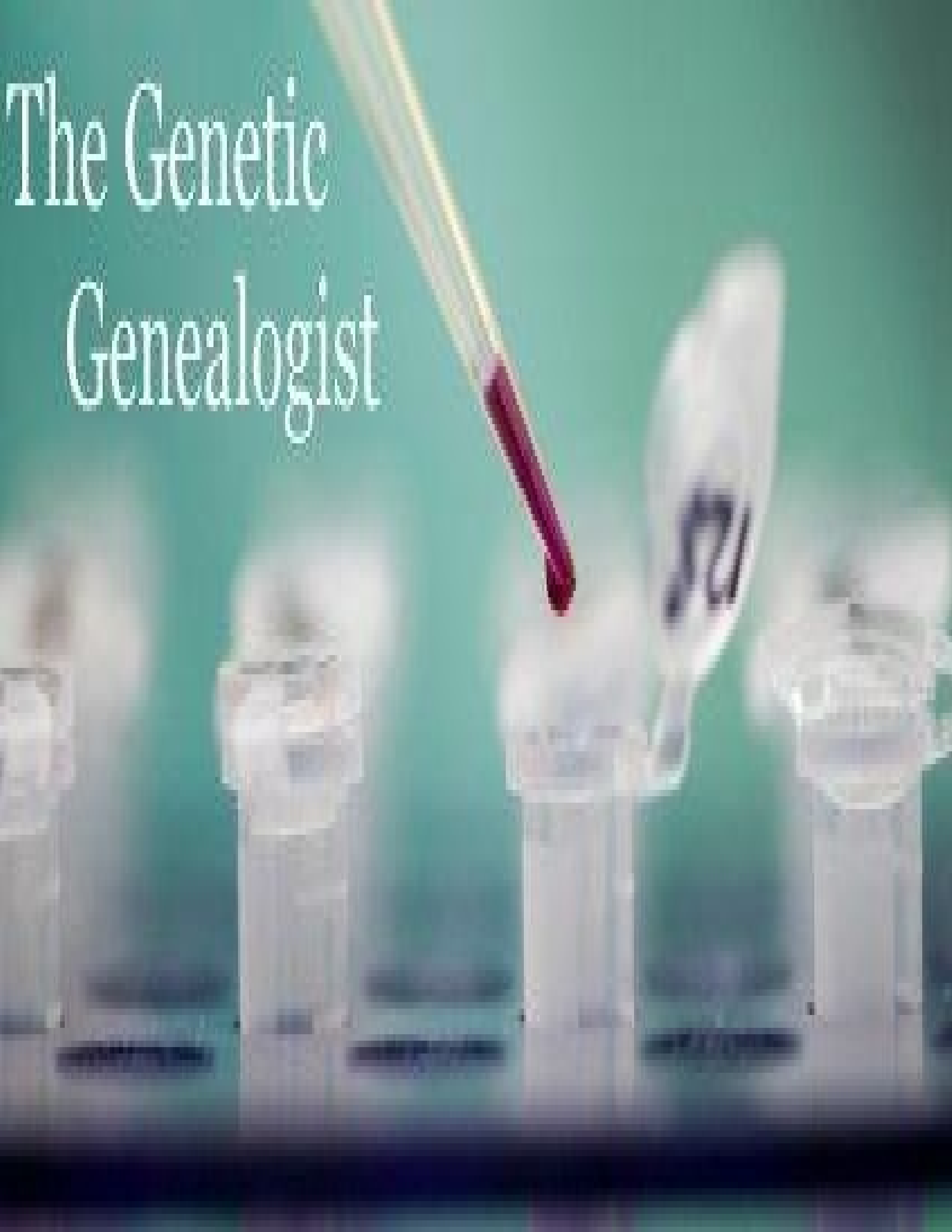
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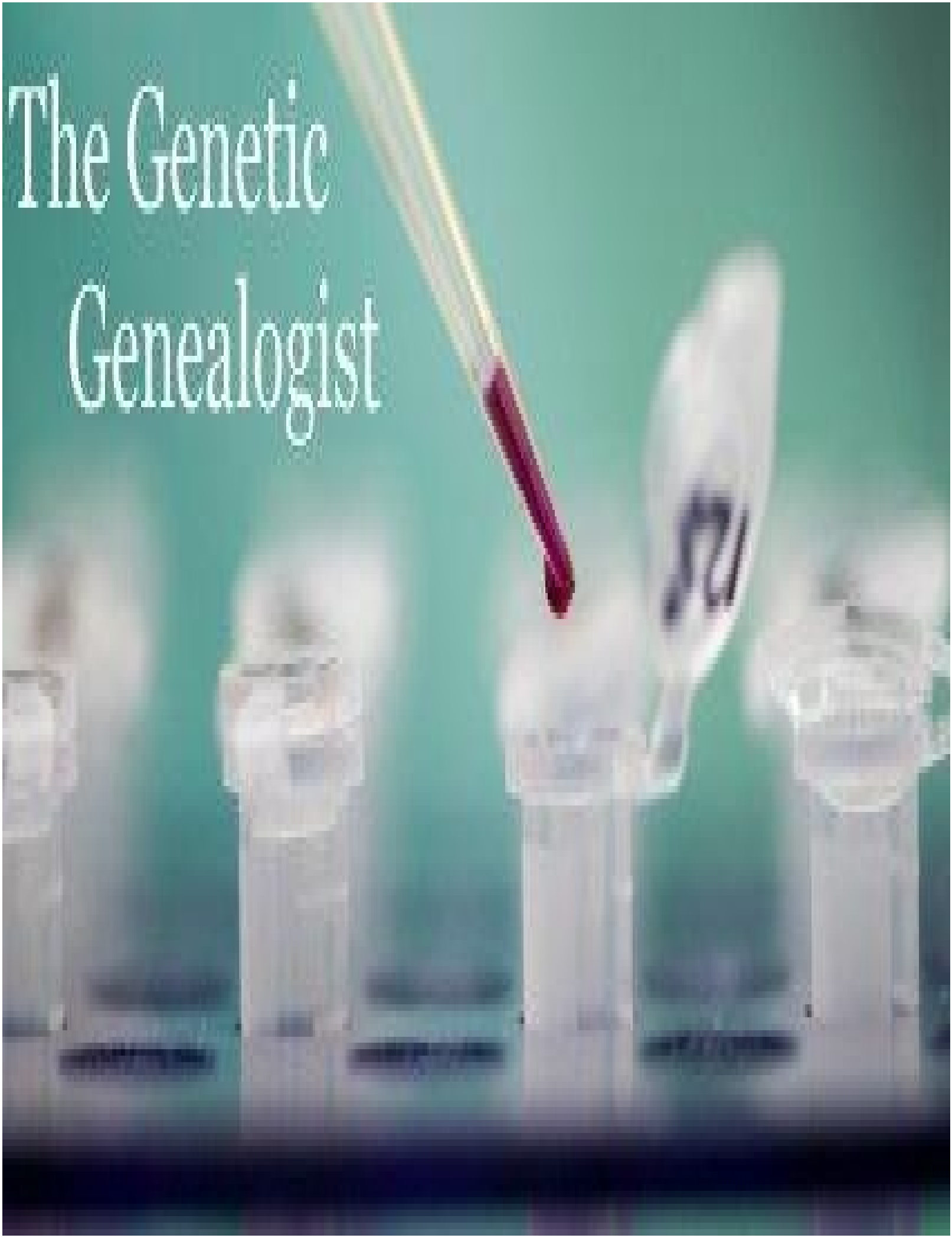

