PXE Awareness

National Association for Pseudoxanthoma Elasticum (NAPE, Inc.)

Volume 16, No. 2, July 2010

Coping Until the Cure:

A PXE Patient-Centered Conference

Philadelphia, Pennsylvania

October 22 and 23, 2010

Gene Patents Ruled Illegal - see page 8

National Association for Pseudoxanthoma Elasticum (NAPE, Inc.)

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NAPE, a non-profit 501(c)(3) support group whose mission is to provide education and support for PXE-affected persons, publishes *PXE Awareness*. Articles in this newsletter are provided for information only and are not a substitute for professional medical advice. You should not use information in this newsletter to diagnose or treat medical or health conditions. Please consult your healthcare provider before beginning or changing any course of treatment.

Board of Directors

Board of Medical Advisors

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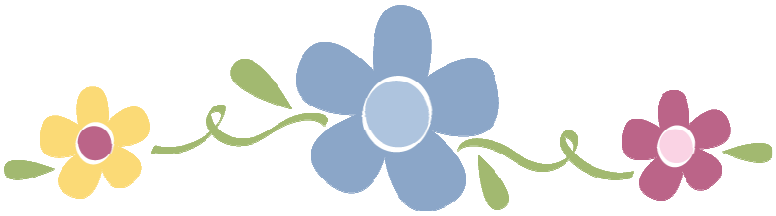


President's Message

It's time to begin thinking of our fall conference scheduled for October 22 and 23 in Philadelphia. Our meeting, focused on patient concerns, features three new partnerships. Matthew Lange, long-term NAPE member, will share his research on PXE and individualized nutrition. Lee Ducat of the National Disease Resource Interchange (NDRI) will share NDRI's new rare disorder program to provide human biomaterials to scientists. Sandra Park, attorney for the American Civil Liberties Union (ACLU), will discuss the law related to the patenting of human genes. Our faithful guides of many years, Drs.Ken Neldner and Berthold Struk will speak and be available for your questions. Drs. Kattesh Katti and Ravi Shukla will update their research and plans to apply nanotechnology to PXE/AMD treatments. NAPE members in the U.S. and Canada will receive a special mailing later this month. We hope you will join us prepared to participate, to build relationships with peers who live with PXE, and to gain much useful information.

This issue focuses on the patenting of human genes, the lawsuit challenging these patents, the federal district court ruling voiding such patents, the upcoming appeal of that ruling, and NAPE's position in this important matter. This is exceedingly important to NAPE because our ABCC6 gene was patented. Please read our article to learn how you can help to make certain that scientific research on PXE can proceed unfettered.

Hope to greet you in Philadelphia this fall.

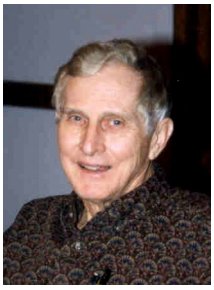
Frances Benham

2010 NAPE CONFERENCE SCHEDULE

Holiday Inn (Fort Washington)
Philadelphia, PA

Friday evening, October 22, 2010

4:00-4:15 pm	Introductions/Conference Information
4:15-5:45 pm	NAPE's Story - Kenneth Neldner with Lenore Seeuwen



6:00-9:00 pm	Dinner, discussion, making new PXE friends
7:00 pm	Gene Patents Ruled Illegal -Sandra Park, American Civil Liberties Union

Saturday, October 23, 2010
(Breakfast on your own)

8:30-8:45 am Introductions/Conference Information

8:45-10:00 am Nanotechnology, AMD and PXE
-Kattesh Katti, PhD, and Ravi Shukla, PhD

10:00-10:20 am Break

10:20-12:00 noon What Patients Need to Know
And Do About PXE
- Berthold Struk, MD, PhD

12:00-12:15 pm Break

12:15-1:45 pm Lunch

1:45-3:00 pm Supporting Research with Human
Biomaterials
-Lee Ducat with NDRI Staff

3:00-3:15 pm Break

3:15-4:30 pm PXE and Nutrition Research
-Matthew Lange

4:30-5:00 pm Board Update

5:00 pm Conference Adjourns

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REGISTRATION FORM – 2010 NATIONAL MEETING

Friday, October 22 – Saturday, October 23, 2010

The registration fee is $45 per person and includes Friday evening dinner, Saturday lunch and breaks, plus all handouts

NAME _____ **PHONE** _____

ADDRESS _____ **EMAIL** _____

CITY _____ **STATE** _____ **ZIP** _____

NUMBER ATTENDING MEETING _____ x $45.00 = AMOUNT ENCLOSED $_____

NAME(S) OF GUEST(S) ATTENDING WITH YOU:

You are responsible for making your own hotel reservations. Please call the **Holiday Inn, Fort Washington, Philadelphia, PA, at 215-643-3000 or 1-800-339-0209**. Be sure to **call by October 10, 2010**, and say you are with NAPE to get the group rate of $89 per night (single or double) plus tax. Please indicate that you are with the NAPE conference. Parking on site is free.

