Thank you for your support and participation!

The National Down Syndrome Project (NDSP) celebrates its fourteenth year of research in 2002. We have recently expanded our study to include families from New York, New Jersey, Arkansas, Iowa and California, in addition to our Atlanta families. Each year we send this newsletter to the families, doctors, counselors and others who have joined us in the study of Down syndrome (DS). Our goal in doing so is two-fold; first, to keep in touch with you and thank you for your vital participation and support of our project. Your help leads to the ability to better understand DS and its health complications. We also use this newsletter to inform you. We provide updates about the progress of our study and the accomplishments that result. We also give you updates about other research that involves DS or chromosome 21. In this issue you will find an explanation of the Human Genome Project, something you may have heard a great deal about in the news. We discuss the goals of the project and how it will impact the future of medicine both for those with DS and others. You will also find an article describing the different types of research currently going on in the field of DS. Researchers world-wide are studying DS and the interaction of the different genes of chromosome 21 that may lead to the specific characteristics of individuals with DS.

Inside these pages you will find information about protecting individuals who participate in genetic studies. The issue of "genetic privacy" is of concern to us all and we want to let you know how we protect your information as a study participant.

Finally, on page three you can read our mission statement that describes the questions we are investigating, and affirms our aims for the future. None of our goals would happen without your support and participation. Thanks to you we are working together to further our understanding of DS and the role our genes play in development.

Many thanks,

the National Down Syndrome Project team
Beyond the National Down Syndrome Project

What else is happening in DS research?

Worldwide, our study is now one of the largest projects devoted to a better understanding of Down syndrome (DS), but it is certainly not the only one. A survey of the National Library of Medicine's online database of articles from major scientific and medical publications (PubMed via www.ncbi.nlm.nih.gov/entrez) provides a fascinating list of topics attracting the attention of scientists and physicians involved in DS research.

For the two-year period from January 1999 to January 2001, PubMed lists over 600 research papers published world-wide on issues related to understanding more about DS. Because PubMed focuses primarily on medical and basic science topics, articles published in journals devoted to psychological, sociological, or educational issues are not included in this count. Listed below are the general areas covered in these 600 articles, beginning with the most common.

- General medical topics: 20%
- Development/behavior/learning: 16%
- Ageing/Alzheimer disease: 13%
- Leukemia/cancer: 10%
- Identifying chromosome 21 genes: 8%
- Chromosome function: 6%
- Speech/communication: 5%
- Nutrition/diet: 5%
- Mouse models (see below): 4%
- Heart defects: 3%
- Risk factors/oocurrence/epidemiology: 3%
- Oral health/dentistry: 2%
- Education: 1%
- Other: 11%

Are there racial differences in the frequency of Down syndrome?

The second in our series of frequently asked questions

Although Down syndrome (DS) has been identified across all racial and ethnic groups studied, recent studies seem to suggest the frequency of DS varies somewhat from group to group. Although such results are still preliminary, when compared with Caucasians, the frequency of babies born with DS in the United States appears to be slightly higher among Hispanics and slightly lower among African Americans. What do such findings mean? If these differences are due to biological reasons, it could point to differences among racial groups in the rate of chromosome nondisjunction (errors in the chromosome distribution in eggs and sperm). Or, DS pregnancies may differ among certain ethnic groups in their chance of survival to birth. However, because these studies examine the frequency of DS at birth, the differences among the groups may not actually be due to biological reasons. The difference in frequency could be related to the use of prenatal diagnosis or the reporting of this condition. Clearly, additional research must be carried out before we can understand the reasons for these differences.

What in the world is a mouse model of Down syndrome?

Medical research presents a problem! Scientists and physicians who want to learn about conditions important to health and well-being don't experiment on their "subjects" - that is, on humans! Additionally, the human system is so incredibly complicated that researchers often wish they could begin their work with a simpler system that can act as a model for conditions seen in humans.

Enter the mouse! Mice have chromosomes just as humans do. They have a different number of chromosomes, but we share many genes in common, and the genes are arranged along the chromosomes similarly. For example, mouse chromosome 16 has many of the same genes found on chromosome 21 in humans and these genes are in the same order. If someone could create a mouse with an extra chromosome 16 (that is, trisomy 16), would that mouse have any of the features, such as heart defects and developmental delays, found in trisomy 21 (Down syndrome) in humans?

Yes and no. Scientists have "made" a mouse with three copies of the chromosome 16 mouse genes that are similar to genes on human chromosome 21. These mice do not have the heart defects found among many individuals with Down syndrome, but, interestingly, they do show learning problems. Thus, these mice are particularly interesting to researchers who are studying brain development and function in individuals with Down syndrome. In addition, these mice may be useful in testing drugs thought to improve mental performance. There are other genes on human chromosome 21 not found on mouse chromosome 16, but on mouse chromosomes 10 and 17. Work is underway to "make" mice that have extra copies of these genes as well. Work is also progressing on engineering mice with three copies of just one human chromosome 21 specific gene, instead of three copies of many genes. This approach will let us determine the contribution of each gene to the characteristics of Down syndrome. As more and more genes on human chromosome 21 are identified, this type of research holds promise to understand the function of these genes and their role in Down syndrome.
Decoding the secrets of the human genome

Over the past year we have seen a number of exciting discoveries in the field of human genetics. One of the most significant is the publication of the draft sequence of the human genome, announced in February 2001. The sequence is called “draft” because it represents a first look at the data - there are a few gaps to be filled in and a few mistakes to be corrected. The “finished” sequence is expected in 2003.