The Genetic
Genealogist

# 10 DNA Testing Myths Busted, and Other Favorite Posts

*By Blaine T. Bettinger*

Blaine Bettinger is the author of The Genetic Genealogist. He has been using traditional genealogical research for almost 20 years and is interested in the intersection of genealogy and DNA Testing. In 2006 he received his Ph.D. in biochemistry with a concentration in genetics. He is currently a second-year law student.

# 10 DNA Testing Myths Busted

(Originally posted October 25, 2007)

1**. Genetic genealogy is only for hardcore genealogists.**

Wrong! If you've ever wondered about the origins of your DNA, or about your direct paternal or maternal ancestral line, then genetic genealogy might be an interesting way to learn more. Although DNA testing of a single line, such as through an mtDNA test, will only examine one ancestor out of 1024 potential ancestors at 10 generations ago, this is a 100% improvement over 0 ancestors out of 1024. If you add your father's Y-DNA, this is a 200% improvement. Now add your mother's mtDNA, and so on. However, please note the next myth:

**2. I'm going to send in my DNA sample and get back my entire family tree**.

Sorry. DNA alone cannot tell a person who their great-grandmother was, or what Italian village their great-great grandfather came from. Genetic genealogy can be an informative and exciting addition to traditional research, and can sometimes be used to answer specific genealogical mysteries.

**3. I would like to try genetic genealogy, but I'm terrified of needles.**

Good news! Genetic genealogy firms don't use blood samples to collect cells for DNA testing. Instead, these companies send swabs or other means to gently obtain cells from the cheek and saliva.

**4. I would like to test my ancestor's DNA, but they died years ago**.

You don't always need your ancestor's DNA to get useful information from a genetic genealogy test. If you are male, you contain the Y-chromosome (Y-DNA) that was given to you by your father, who received it from his father, and so on. Both males and females have mitochondrial DNA (mtDNA), which was passed on to them by their mother, who received it from her mother, and so on. Everyone of us contains DNA (Y-DNA and/or mtDNA) from our ancestors that can be studied by genetic genealogy.

