



National Alopecia Areata Foundation

An information excerpt from NAAF Newsletter Number 124 | Fall 2006

*Be Part of the Registry!
Be Part of the Cure!*



The Importance of the National Alopecia Areata Registry

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Alopecia areata is an autoimmune disease. It is mediated by nerves and cytokines, which are messenger cells that go around the hair follicle and disrupt the hair pattern. One of the early NAAF research grants went to Dr. Maria Hordinsky and me to start looking at how HLA (human leukocyte antigen) genes may affect alopecia areata; we got funding back in 1987 to start looking at HLA genes in people with alopecia areata and in multiplex families. The HLA is important because it lets T cells recognize foreign proteins by antigen presenting cells (APCs). In alopecia areata we think that the hair follicle or cells in the hair follicle such as melanocytes may be the target for this immune reaction.

Why is this relevant to the National Alopecia Areata Registry? All of these interactions between cells depend on proteins, and those proteins are made by genes, which we can study in patients, comparing patients with alopecia areata to normal patients and looking at different stages of the disease for different protein levels. Alopecia areata is caused by genes. T cells release chemicals that are called interleukins and cytokines that cause the inflammation. These genes make these chemicals and regulate these chemicals. HLA genes also control which proteins our immune system sees, and perhaps the different severity of alopecia areata versus alopecia totalis versus alopecia universalis is due to interactions of different genes. There may be genes that make you lose your hair or react to something in the environment, there may be genes that cause the hair loss to continue for a long period of time, and there may be genes that let you grow your hair back. There could be as many as 6 or 12 genes that cause this.

We did another study, which was also funded by NAAF, that looked at alopecia areata in identical twins and it was very fascinating to learn that only half of identical twins both get alopecia areata. The first twin gets it more severely. We think that means that there's an

HLA association; all of the twins had DQ 302, which is an HLA molecule that's very common in 80 percent of alopecia areata patients. Many of the twins reported stress as a precipitating factor. We looked at one virus called CMV and found no association, but there are other viruses and vaccines that might trigger alopecia areata.

What is the National Alopecia Areata Registry? It is a medical registry that is funded through a contract with the government. More specifically, it is funded through a part of the government called the National Institutes of Health (NIH), and even more specifically, it is funded through the branch of the NIH that is the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS). We competed for the registry. We submitted an application that was four inches thick. This application was created with the collaboration of Drs. Vera Price, Maria Hordinsky, David Norris and Angela Christiano, with our center, the M. D. Anderson Cancer Center, as the principal investigator. We applied for and were awarded this registry in September of 2000. Because of all the regulations, it took us between 6 and 12 months to get going and to get everybody onboard, to get Institutional Review Board approval for everything, and to get all the paperwork done. The registry was funded in two parts. The first part is self-registration for patients, and the second involves blood sampling of patients for research studies. There are five registry locations all around the country where this takes place — at the University of California, San Francisco with Dr. Vera Price; at the University of

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Colorado in Denver with Dr. David Norris; at the University of Minnesota in Minneapolis with Dr. Maria Hordinsky; at M. D. Anderson Cancer Center in Houston with me; and at Columbia University in New York with Dr. Angela Christiano.

We mentioned the HLA genes that have been discovered in alopecia areata. It is possible that HLA genes 4 and 5 may together cause the more severe form of alopecia areata, whereas genes 1 and 5 together might cause patchy alopecia areata. That is the kind of hypothesis that can be tested utilizing information and blood samples in the registry. You look at the genes and at who gets the disease, and you determine where the genes and the numbers of people with the disease localize together.

Multiplex families are families where three or more members have alopecia areata, and multiplex families of many members are the most powerful tools for doing genetic linkage. It is important that we register not only all the people with alopecia areata in such families but also all siblings and the parents. Through the registry, we have identified 200 multiplex families, which is fantastic, and we've acquired all the members in about 20 of these families. We would like to get at least 100 totally ascertained families, which means that everybody in the family has given a blood sample. With this linkage power, we should be able to find almost all of the genes that cause alopecia areata in a very short time. Dr. Christiano has just been given another grant by the NIH to actually study linkage in these families, looking at the genes that track, so now is the time for you to call your relatives who have alopecia areata and ask them if they have registered. Get your whole family registered. Let's do all we can to get the samples into the registry, so Dr. Christiano can continue this important work.



Dr. Madeleine Duvic speaks with conference attendees at the Medical Questions and Answers Session.