What is a genome?

A “genome” represents the DNA found in a person, animal, plant, virus or bacteria. By examining the genome, scientists can identify the genes found in that DNA. Genes carry the information for making an individual. They determine how we look, how we grow and develop and how we break down food into energy for our cells.

What has the genome told us?

The sequence of the human genome has been compiled by many scientists from across the globe over the past 11 years. A first look at the draft provides some interesting results. Among them:

- Less than 2% of all the DNA in our genome actually directs the production of proteins. The other 98% either regulates this production or has no known function.
- There are only about 40,000-50,000 genes in the Human genome, many fewer than previously estimated. This compares with 6,000 genes for yeast, 13,000 for flies, 18,000 for worms, and 26,000 for the plants in our gardens. Understanding which genes make us so different from these other creatures remains a challenge for the future. In addition, we know the function of fewer than half of the identified genes. Work in this area promises to keep scientists busy for years.

What possible benefits can come from knowing the sequence and function of all our genes? As we learn more about the ways specific forms of genes interact with each other and with our surroundings, we will better understand the ways our genes can cause diseases like cancer, Alzheimers, heart defects and so on. Doctors can begin to treat diseases by looking at their basic causes, rather than just treating the symptoms they see.

What can we learn about Down syndrome?

How does the sequencing of the human genome affect our research with Down syndrome? Thanks to the efforts and support of families, doctors and researchers worldwide, chromosome 21 is among the first of the chromosomes to be “finished”. The sequence tells us that there are about 250 genes on chromosome 21. Scientists are working to identify the function of each. Work is also underway to understand what occurs when three copies of each gene are present, as in individuals with Down syndrome (see article on page two for a list of other types of research involving DS).

Our mission statement

Trisomy 21, the leading cause of Down syndrome, occurs when a child receives three copies of chromosome 21 instead of the usual two copies. This is almost always due to a chromosome error during the formation of either the egg or the sperm (see figure at right). Our first goal is to discover how these errors occur and identify risk factors that affect this process.

Secondly, we want to understand why an extra chromosome 21 causes the characteristic developmental pattern that we know as Down syndrome. We hope to identify specific genes on chromosome 21 that alter development and produce the mental retardation, congenital heart defects, and other clinical problems associated with Down syndrome.

Our hope is that increased knowledge about Down syndrome will benefit families, educators, and health professionals.

Both father and mother have the usual number of chromosomes, including two copies of chromosome 21. Here we show only chromosome 21.

The father’s sperm have one copy of each pair of chromosomes, including chromosome 21.

The mother’s eggs have one copy of each pair of chromosomes, including chromosome 21.

Occasionally, an egg or sperm is formed with an extra copy of chromosome 21.

This example shows the extra chromosome forming in the egg.

Union of this egg with a normal sperm leads to a child with three copies of chromosome 21 - Down syndrome.
Protecting human research participants:
“If I agree to be in the study, how do I know you won’t test me for all kinds of things?”

Earlier this year, the national news (6/6/01, PBS) told a story of the misuse of genetic testing. After several workers at the Burlington Northern and Santa Fe Railroad reported developing work-related carpal tunnel syndrome, a type of hand injury usually caused by repeated motion, company officials ordered medical exams and blood sample collection. Reportedly, without the employees’ knowledge, the blood was used to test for a genetic defect that might explain the carpal tunnel syndrome. The news report implied that the company would not be responsible for the injuries if a gene was found to “cause” the syndrome. Leaders in the field of genetics who were interviewed for the story strongly stated it was unethical to do this type of genetic testing without the knowledge and consent of the individual.

Medical researchers know that each time these issues are identified and reported, the job of recruiting study participants becomes harder. The increased interest resulting from the successful mapping of the human genome (see the article on page 3) has also made the public increasingly aware of the possible misuse of personal genetic information by insurance companies and employers. Accordingly, researchers must tell the people in their study about the specific purpose of the study, the limits of any genetic testing, and the methods used to safeguard privacy. To make sure that this responsibility is carried out faithfully, most research institutions have an Institutional Review Board (IRB).

The statement of purpose from the Emory University IRB is “To assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in research.” In just a few words this sums up a very important, but very lengthy and difficult process that researchers must complete before they can begin any study that involves humans. Research plans ranging from the simplest, such as completing questionnaires, to complicated clinical trials of promising new drugs and experimental procedures are all closely examined by an institution’s IRB to make sure the proper safeguards are in place. The IRB reviews a detailed description of the project, as well as all consent forms, recruitment brochures, letters, and any other documents to be used in the research study.

In the National Down Syndrome Project, every site involved in the research has had to obtain approval from at least one local IRB, often more. In all cases, the approved research proposals clearly state that the purpose of our research is confined to the study of Down syndrome and that the privacy and confidentiality of participants are strictly guarded. Everyone on the National Down Syndrome Project, including recruiters, lab personnel and data analysts take every effort to uphold these goals and to make sure that the research accomplished is of the highest standard.

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