**5. I want to test my mother's father's Y-DNA, but since he didn't pass on his Y-chromosome to my mother, I'm out of luck.**

Wrong! There is a very good chance that there is another source of that same Y-DNA. For instance, does your mother have a brother (your uncle) who inherited the Y-DNA from his father? Or does your mother's father have a brother (your great-uncle) who would be willing to submit DNA for the test? Sometimes there might not be an obvious source of "lost" Y-DNA, or no one in the family is willing to take a DNA test. The secret to solving this problem is to do what every good genealogist does – use traditional genealogical research (paper records, census information, etc) to "trace the DNA". Follow the line back while tracing descendants in order to find someone who is interested in learning more about their Y-DNA. This applies to finding a source of mtDNA as well.

**6. Only men can submit DNA for genetic genealogy tests, since women do not have the Y-chromosome.**

Wrong! Most genetic genealogy testing companies also offer mtDNA testing. Both men and women have mtDNA in their cells and can submit that DNA for testing. In addition, women can test their father's or some other male relative's Y-DNA to learn more about their paternal ancestral line, even though they did not inherit the Y-chromosome.

**7. My genetic genealogy test will also reveal my propensity for diseases associated with the Ychromosome and mtDNA.**

Wrong, thank goodness. Most of the information obtained by genetic genealogy tests has no known medical relevancy, and these firms are not actively looking for medical information. It is important to note, however, that some medical information (such as infertility detected by DYS464 testing or other diseases detectable by a full mtDNA sequence) might inadvertently be revealed by a genetic genealogy test.

**8. I don't like the thought of a company having my DNA on file or my losing control over my DNA sample.**

This is, of course, an understandable concern. However, most testing firms give a client two options: the DNA is either immediately destroyed once the tests are run, or it is securely stored for future testing. If the DNA is stored, the firm will typically destroy the DNA upon request. If the long-term storage of DNA is a concern, be sure to research the company's policy before sending in a sample.

**9. If my test reveals Native American ancestry, I plan to join a particular Native American affiliation group.**

Although genetic genealogy can potentially reveal Native American ancestry (for instance, my mtDNA belongs to the Native American haplogroup A2), it is incredibly unlikely that this information will be sufficient to positively identify the specific source of the lineage (such as a tribe) or allow membership in a particular Native American affiliation.

**10. My DNA is so boring that genetic genealogy would be a waste of time and money.**

Very wrong! A person's DNA is a very special possession – although everyone has DNA, everyone's DNA is different (okay, except identical twins – if your identical twin has been tested, you should think twice about buying the same test!). As humans settled the world, Y-DNA and mtDNA spread and mixed randomly. As a result, it is impossible to guess with 100% assurance that a person's Y-DNA or mtDNA belongs to a particular haplogroup (a related family of DNA sequences) without DNA testing.

**BONUS MYTH: My genetic genealogy test says that my mtDNA belongs to Haplogroup A2. Juanita the Ice Maiden, a frozen mummy discovered in the Andes Mountains in Peru, also has Haplogroup A2 mtDNA. Therefore, she must be my ancestor!**

Unfortunately, although genetic genealogy can reveal that a person is RELATED to an ancient DNA source, it cannot prove that a person is a DESCENDANT of an ancient DNA source. For instance, perhaps you are descended from Juanita's sister, or her 5th cousin. Thus, although Juanita might be your great-great-great-great…great-grandmother, she might instead be your great-great-great-great…great-aunt. And since Juanita died when she was just 12 to 14, it is unlikely she has any descendants.

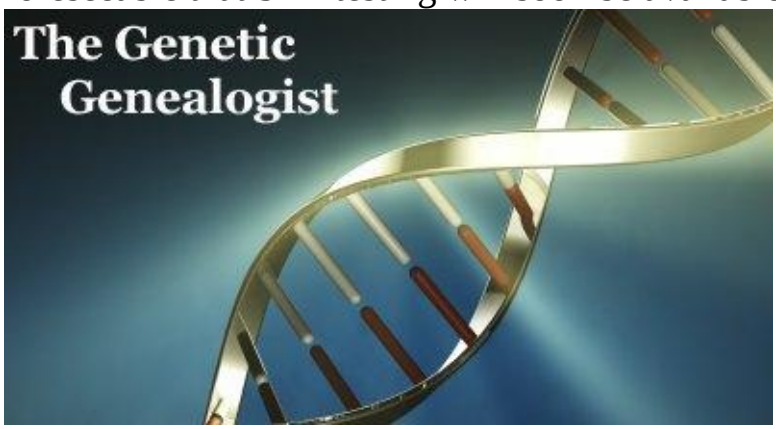
If you understand the risks associated with genetic genealogy (such as the detection of non-paternal events) and other risks) and are ready and willing to embrace the results to learn more about your genetic ancestry, then genetic genealogy might be for you. I recommend that you read archived posts here at The Genetic Genealogist, and do some online research through one of the many companies that offer genetic genealogy testing