Payment of the registration fee must accompany this form. Please make your check payable to NAPE, Inc., in U.S. currency. We cannot accept credit card payments. Mail your registration and check to NAPE at the address shown above. We will send you a confirmation packet if registration is received by October 10.

Check here _____ if need vegetarian meals. If you require special assistance to participate fully, please provide a written description of your needs on the back of this form.

If you are willing to share a room and its associated cost, check here _____. NAPE will provide your contact information to others who are willing to share a room. It will be your responsibility to make contact and decide if you are willing to share a room. NAPE will not be involved other than to provide contact information of those who provide permission.

SIGNATURE _____ **DATE** _____

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CANCELLATIONS ARE NOT REFUNDABLE AFTER OCTOBER 10, 2010

Gene Patents Ruled Illegal

The following article has been derived with permission from the American Civil Liberties Union (ACLU) website (www.aclu.org/brca). It has been edited and information about pseudoxanthoma elasticum has been added where appropriate. NAPE is grateful to the ACLU for providing permission to share this material with the NAPE family. Additional information regarding the content of this article is provided at the end of the article.

On Sunday, April 4, 2010, CBS's *60 Minutes* featured the story of biotech companies patenting human genes, thus controlling testing for them as well as research to develop better, perhaps cheaper, tests and possible treatments for genetic disorders. The program focused on hereditary breast and ovarian cancer, believed in many women who develop it to be caused by a gene mutation. Myriad Genetics patented the genes involved, creating their own tests which were not authorized for use unless their full price was paid. And Myriad was not alone. Twenty percent of human genes have been patented by biotech companies, other organizations and even some by individuals.

The U.S. Patent and Trademark Office (USPTO) granted thousands of patents on human genes which gave patent holders exclusive rights to genetic sequences, their usage, and their chemical composition. Anyone who used a patented gene without permission of the patent holder – whether for commercial or noncommercial purposes – was committing patent infringement and could be sued by the patent holder for such infringement.

Because the USPTO granted patents on the genes themselves, it essentially gave patent holders a monopoly over the patented genes and all of the information contained within them. Gene patent holders had the right to prevent anyone from studying, testing or even examining a gene. As a result, scientific research and genetic testing have been delayed, limited, or even shut down due to concerns about gene patents, and patients' options regarding their medical care have been restricted.

On May 12, 2009, the ACLU and the Public Patent Foundation (PUBPAT) filed a lawsuit challenging the USPTO's practice of granting patents on human genes – specifically, the BRCA1 and BRCA2 genes, which are associated with breast and ovarian cancer. The lawsuit was filed on behalf of scientific organizations representing more than 150,000 geneticists, pathologists, and laboratory professionals, as well as individual researchers, breast cancer and women's health groups, genetic counselors, and individual

women. Groups supporting the plaintiffs include the American Medical Association, the American Society of Human Genetics, March of Dimes and the National Organization for Rare Disorders (NORD), among many others.

So, what exactly is a gene? Genes are the basic units of heredity in all living organisms. A gene is a segment of DNA, the molecules that contain instructions for the development and functioning of living organisms. It is estimated that humans have approximately 25,000 genes that make up our genome. DNA is found inside each cell's nucleus, and is organized into structures called chromosomes. Humans have 46 chromosomes – two sets of 23, with one set coming from each parent. The human genome can be thought of as a set of encyclopedias with 23 volumes, where each chromosome represents one volume. The DNA code is like the letters that are used to build the words, paragraphs, and pages of text in those volumes. Because genes vary in size, they can be thought of as a single paragraph or an entire chapter inside each volume.

The BRCA genes – BRCA1 and BRCA2 – are two genes that have been associated with hereditary forms of breast and ovarian cancer. Everyone has these genes. BRCA1 and BRCA2 are believed to be tumor suppressor genes, which means that when they are functioning normally, they suppress the growth of cancerous cells. Women who have certain mutations along these genes have an elevated lifetime risk of developing breast and ovarian cancer because their ability to suppress cancerous growth has been reduced. A woman with a BRCA mutation faces a 36 to 85 percent chance of contracting breast cancer and a 16 to 60 percent chance of ovarian cancer.[1] BRCA mutations are also linked to breast and prostate cancer in men.

