blue print for everybody's genetic material and you could just go in there and repair things // I think you have to realize that first of all there's so many interactions that happen between genes and each other and everything in a cell that it's not really that straight forward.

David Hafler

Now it still could be a few rare genes that are causing it but most geneticists feel, and I would agree, that it's more likely to be common variance of common genes which together lead to the risk of developing the disease.

David Hafler

If you have Muscular Dystrophy there is a defect in the gene that codes for protein that makes muscle. So if you have that gene not working you will get the disease. Its one gene, one disease.

David Hafler

Common immunological diseases such as rheumatoid arthritis, autoimmune diabetes, they're all complex genetic diseases. So it's not one gene, one disease but a series of common genes or variance of the common gene which come together and lead to the risk of developing the disease

HOST

Note that Dr. Hafler said that these variances "lead to the risk of developing the disease." What that means is that if you have the genetic variances that may be linked to MS, you have the *susceptibility*, to contract the disease, but it doesn't necessarily mean that you will.

Dessa Sadovnick

There are a lot of different risk factors for people with MS. There are genetic factors, which seem to be involved in susceptibility. There are also environmental factors that often in somebody who has the genetic susceptibility together the genetic and environmental factors will push a person over the threshold to show clinical disease.

Dessa Sadovnick

I honestly can say I don't think there is a specific universal trigger. I think it's very different in different people and what I also think is very interesting is we're finding more and more in our research that the trigger or what predestines you to eventually develop MS could possibly even be as early as when you're in the uterus.

David Hafler

Well it clearly is a complex interaction between the environment and genetics. One thing that Einstein said is that one wants to study the problems that are important and study problems that one can solve. Clearly understanding the environmental causes of MS is very important but it's a very difficult problem to solve and we don't really have the tools right now to solve it.

David Hafler

So the question often arises with patients // Is it a genetic disease or not?

David Hafler

What's very special in this moment in time is that we now have the tools to potentially answer the question.

HOST

Dr Hafler talks about having the tools to potentially answer the question. Dr Hauser how will we find the genes that unlock MS.

Dr Hauser:

Well using these wonderful new tools of molecular biology we can very efficiently map the variation between people with MS and people without MS. Across the 23 pairs of chromosomes and 3 billion building blocks of DNA that we all have inherited from our ancestors, we can do this in 2 ways. In people with MS who are unrelated to each other and in large families where multiple people have MS and both methods of genetic analysis, association and linkage are going to be complimentary in letting us pinpoint for the first time exactly which genetic changes predispose people to this disease.

Host:

Dr Rickert what is the National MS Society doing to stimulate genetic research around the world?

Dr Rickert:

The National MS Society has funded grants related to genetics for many years. In recent years we have decided that the field has moved to a point at which large scale projects would be very import // so we have targeted genetics as one of the areas that want to emphasize and that has allowed us to fund large scale projects related to MS. We have also felt that it is important to get the major investigators from around the world together and in the same room and talking together and putting together a strategy. So recently we have put together an international conference in conjunction with the National Institutes of Health at which the major investigators of MS genetics from around the world got together and began to develop strategies so there are all pulling together. One of the issues has been that there have been some very important major groups of MS geneticists who have been in competing research groups and we felt that it was important to the extent possible that they work together. So we provided a planning grant to a group of those investigators who have put together an international MS genetics consortium which has now successfully applied NIH funding on a large scale and this will move the field forward to a tremendous degree.

Tom

Indeed genetics research offers a lot of hope.

Tracey

Hope not only in the understanding of why people get MS but what therapies are best suited for people. Fascinating!

We'd like to thank all of you for joining us today for the first installment of MS: The Genetic Connection.

Tom

Yes and join us for part two when we'll learn more about the hope that lies in genetic research.