# To Sequence or Not to Sequence - That is the Question

(Originally posted October 15, 2007)

An article appearing Sunday at Bloomberg.com, "Cheap, Detailed Genetic Testing Might Soon Be Ready for Market", highlights some of the recent developments in DNA sequencing. The article is a response to three studies published at Nature Methods which reportedly "explore cheap technologies to decipher and analyze individual patients' DNA by allowing researchers to quickly find the small portions of the human genome that make protein and describe them, while discarding irrelevant data."

According to the author of the Bloomberg article, "complete" DNA sequencing for as little as $300 could be ready within months. Although it is unclear what the author means by "complete", it is entirely foreseeable that SNP testing will soon be available for a reasonable price.



## All this leads to the question which is so hotly debated in the blogosphere - if inefficient sequencing becomes available to the average consumer, should they get their genome sequenced?

As the article points out, there are already around 1,000 different DNA sequencing tests which range in price from $200 to $3,000. However, Cathy Wicklund, the president of the National Society of Genetic Counselors, believes that people should "think hard before asking for complete genome testing":
"Just because we have the technology doesn't necessarily mean that we should jump to offer it," she said. "Consumers should ask themselves, `What is this going to tell me, is it going to give me information that's helpful right now?' "
There are a number of strong voices in this arena, others who believe that genomic sequencing without further extensive studies that link genotype and phenotype is useless and potentially harmful to any consumer who does not have a strong genetics background. Although I respect this position, I believe that attempting to ward people away from genomic sequencing will prove to be ineffective. Genetics is about to leave the hands of the medical professional, and there's nothing we can (or perhaps should) do about it.
Fortunately or unfortunately, the wave is coming. In just months or a few short years, anyone will be able to open an envelope or log into a website and see their entire genomic sequence, from the very first nucleotide to the very last. **Thus the question is not whether people should get their genome sequenced - because they invariably will - but rather what can be done to educate consumers**. With a background in genetics, I know better than many consumers all the dangers that my genetic sequence will reveal. But I'll still be ready to swab my cheeks the instant I can afford a complete genomic sequence.
Is there really no proper place for the average non-geneticist, non-physician-assisted consumer in the whole genome market? What if I can't afford a genetic specialist - should I be denied the opportunity to sequence my genome? What if my health insurer refuses to pay for genetic sequencing? Should only the knowledgeable or the rich be allowed to learn more about their genes?
I would argue that there is a place for the "early consumer." Early consumers are the pioneers, the curious who do something because it is new and exciting and they want to learn more about the technology and about themselves. For instance, there are so many people that get into genetic genealogy even though they don't know the first thing about genetics. When they get their results back, they do what the human mind was designed to do - they go out and attempt to learn more (and helping educate them is exactly why I started The Genetic Genealogist in the first place). Luckily, there are already others who are leading the consumer education front.
All new technology comes with risks. Even genetic genealogy, the sequencing of a few SNPs or a few 100 base pairs, can reveal unexpected or unwanted results. But should the risks really cause so much fear and caution? We are who we are regardless of whether or not we get sequenced. Sequencing just arms us with information that could, now or in the future, be useful. For me, the benefits far outweigh the risks.
In my opinion, the answer is to educate, educate, educate. Convincing people that their genome is scary or useless will dissuade very few from sequencing and will likely only alienate the pioneers.

# Top 5 Reasons to Save Your Grandmother's DNA

(Originally posted May 10, 2007)

**1. You got those big blue eyes from your grandmother, but chances are you inherited less desirable genes as well.** We inherit our DNA from our parents, who inherited it from their parents. Since we all possess genes that can cause or contribute to disease, knowing one's DNA and family medical history can be a great resource for someone who learns they have a genetic disorder.

**2. Full genome sequencing is right around the corner!** The X-prize quest for the $1000 genome will lead to efficient and affordable whole-genome sequencing. As commercial companies crop up and compete for customer's business, leading to even lower prices.

**3. Your grandmother's DNA contains clues to her ancestry.** X-chromosome, mtDNA, and autosomal genealogy tests contain clues to a person's ancestry, both recent and ancient.

**4. Even if you aren't interested in this whole genetic genealogy craze, somebody you know will be** ! Genealogy is one of the most popular hobbies in America, and the use of DNA to augment traditional genealogical research is growing faster than ever. Chances are that someone you know will someday be interested in your grandmother's DNA!

