

## Genetics, Environment and Lifestyles of People with Spondyloarthritis—Unlocking the Secrets

# WHAT IS TASC (TRIPLE “A” ANKYLOSING SPONDYLOARTHRITIS CONSORTIUM)?

As many of you know from scanning these pages and by attending the SAA Patient Educational Seminars during the past several years, a great deal has been happening in spondyloarthritis research. In brief, up until June 1998, there was very little activity in AS research in the U.S. except for a very small dedicated group of researchers. Then in 1998, under the guidance of Dr. John D. Reveille, the SAA initiated, with member support, the AS Family Genetic Project. Following suit, during the next ten years, the situation in AS research in the United States vastly improved as interest grew and activity increased as more researchers became involved in this group of diseases:

- In 1999, the AS Family Genetic Study evolved into an National Institute of Musculoskeletal and Skin Diseases (NIAMS) multimillion dollar funded consortium of eleven medical centers nationwide called NASC, out of which came the identification of the regions on several chromosomes implicated in AS;
- in 2001, NIAMS funded the first prognostic study of outcomes in AS, called PSOAS;
- in 2002, the first genome-wide scan results from the NASC study were presented and were subsequently published in a peer-review publication;
- in 2003, a group of AS “thought leaders,” comprised of researchers, clinicians and the SAA, joined forces to form SPARTAN, which stands for the Spondyloarthritis Research and Treatment Network;
- in 2004, the genome scan results from the NASC study were combined with a large British genome-scan and a smaller scan from France—soon to be published;
- in 2006, the NIH and the SAA co-sponsored the “Spondyloarthritis: The Unmet Needs” conference which led to a more comprehensive picture of where spondyloarthritis research needed to be heading.

### What is a Genome-Wide Scan?

In diseases and other characteristics that form who we are as individuals, it is our chromosomes that determine what gets passed on to the next generation. Most people have two sets of 22 chromosomes, each inherited from a parent. Then there are the chromosomes that determine our sex. These are called the X and Y chromosomes. During a Genome-Wide Scan, the DNA, which has been extracted from the blood sample, has markers placed along the chromosomes, each of which are different sizes. This method of observation allows researchers to see whether a gene for the disease lies near one of the markers to determine risk areas—in our case—for AS. For example, the HLA-B27 gene, which is very much implicated in AS, is located in a group of genes called major histocompatibility complex (MHC). This is a large genomic region or gene family found in most vertebrates and is located on chromosome 6 in humans. Genome-Wide Scanning technology has vastly improved in recent years. This improvement allows for more efficient scanning with less likelihood of missing information in between the markers, which means, potentially, good news with regard to all of our efforts. For more information, please visit an online tutorial called “What is Inheritance?” <http://learn.genetics.utah.edu/units/basics/tour/inheritance.swf>

- concurrently, along with these events, a new class of drugs, called biologics or TNF-blockers, was brought to market that immediately began to show tremendous promise in the treatment of spondyloarthritis patients.

Furthermore, the results of the NASC study eventually formed the building blocks upon which Dr. John Reveille and his colleagues were able to found a new NIAMS-funded AS genetic study called TASC (Triple “A” (Anglo/Australian/American) Ankylosing Spondylitis Consortium). In addition, during this time span, doctors also learned how to

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take better care of spondyloarthritis patients by developing scoring systems to measure disease activity, functional impairment and spinal mobility, as well as by improving techniques in radiography. What these scoring systems potentially enable doctors to do is to listen more carefully to how people with spondyloarthritis are functioning in their daily lives and responding to treatments.

There is still much work to do—we are not out of the woods with regard to early diagnosis, better treatments and access to those treatments for all, and ultimately to learn what causes this disease in the first place. Even so, many doctors now believe that today they are much better equipped to care for people with spondyloarthritis than they were ten years ago.

As we move forward, the researchers who lead the TASC study believe that the future burns bright in spondyloarthritis and that this project, with its multiple components, will truly make a difference, not only on the research bench, but more specifically in the lives of people living with AS and its related diseases.

#### **What is TASC and what is it seeking to accomplish?**

The purpose of the TASC Genetic Study, which is supported by a grant from NIAMS and led by Dr. John D. Reveille,

is to characterize the genes and genetic networks involved in predisposition, cause and outcome of ankylosing spondylitis. The study will span five years from 2007 through mid-2011. In the initial phase of the study, Dr. John Reveille in Houston, Dr. Matt Brown in Australia and Dr. Paul Wordsworth in Oxford will be comparing data, via a genome-scan, from 1,000 people in the United States with ankylosing spondylitis, and 1,000 people from the U.K. who have ankylosing spondylitis to uncover all of the genes throughout the entire genome that are associated with the disease

The big difference between the old techniques and what we are able to do today is that in the old scan, researchers were looking at 400 markers and today, Dr. Reveille's team will be looking at 317,000 markers. What this means is that a much wider area of the genome will be covered and hence, the spaces in between the markers will be much, much smaller.

In the next segment of the study, the researchers will be looking at family members of people with AS to find out more about the associated diseases such as reactive arthritis, inflammatory bowel disease in spondylitis and psoriatic spondylitis to try to find out how all of these work together within the family group. Later in the study, the researchers will be looking at the data from 900

### **We need you!**

Moving forward, we would like to thank all of the people who have already so generously participated either in NASC or in TASC. We could not have gotten this far without you. We still need to enroll more patients and their non-affected family members or friends in order to meet our goals. If you have not yet participated in an AS Genetic Study and would like to help, please turn to the back cover of this issue of your Spondylitis Plus to find out how to contact us in order to help. Thank you.

patients to examine the non-genetic factors and how these may relate to disease severity. For instance, socio-economic factors will be examined—mood, and different personality traits will be plotted. All of these things will be identified to see how they may influence disease progression. The objectives of this part of the study will be to determine whether in the future, it might be possible find out whether certain behaviors or lifestyles might have an impact on disease severity, and if so, what potential changes might be adopted in order to improve the outcome or prognosis of the disease in the individual.