Myriad Genetics, a private biotechnology company based in Utah, controlled patents on the BRCA1 and BRCA2 genes. Because of its patents, Myriad had the right to prevent anyone else from testing, studying, or even looking at these genes. It also held the exclusive rights to any mutations along those genes. No one was allowed to do anything with the BRCA genes without Myriad's permission. Such patents are awarded for twenty years.

A 2005 study found that 4,382 of the 23,688 human genes in the National Center for Biotechnology Information's gene database are explicitly claimed as intellectual property.[2] This means that nearly 20% of human genes are patented. In addition to the BRCA genes, genes

associated with numerous diseases, both common and rare, are patented, including Alzheimer's disease, asthma, some forms of colon cancer, Canavan disease, hemochromatosis, some forms of muscular dystrophy, Long QT Syndrome, pseudoxanthoma elasticum and many others.[3,4,5,6,7]

The patent system was designed to grant certain rights to inventors for their inventions in order to reward and encourage human ingenuity. But genes are naturally-occurring parts of our bodies, not inventions. Researchers identify genes; they don't invent them. U.S. law recognizes this difference. There is long-standing legal precedent that "products of nature" are not patentable. You can't patent gold or other basic elements, for example.

Nevertheless, the USPTO ignored this obvious discrepancy for roughly 20 years and issued gene patents on the basis that genetic sequences are "isolated and purified." But all this means is that the gene has been removed from the human body and the non-coding regions of the gene stripped away. These steps – simple enough for any graduate student in genetics or a related field to perform – do not make a gene patentable, any more than removing gold from a mountain makes gold patentable. This is why the ACLU sued the USPTO, to get them to stop issuing such patents which are contrary to the law.

BRCA1 and BRCA2 are not the only genes involved in breast and ovarian cancer. There are other genes that are involved, though perhaps not as strongly linked as the BRCA1 and BRCA2 genes. In addition, there are most likely additional cancer-related mutations along the BRCA1 and BRCA2 genes than those for which tests are currently conducted, including mutations that have not yet been identified. Nearly 2,000 distinct mutations and sequence variations have been found along BRCA1 and BRCA2.[8] However, due in part to the limitations that gene patents have placed on studying the two genes, the significance of many of these mutations is unknown.

Many researchers around the world were involved in identifying the BRCA1 and BRCA2 genes. Most of them did not seek patents or did not enforce any patents obtained by their universities because they wanted research and testing to continue openly and unfettered by exclusive monopoly rights.

Myriad was granted patents on both the BRCA1 and BRCA2 genetic sequences, as well as any mutations along those genes. That means, if you were to take the gene you have in your body and remove it from all the other biological material that surrounds it, you would be committing patent infringement regardless of how or why you did it. Myriad also was given

patents on any methods for locating mutations, whether those methods are known now or not, and they also held patents on correlations between mutations and breast and ovarian cancer. The plaintiffs in this case did not challenge any patent claims over specific tests for mutations.

The ACLU and PUBPAT argued that gene patents violate both existing patent law and the Constitution. Patent law has long held that products of nature and laws of nature are not patentable subject matter. The USPTO failed to abide by this precedent when it granted patents on human genes. Human genes, even when removed from the body, are still products of nature, and their associations with diseases are laws of nature. The First Amendment protects freedom of thought, academic inquiry, and the exchange of knowledge and ideas. Gene patents implicate the First Amendment because the very *thought* that there is a relationship between specific genetic mutations and diseases has been patented and because scientific inquiry is limited.

The Patent Clause in Article 1, Section 8 of the U.S. Constitution gives Congress the power to award patents "to promote the Progress of Science and useful Arts, by securing for limited Times to Authors and Inventors the exclusive Right to their respective Writings and Discoveries." Human genes are not inventions, and awarding patents on them does not promote the progress of science. Instead, gene patents slow scientific advancement, because there is no way to invent around a gene – the gene is the basis for all subsequent research.

Scientific researchers' rights are violated because gene patents prevent them from freely engaging in research and exchanging information about patented genes. If a researcher wanted to study a gene that had been patented, s/he must obtain permission from the patent holder or risk being sued for violating the patent. The USPTO gave patent holders the unrestricted authority to refuse research licenses, to charge high licensing fees, and to sue and/or shut down researchers who do not have a license. Using the patent power granted to it by the USPTO, Myriad forced researchers to pay for Myriad's testing services if they wanted to tell genetic test results to women participating in their studies.