**5. All the undiscovered possibilities.** No one knows what uses will be discovered for DNA in the future. Save that DNA just in case!

Disclaimer: Some people are very uncomfortable with the thought of gathering and storing a loved one's DNA, and those beliefs should be honored and respected. It is ALWAYS best to obtain your grandmother's permission before you gather her DNA. So don't delay, call her now!

# Famous DNA Review – Genghis Khan

(Originally posted May 21, 2007)

In 2003, researchers from around the world released a paper that suggested that 8% of all Mongolian males have a common Y chromosome because they are the descendants of Genghis Khan (See "The Genetic Legacy of the Mongols," 2003, Zerjal, et. al., *American Journal of Human Genetics*, 72: 717-721). The researchers examined the Y chromosome variability of over 2000 people from different regions in Asia and discovered a grouping of closely related lines. The cluster is believed to have originated about 1,000 years ago in Mongolia and its distribution coincides with the boundaries of the Mongol Empire.

Genghis Khan's empire (he ruled from 1206 – 1227) stretched across Asia from the Pacific Ocean to the Caspian Sea and was reportedly extremely prolific. Khan's son Tushi had as many as 40 sons. His grandson Kublai Khan is reported to have had as many as 22 sons, and perhaps many more. Together this family may have as many as 16 million descendants alive in Asia today. **It is extremely important to note that until DNA can be extracted from Khan's bones (which have never been found), there is no definitive proof that this Y chromosome cluster is actually descended from Genghis Khan**.

When Family Tree DNA compared the markers in the paper to their database, they determined that the Y chromosome cluster belongs to Haplogroup C3 (M217+). Forty-seven samples in their database at that time exactly matched the markers identified in the paper. The company has summarized the marker results from the paper and have made that information freely available.

A newly released study from Russian scientists examined the Y chromosomes of 1,437 men from 18 Asian ethnic groups (Altai Kazakhs, Altai-Khizhis, Teleuts, Khakasses, Shor, Tuvinians, Todjins, Tofalars, Soyotes, Buryats, Khamnigans, Evenks, Mongolians, Kalmyks, Tajiks, Kurds, Persians and Russians). The researchers discovered that approximately 35% of Mongolians possess the "Khan" Y chromosome. Surprisingly, the results of the study suggest that although the Mongol Empire held eastern Russia for 250 years, there are few "Khan" Y chromosome carriers in that region.

You can read more about the 2007 study at UK Channel 4.

# You and the $1000 Genome - Part I: The Archon X PRIZE for Genomics

(Originally posted May 22, 2007)

The Archon X PRIZE is a challenge from the Archon X PRIZE Foundation to foster the development of efficient and inexpensive genomic sequencing. Not only will the X PRIZE for Genomics change the face of medicine, but it will also have an ENORMOUS impact on the field of genetic genealogy, which we'll discuss in Part IV of this series.

**History of the Archon X PRIZE for Genomics:**

In 2003 the J. Craig Venter Science Foundation announced a $500,000 Genomic Technology Prize that would be awarded to an the group whose technology significantly enhanced "the field of high throughput DNA sequencing by enabling a human genome to be sequenced for $1,000 or less." The Foundation believed that crossing this threshold would enable the majority of individuals to afford genomic sequencing as part of medical treatment.

By 2006, Dr. Ventor's $1000 genome challenge was picked up by the X PRIZE Foundation to create the Archon X PRIZE for Genomics, a $10 million dollar incentive for the first successful team. **To win the prize purse, the registered group must build a device and use it to sequence 100 human genomes within 10 days or less, with an accuracy of no more than one error in every 100,000 bases sequenced (that's just 0.001%!!) for no more than $10,000 per genome**. As of May 2007 there are three teams registered for the competition; VisiGen, 454 Life Sciences, The Foundation for Applied Molecular Evolution (FfAME), and Reveo, Inc. If you're curious, Genomics & Proteomics Magazine has summarized a number of the leading technologies that are being developed in pursuit of the X PRIZE (very technical information).

In August 2005, the National Human Genome Research Institute announced that it had awarded grants in excess of $32 million to promote the development of sequencing technologies that would significantly lower the cost of whole-genome sequencing. At the time, it cost roughly $10 million to sequence a human genome (a 50-fold decrease from the previous decade), and the NHGRI set a final goal of $1000 or less for an entire genome. As the NHGRI pointed out, "the ability to sequence an individual genome cost-effectively could enable health care professionals to tailor diagnosis, treatment, and prevention to each person's unique genetic profile."

