FIA NEWS

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A Newsletter for the Familial Intracranial Aneurysm Study

An Up-Date from the Desk of Laura Sauerbeck, RN, MS, CCRC, FIA Study Manager

The Familial Intracranial Aneurysm (FIA) Study has completed enrollment for the first phase and is currently resubmitting to the National Institute of Health for an additional 5 years of funding. This will allow the researchers to duplicate the findings of the first phase and to continue to follow the participants already enrolled while entering additional participants to give us further answers into the genetics of brain aneurysms. Below is an overview of the important findings from this study to-date.

Genetic findings:

To understand how these findings where obtained please read "New approaches to try to find genes that increase the risk for Intracranial Aneurysms" in this issue of the FIA Participant Newsletter.

Genome Screen to Detect Linkage to Intracranial Aneurysm Susceptibility Genes: The Familial Intracranial Aneurysm (FIA) Study

The genome screen has been completed on the first 192 completed families; thus far we have detected possible evidence of chromosomal regions contributing to the formation and/or rupture of brain aneurysm on 4 of the 23 pairs of chromosomes in humans. We also found potential evidence that smoking interacts with the genes in 3 of these areas. Attempts are underway to duplicate these findings and to identify the actual genes involved. For the published article on these findings please go to: http://stroke.ahajournals.org/cgi/reprint/39/5/1434.

Genome Screen to Detect Linkage to Common Susceptibility Genes for Intracranial and Aortic Aneurysms

In addition to reporting brain aneurysms families have also been reporting aneurysms elsewhere in the body including the chest and abdomen. The genome screen has been completed in 29 of these families and the findings suggest that a common genes maybe responsible for both Intracranial aneurysm as well as abdominal aortic aneurysms. The two chromosomes involved include chromosome 11 (which has been report previously by other genetic investigators) and chromosome 6. Attempts are underway to identify the actual genes involved. This article is in press and will be posted on the study website as soon as it is published).

The identification of the actual genes involved in the above results will allow for a rapid and cost-effective genetic screening test. Such a test will allow physicians to identify who is at risk for aneurysm development and who would benefit from further diagnostic testing.

Magnetic Resonance Angiography (MRA) Findings:

Screening for Brain Aneurysm in the Familial Intracranial Aneurysm Study: Frequency and Predictors of Lesion Detection

In the first degree relatives (parents, siblings, and children) of a person who has been diagnosed with an intracranial aneurysm, we found that between 19-20% of the participants who received a study MRA has an aneurysm that was previously undiagnosed. Those diagnosed with an aneurysm were over the age of 30 years, female or who had a history of smoking and/or high blood pressure.

This rate is much higher than the 1-2% prevalence of undiagnosed intracranial aneurysm in the general population which has been previously reported. This finding provides guidance to health care professionals for screening high-risk individuals, based on family and medical history, and will reduce the morbidity and mortality associated with intracranial aneurysm. For the published article on these findings please go to: http://thejns.org/doi/pdf/10.3171/JNS/2008/108/6/1130

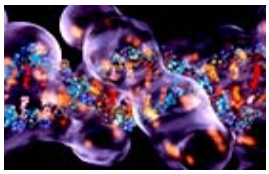
The Effects of Study Participation on in the Familial Intracranial Aneurysm Study on Cigarette Smoking

We found that after 3 years of follow-up participants in the FIA study had significantly decreased their smoking rates, in both those with a diagnosis of intracranial aneurysm, and to a lesser degree those without a known aneurysm. This demonstrates that high-risk individuals are willing to change to reduce their risk of a potentially life-threatening condition. Health care professionals should provide more aggressive risk factors education and smoking cessation strategies in this high risk group. (This article is in press and will be posted on the study website as soon as it is published).

The coordinating center encourages all FIA participants to monitor the study website for further findings.
http://www.fiastudy.org

New Approaches to try to Find Genes that Increase the Risk for Familial Intracranial Aneurysms

By: Tatiana Foroud, Ph.D.



In the past few years, there has been a revolution in the ways that researchers can study DNA, our genetic material. In the past, when we would begin to hunt for genes that increase the risk for Familial Intracranial Aneurysms we would analyze about 400 different positions along an individual's DNA. Today, it is now possible to test hundreds of thousands or in some cases even a million different positions along our DNA.

How are we able to do this? Let's begin with a review of DNA. Each cell in our body, with a few exceptions, contains deoxyribonucleic acid (DNA), which is the genetic building block. DNA is often depicted as a ladder. The rungs of the ladder are made up of a series of four nucleotides, coded by four different letters: A (adenine), T (thymine), G (guanine), and C (cytosine). The DNA sequence consists of over three billion letters. Within this sequence are particular stretches of DNA, called genes, that determine things such as eye color, hair color, and we believe influence an individual risk for Intracranial Aneurysms.

Researchers have known about the basic structure of DNA for nearly 50 years. However, we have only slowly been able to develop tools and techniques for the laboratory that will allow us to critically examine the DNA to identify very small changes in the DNA sequence that result in some individuals have an increased risk for a particular disease, such as Intracranial Aneurysms.

An important breakthrough that has greatly helped in the development of new methods to analyze DNA was the sequencing of the human genome. One of the unexpected discoveries from the Human Genome Project was that individuals have more variation in their DNA sequence than was originally thought – millions of changes have now been found in the DNA sequence. Most of these DNA sequence changes are likely to be benign with regard to health, but scientists have quickly learned to use this information to improve the ability to perform scientific research. New methods were developed and gradually improved to the point that we can now test hundreds of thousands of different positions along the DNA sequence in a single laboratory test.

It is important to note that even when a researcher is able to test hundreds of thousands of positions along the DNA sequence, there are still millions of positions that are not being tested. We are still just sampling some of an individual's genetic information.

What can we do with all of this new technology?
One of the important things that we want to do is help identify genes that increase the risk for Intracranial Aneurysms. One way to do this is to compare the DNA of individuals with a Intracranial Aneurysm with the DNA of individuals who do not have an Intracranial Aneurysm. While we cannot compare the entire DNA sequence of the individuals with a Intracranial Aneurysm and those without a Intracranial Aneurysm, we can compare the DNA at several hundred thousand positions. This is exactly what we are doing in the FIA study.

We are currently completing a study that compares the DNA at these many different positions in about 840 individuals with an Intracranial Aneurysm and 900 individuals who do not have an Intracranial Aneurysm. We are looking for variations at any one or more of these positions that occur more frequently in individuals with an Intracranial Aneurysm than in those without an Intracranial Aneurysm. We hope that through this analysis, we can get clues that will help us identify new genes that have made it more likely that some individuals will develop an Intracranial Aneurysm and others will not.

Glossary

Autosome - Any of the non sex determining chromosomes.

Cell - Small, watery membrane-bound compartment filled with chemicals; the basic subunit of any living thing.

Chromosome – Structures found in the nucleus of a cell. Normal human cells contain 46 chromosomes, 22 pairs of autosomes and 2 sex chromosomes.

DNA – A large molecule that carries the genetic information that cells need to replicate and to produce proteins.

DNA Sequence – Determines the exact order of the base pairs in a segment of DNA.

Genetics – the scientific study of heredity.

Genome – The substance of heredity. All the genetic material in the chromosomes of a particular organism.