Clinical geneticists' and genetic counselors' rights are violated because gene patents infringe on their freedom to provide patients with information about their susceptibility to genetic diseases. Like researchers, clinicians must obtain licenses to conduct clinical testing,

and as with research licenses, the USPTO gave the patent holders the authority to refuse to grant testing licenses, to charge high fees, and to shut down un-licensed testing. Genetic counselors are forced to refer their patients to the laboratory dictated by the patent holder and are restricted in the service they can provide patients. Myriad did not allow anyone else to conduct full sequencing testing on the BRCA genes, which means that, although there are many qualified geneticists who could conduct tests and provide patients with results, no one but Myriad was allowed to do so. Myriad sent cease-and-desist letters to several laboratories in the United States to stop them from providing BRCA testing.

Individual patients' rights were violated because gene patents impede access to medical information and care. The patent holder controls what information people can obtain about their own genes, how they may obtain the information, and from whom. The USPTO allowed gene patent holders to control the price of diagnostic testing, whether the quality of their tests can be assessed, whether testing can be improved and alternative tests developed through research, and whether patients can get a second opinion. The monopoly the USPTO granted to Myriad on BRCA allowed Myriad to charge high rates for its testing – over $3,000. Women who could not afford this price and whose insurance companies did not cover the test had no access to BRCA testing. The USPTO also gave Myriad the power to decide that it would not contract with particular insurance providers. There are many qualified geneticists who could do the testing for less, but were not allowed to because of Myriad's enforcement of its patents. Myriad did not allow anyone else to conduct full sequencing testing on the BRCA genes, so Myriad alone could examine a woman's genes to determine if she had mutations that have so far been associated with a higher risk of hereditary breast cancer. There was no way for a woman to know if the test had been done properly, to verify that the results received from Myriad were accurate, or to undergo an alternative method of testing.

The USPTO allowed Myriad alone to determine which mutations on the BRCA genes to look for. For a period of time, Myriad's method of testing had a false negative rate that was estimated to be as high as 12%.[9] When Myriad decided to extend its testing to look for the mutations its standard test was missing, it chose to offer the new testing as a separate test, at an additional cost. The USPTO gave Myriad the sole power to determine what to do with the data it collected from people who were tested. Women who received test results indicating that they had a "variant of uncertain significance" had no way to access further testing to find out if they were at elevated risk for cancer or to force Myriad to share their data with other researchers. African-

Americans, Hispanics, and Asian-Americans were disproportionately likely to receive these ambiguous test results.

The American public's rights were violated because gene patents permitted an unfair monopoly that limited the public's right to benefit from scientific breakthroughs that advance medical research. This monopoly had a chilling impact on other researchers' ability to conduct medical research, undermining advances towards better treatments, cures, and more accessible, affordable genetic testing. This blocked the public's right to know about, share, and benefit from research that helps lead to better medical care for cancer and other life-threatening diseases. Such a monopoly serves to profit one company at the expense of the public good.

The primary purpose of the patent system is to foster innovation. The USPTO awards the patent holder certain exclusive rights over his/her invention in return for sharing information about the invention so that others can "invent around" it – that is, improve upon the original invention and design alternatives. This is best illustrated by an example: When the first cell phone was invented in 1973, the inventor, Martin Cooper of Motorola, was able to patent his particular device. He was required to publish information about the device so that other inventors could learn from it and invent their own alternative devices. Hence the plethora of cell phone companies and options we have today. But genes are different from cell phones and other things that are patented because they are not inventions, and other researchers cannot invent alternative genes. Even if patent-holders publish information about the genes they have identified, there is nothing to invent around – the genetic material contained in the gene *is* the information. Because this information is the foundation for future diagnostic tests and potential treatments, tying it up as intellectual property can inhibit, rather than stimulate, advances in biomedical research.

People who support gene patents often argue that genetic investigation is like drug development and will not take place without the incentive of the patent system. But studies sponsored by the federal government have established that gene patents, unlike other patents, are not required to incentivize research.[10] The Human Genome Project sequenced the *entire human genetic sequence* and did not patent any of the genes it identified. More than five million dollars of federal tax money funded the pursuit of the BRCA1 gene specifically.[11] Overall, much of the world of science has progressed

without any expectation of patents: Einstein's equation, $E=MC^2$, and his theory of general relativity were developed without any patent incentives.