**Four years later, has there been progress?**

454 Life Sciences, for example, has just announced in March that they have essentially completed sequencing of James Watson's genome, arguably the first time a single person's genome has been sequenced (the Human Genome Project's source of DNA was reportedly an amalgam of different sources). For those that don't know (can there be anyone?), James Watson is famous for having discovered the structure of DNA over 50 years ago. **Interestingly, Watson has asked 454 to withhold his results for the *apoE* gene - associated with Alzheimer's disease - as well as a number of other results, citing privacy concerns**. Watson, after all, has a son who received 50% of his genetic makeup from Watson's genome. In light of this, 454 has decided to hand over the results to Watson, who will then decided what to release to the public. (See Marshall, Eliot, "Sequencers of a Famous Genome Confront Privacy Issues" *Science* 30 March 2007:Vol. 315. no. 5820, p. 1780DOI: 10.1126/science.315.5820.1780). 454 estimates that the six-fold coverage of Watson's genome cost an estimated $1 million. Still a long way to go to reach the $1000 goal.

Meanwhile, Reveo, Inc. just joined the competition on April 30th of this year, but Reveo's founder, Dr. Sadeg M. Faris, believes that their technology will eventually be able to read an entire human genome "in minutes for pennies per genome."

The X PRIZE Foundation has released a video that explains the aims of the project. In the next post I will be examining whether or not the $1000 genome is really necessary considering recent developments in a related field.

# You and the $1000 Genome – Part II: The International HapMap Project

(Originally posted May 24, 2007)

In Part I of the "You and the $1000 Genome" series we examined the Archon X PRIZE for Genomics, a $10 million purse for the group that can sequence 100 genomes in 10 days for no more than $10,000/genome with an error rate below 0.001%. With today's technology this goal is still a few years away.

But do we need an entire genomic sequence to obtain all the relevant medical information that our DNA contains? **After all, 99.9% of my DNA is exactly the same as everyone else's! Why sequence that 99.9% over and over and over if the results are the same every time?** Wouldn't it be cheaper to just sequence and then decode the 0.1%?

Sequencing that 0.1% is the goal of the International HapMap Project. HapMap stands for "Haplotype Map", and those of you who are genetic genealogists will instantly recognize the importance of the word haplotype. The goal of the HapMap Project, begun in 2002, is to identify SNP groups (haplotypes) from a total of 270 individuals representing the Yoruba people of Nigeria, the Han Chinese in Beijing, the Japanese, and U.S. residents with northern and western European ancestry. **The HapMap is essentially a catalog of all the common genetic variants in human beings.**

Phase I of the HapMap project, which is complete, identified 1 million SNPs in the human genome. SNPs are "single nucleotide polymorphisms", a single variation in the genetic code. According to some scientists, 1 million SNPs is about 10% of the total SNPs in the human genome. Interestingly, the results of Phase I of the HapMap suggested that SNPs tend to cluster together at certain locations and may be passed onto the next generation in groups. For many regions of our DNA there are only a few different haplotypes in most humans, and researchers can identify these haplotypes using just a few single SNPs. **As a result, a single person's genotype (collection of haplotypes) can be created by sequencing as few as 300,000 to 600,000 SNPs**. For a recent review of Phase I of the HapMap Project, read this 2005 article in PLoS Genetics (open access).

Phase II of the HapMap Project identified close to 2.5 million SNPs using the same 270 samples. Although data acquisition for Phase II has been completed, analysis is still continuing.

As the HapMap data becomes available, researchers can use it to identify genes and SNPs that are involved in disease. If most people with colon cancer share a certain haplotype, researchers can use that information to identify the genes involved and doctors can use that information to predict who might be susceptible to colon cancer long before the disease develops. I've previously written about two studies using information from the HapMap to identify a locus associated with diabetes and prostate cancer.

So with the huge success of the HapMap Project, do we really need genome sequencing? Some would argue that haplotyping is not sufficient, especially when a genetic disease is found at very low frequencies in the population. According to Jonathan Rothberg, the founder and chairman of 454 Life Sciences, "genotyping rests on the hypothesis that common alleles contribute to common diseases. What if very uncommon alleles contribute to common diseases? Only deep sequencing would be able to answer this question. The deeper the sequencing, the less frequent variant you can find. You need deep coverage to ensure the statistical likelihood of finding rare mutations." Indeed, some mutations are so rare that they are only found within specific families or populations. **If these families aren't part of the HapMap Project, there is the potential that their personal SNPs won't be identified.**

Despite the concerns, there is little doubt that the HapMap Project is a valuable contribution to the field of personalized medicine. It has already produced results that will further our understanding of the genetic component of diseases such as diabetes and prostate cancer. While HapMap sequencing has

limitations that differentiate it from whole-genome sequencing, it is a much cheaper and immensely useful tool for scientists and medical specialists.