Sibling pairs with alopecia areata are also very important to us. And again, we hope to register not only the two children with alopecia areata but all of the children in the family plus the parents.

When just one person in a family has alopecia areata, we can combine the information from that single individual with other single individuals who have alopecia areata and compare it to singles who are unrelated match controls and find differences in the increases or decreases of genes that cause alopecia areata. Even if you don't have a family history of alopecia areata or a brother or sister with alopecia areata, you're still important to our effort, so please register.

The purpose of the registry is to find and collect samples from multiplex families, sibling pairs, and individuals and to encourage research by investigators. The samples that we collect are available for any researchers who have grants and want to study alopecia areata. We can also notify registry participants when there's a drug study that needs a lot of patients.

If we have your permission to do so, we mail you a postcard describing the study, and then, if you want to participate, you can contact the centers that are doing the study. That's another part of the registry that I don't think has been given enough vocalization.

Who funds the registry? You do. It's your tax dollars that fund the registry, and that money comes to us through the National Institutes of Health. The registry is very user friendly. If you go to alopeciaareataregistry.org, you'll get our registration site. You can complete the initial registration form online, or you can print out a copy of the form and complete it and mail or fax it to us. The main registry e-mail address is alopeciaregistry@mdanderson.org if you have questions. The telephone numbers and additional contact information can be found on our Web site and on the NAAF Web site.

If you've registered in the past and you want to update your information, you can go back online and give us some more



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information. If you want to participate in the second phase of registration, providing us with a blood sample, you can go to your dermatologist's office and have your blood drawn locally if you can't make it to a center. We allow that. We have to get your consent over the phone but you can have the blood work done locally. We also look at your pattern of alopecia areata, your skin, and your nails. And in some cases, we seek photos to confirm a diagnosis.

We are collecting a lot of epidemiology data through the registry. We don't know what causes alopecia areata in addition to genes, so we want to look at different aspects like who got virus vaccinations before they got it and who got stressed. So eventually we will be able to analyze the epidemiology data for all the people who registered.

Confidentiality is important to us. Everyone who registers is assigned a code number. No one except the registry personnel knows your name or your addresses. It's all anonymous. Your name will never be given out to anybody unless we contact you and get your permission to do that.

Anyone who is a US resident can register in the first tier. Anyone with any kind of alopecia areata can register in the first tier. Eventually you have to have a diagnosis confirmed by a dermatologist or someone who's a hair specialist. We have a number of incomplete registrations where people have completed part of the registration, but they have not finished it. As of the start of the NAAF conference, we had about 5,000 completed first-tier registrations. We want to increase our enrollment of minorities in the coming year. And we want to get more men involved. There are more women than men who have registered, and we want to balance that out; we want the same numbers of men and women because that is in accord with the epidemiology of this disease.

People with alopecia universalis are really heavily represented in the registry, but we also want to register people who have transient alopecia areata—people who have just one patch of hair loss that goes away. We want to understand the genes involved in every type of hair loss and regrowth, and we also want to get controls. So if you have a friend who doesn't have alopecia areata, ask them to register and be a control.

For the second tier of the registry, we need 500 patients with each

kind of alopecia areata and we're not there yet. We're about halfway there. We need multiplex families, sibling pairs and twins.

We now have blood samples from 1,451 patients, so we really have a lot of work to do in the next four or five years.

We also have quality of life questionnaires. Quality of life is very, very important, and we have already done one study on quality of life with Stephanie Austin, one of Maria Hordinsky's fellows.

I want to underscore some of the progress that has taken place because of the registry:

- We've confirmed the HLA associations that were previously reported in our alopecia areata patients, so we know these HLA associations are real and that we're collecting information that's real.
- We've studied cytokine profiles in patients with alopecia areata and atopy.
- We've looked at the incidence of self-reported alopecia areata in the alopecia areata patient population.
- We've undertaken a quality of life study in teenagers with alopecia areata.
- Dr. Christiano has found four new regions in the chromosomal DNA that are associated with alopecia areata and she's looking for the genes in these regions right now.

The opportunity is now. If you want effective treatment and a cure for alopecia areata, this is the time to register. I also want to thank everyone who has already registered for their support. I think that through the registry genetic studies will actually find the genes that cause alopecia areata, and once we know the genes, we will be able to create small molecules or antibodies and things that interfere with those genes and improve therapy. This can't happen without you all being part of the registry, so thank you. ■