The ACLU lawsuit was filed in May 2009, challenging the grant of patents on human genes. More specifically, plaintiffs challenged the granting of patents to Myriad Genetics over two genes (BRCA1 and BRCA2) that correlate with an increased risk of breast and/or ovarian cancer. In March 2010, a United States District Court in New York held that human genes were not patentable and voided the patent claims that had been challenged. The defendants have appealed to the United States Court of Appeals for the Federal Circuit.

The Board of Directors of NAPE (the National Association for Pseudoxanthoma Elasticum) voted to strongly support the position that no human gene should ever be patented. Representative Xavier Becerra (Democrat of California) introduced H.R. 977, the "Genomic Research and Accessibility Act" during the 110th Congress to bar the issuance of gene patents. He would like to reintroduce a new version of the bill this year, but needs our help. Representative Becerra needs support from colleagues on both sides of the aisle if his bill has any chance of being enacted. Please urge your members of Congress to join Representative Becerra by signing on as a cosponsor of this important piece of legislation. In this way you will be helping to assure that scientific research on PXE will continue unfettered.

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1 National Cancer Institute, "Genetic Testing for BRCA1 and BRCA2: It's Your Choice." *Available at* http://www.cancer.gov/cancertopics/factsheet/risk/brca.

2 Kyle Jensen & Fiona Murray, "Intellectual Property Landscape of the Human Genome," *Science* 310(5746):239-240 (October 14, 2005).

3 Ronald Kotulak, "Taking License with Your Genes: Biotech Firms Say They Need Protection," *Chicago Tribune*, September 12, 1999.

4 US Patent No. 6,037,149 (issued March 14, 2000).

5 Mildred K. Cho, et al., "Effects of Patents and Licenses on the Provision of Clinical Genetic Testing Services," *Journal of Molecular Diagnostics* 5(1):3-8 (February 2003).

6 Arthur Allen, "Who Owns My Disease?" *Mother Jones* 26(6):52-59 (November/December 2001).

7 Wendy Chung, "Statement to the House Judiciary Subcommittee on Courts, the Internet and Intellectual Property in Connection with a Hearing on Stifling or Stimulating – The Role of Gene Patents in Research and Genetic Testing," October 25, 2007.

8 National Cancer Institute, "Genetics of Breast and Ovarian Cancer (PDQ): Major Genes: Mutations in BRCA1 and BRCA2." *Available at* http://www.cancer.gov/cancertopics/pdq/genetics/breast-and-ovarian/HealthProfessional/page3.

9 Tom Walsh, et al., "Spectrum of Mutations in BRCA1, BRCA2, CHEK2, and TP53 in Families at High Risk of Breast Cancer," *JAMA* 295(12):1379-1388 (March 22, 2006).

[10] Secretary's Advisory Committee on Genetics, Health, and Society, "Public Consultation Draft Report on Gene Patents and Licensing Practices and Their Impact on Patient Access to Genetic Tests," March 2009.
[11] Bryn Williams-Jones, "History of a Gene Patent: Tracing the Development and Application of Commercial BRCA
Testing," 10 *Health Law Journal* 123, 131 (2002).

Additional sources of information about gene patenting:

Action alert to encourage Congress people to co-sponsor a bill prohibiting patents on genes:
https://secure.aclu.org/site/Advocacy?cmd=display&page=UserAction&id=2281

A Facebook page has been created for discussion and more frequent updates:
http://www.facebook.com/pages/Dont-Patent-My-Genes-Liberate-the-Breast-Cancer-Genes/111528515533018

Blog which rounds up recent media coverage on the BRCA gene patents lawsuit, with links to a 60 Minutes story and a Stephen Colbert clip:
http://www.aclu.org/blog/free-speech-womens-rights/scientists-pundits-and-journos-weigh-dont-patent-our-genes

Other blogposts are linked here:

Court decision invalidating the BRCA patents (March 2010)
http://www.aclu.org/blog/free-speech-womens-rights/who-owns-your-genes-you-do

First federal court hearing on whether genes can be patented (February 2010)
http://www.aclu.org/blog/free-speech-womens-rights/first-federal-court-hearing-whether-human-genes-should-be-patented

Amicus briefs filed by the American Medical Association and March of Dimes (August 2009)
http://www.aclu.org/2009/08/28/how-the-patents-on-the-breast-cancer-genes-harm-physicians-and-patients

Video of the plaintiffs who brought the gene patent lawsuit (May 2009)
http://www.aclu.org/2009/05/13/liberate-the-breast-cancer-genes

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