# You and the $1000 Genome – Part III: Ethical Issues

(Originally posted 26 May 2007)

In Part I and Part II of the "You and the $1000 Genome" series we examined the history of the Archon X PRIZE for Genomics and the success of the International HapMap Project. Here we'll talk about some of the ethical issues associated with efficient and inexpensive genome sequencing. The value of whole genome sequencing will only be realized if individuals believe they have complete and legal control over their genetic information. I am greatly indebted to a thorough analysis of this issue by John A. Robertson at the University of Texas School of Law ("The $1000 Genome: Ethical and Legal Issues in Whole Genome Sequencing of Individuals (pdf)." 2003 *The American Journal of Bioethics* 3(3):InFocus). Note that this analysis is not intended to constitute answers to any of the ethical questions - it is only meant to be part of the discourse.

The ethics surrounding the X PRIZE competition has led the Foundation to establish an Ethics Advisory Board to identify issues that may be involved in whole genome sequencing and the conduct of the X PRIZE competition. The goal of the Ethics Advisory Board is to not only "comply with existing ethical and legal standards, but to promote public dialogue about some of the more controversial ethical, legal, and social implications of emerging genomic technology and to actively participate in setting standards for the future use of these technologies in research and clinical care."

**Ownership of DNA and Sequencing:**

It is probably obvious that a person has almost total control over their own DNA as long as it is attached to their body. However, all day long we are continuously shedding our DNA into our surroundings, leading to the more difficult question; who owns DNA once it has left the body? If I find DNA on the sidewalk (such as a cigarette, a coffee cup, a piece of hair), does it belong to me or does it belong to the 'shedder'? This was one facet of a recent New York Times article addressing the extreme tactics that some genetic genealogists have employed to obtain DNA from (potential) family members ("Stalking Stranger's DNA to Fill in the Family Tree" 2 April 2007, Amy Harmon). Since DNA contains information that can be used to specifically identify a person, should we have total and complete control over our DNA unless we knowingly waive that right?

**Informed Consent:**

It goes without saying that written informed consent is a vital component of genomic sequencing. Consent is necessary for sequencing, interpretation, and any eventual research. Unique to genomic sequencing and interpretation, however, is the potential for emotional and psychological distress. There are always risks involved with discovering the information contained within our own genomes. As a result, entities, especially commercial enterprises, will have to delicately balance protecting their clients from the emotional consequences of genomic sequencing with protecting themselves from liability. This will necessitate educating their clients of the potential risks of sequencing and interpretation while obtaining legally sufficient informed consent.

The X PRIZE Foundation has directed that the "Genome 100 ", the 100 volunteers who will contribute DNA to the sequencing competition, must give fully informed consent. Members of the Genome 100 (who will theoretically remain anonymous) will also be asked if they would be willing to contribute their results to a database that will be accessible to others.

The HapMap Project is also concerned about informed consent and has even provided an example of the consent form that they used when obtaining samples for the Project. According to the Project, "[e]ach of the DNA donors gave individual consent to participate in the Project and signed a consent form that grants permission for the DNA samples to be used in future studies approved by relevant ethics committees." Interestingly, the Project also used teams of geneticists and ethicists to work in the

communities to discuss the issues and educate the public about the science of the HapMap Project. Although the process was different in each country, "it involved a combination of individual interviews, focus group discussions, community meetings, and public surveys… and …created a climate in which research could proceed in an atmosphere of greater openness and trust." This might be a good model for companies engaging in whole genome sequencing and/or genome interpretation.

**Risks and Genetic Counseling:**

There are numerous risks involved in whole genome sequencing and interpretation, including the discovery of medical and/or behavioral disorders, both present and future. These risks should be addressed by both informed consent (to warn customers of potential dangers) and genetic counselors (to help customers deal with the results of sequencing). The UCSC Genome Bioinformatics Group, for instance, has strongly supported the efforts of the National Human Genome Research Institute to train individuals to provide professional genetic counseling.

**Storage:**

How should samples be used once the DNA has been sequenced? Should they be stored or should they be destroyed? This will undoubtedly be an issue requiring informed consent.

Perhaps more importantly, how should results be stored? It is vital that results be protected from unlawful detection or use under any circumstances. Online storage will require advanced theft protection measures. Results shared in hard copy, such as via DVD, should also be strongly protected to avoid theft (a whole new type of identity theft). According to the X PRIZE Foundation, "[a]ll data generated as part of the X PRIZE competition will be stored in secure databases. The X PRIZE Foundation encourages continued research into creative and secure database structures."

**Discrimination:**

Almost everyone would argue that discrimination on the basis of genetic information is not an acceptable use of genomic sequencing. Although there is no federal prohibition of this type of discrimination, many states have their own laws that prevent genetic information discrimination. And it appears that the federal government will soon pass the Genetic Information Nondiscrimination Act (See "GINA, A Primer") to create an extensive nationwide prohibition of discrimination on the basis of genetic information.

**Sequencing the Genomes of Minors:**

Minors often have little choice in their medical treatment because that duty is carried out by their parents or legal guardians. But should parents have the right to sequence their children's genomes? How about the genomes of embryos that are not implanted? What if there is a medical necessity? Perhaps sequencing in those situations should be limited to only those regions that are involved in the medical situation at hand.

**The "Geneticization" of Society:**

In his article, Mr. Robertson coins the phrase "geneticization of society" to address the concern that our genetic information will come to represent our identities. In our society, a person is ideally represented by their goals and achievements, not by their genetic information. Unfortunately, just as people are judged by their physical appearance in today's society, there is the danger that people will be judged by their genetic identity in tomorrow's society. Are we limited by our genetic information, or are we more than our own genome? In my opinion, our identity is what we make it, not a sequence of A,T,C, and G's.

While researching the ethics of the $1000 Genome, I came across a terrific quote at ( Genetic Engineering & biotechnology News) by Chad Nusbaum, Ph.D., co-director of the genome sequencing and analysis program at the **Broad Institute**: **"Science is moving way ahead of the ethics. We can't stop the technological advancements but the gap keeps widening. It is our responsibility to understand the implications of our work and educate the public and elected officials so that a**

**proper dialog can take place.”**

# You and the $1000 Genome – Part IV: The Impact

(Originally posted May 29, 2007)

In Part I, Part II, and Part III of the "You and the $1000 Genome" series we've examined the Archon X PRIZE for Genomics, the International HapMap Project, and the ethical issues associated with both. In this final installment of the series we will examine the potential impact of genomic or SNP sequencing and interpretation on both medicine and genealogy (finally, some genealogy for you patient genealogists out there!).

I believe that whole genome sequencing will have myriad uses. In the paper mentioned in Part III of the series (John A. Robertson, "The $1000 Genome: Ethical and Legal Issues in Whole Genome Sequencing of Individuals (pdf)." 2003 *The American Journal of Bioethics* 3(3):InFocus), Mr. *Robertson suggests that demand for personal genome sequencing outside of the medical context could be quite limited. But that view might fail to take into account uses of genomic information other than identifying or predicting disease, such as the genetic genealogy setting. Very few could have predicted 10 years ago that thousands of genealogists would be submitting their DNA for limited sequencing as they are doing today. If information from whole genome sequencing can be used to analyze genealogy (which it surely will be), then this will create an entire niche that will increase commercial demand outside of the medical context. And this is only one such niche. There might be many many more, some of which will only develop after whole genome sequencing becomes economically available.*

Here is a list of just a few of the uses of genomic sequencing:

1. **Identification of genes involved in disease** - scientists are far from understanding the genetic basis of most human conditions, both normal and disease. Having thousands of genomes in research databases will give researchers the ability to make these types of associations through comparative genomics.

2. **Tailored preventative medicine** - knowing one's propensity for disease(s) will allow scientists and medical specialists to attempt to prevent the formation of these diseases. So see more about personalized genetics, read this informative interview at ScienceRoll with Steven Murphy, MD of the Gene Sherpa. If tailored preventative medicine is to come about, it will require the education of all healthcare specialists in genetics and the relationship between genetics and disease.

3.**Genealogical research** - whole genome sequencing will greatly advance the ability of genealogists to use DNA to study ancestral relationships. This will have a big effect on both autosomal and Y chromosome studies. Genealogical testing using autosomal markers is limited by both the low number of identified markers and the unknown frequency of sequences across all populations. Cheap and efficient genomic sequencing could alleviate both these limitations. Y chromosome studies will greatly benefit by a huge increase in the number of STR markers that could be used for relationship comparisons. Currently companies such as Family Tree DNA offer 67-marker tests. In a few years we will be able to compare all the STRs in the Y chromosome rather than just a few of them.

Recognizing the impact that cheap and efficient whole genome sequencing will have on science and society, *Nature Genetics*' 'Question of the Year' is "What would you do if this sequencing capacity were available immediately?" The website has numerous replies from prominent geneticists and presents a number of interesting thoughts on the topic. evolgen, another member of The DNA Network, has also provided an answer to the question on the evolgen blog. In addition, DNA Direct Talk has a round-up of recent blog discussions regarding the $1000 genome.

Here is a quote from Professor Stephen Hawking in support of the X PRIZE in Genomics:

"As you may know, I have recently expressed my belief that space exploration and the eventual colonization of space is critical for humanity's survival. To bring about breakthroughs for personal

spaceflight is a laudable aim and it is work done by the X PRIZE Foundation that will eventually unleash humanity from the gravitational bonds of earth. You may also know that I am suffering from what is known as Amyotrophic Lateral Sclerosis (ALS), or Lou Gehrig's Disease, which is thought to have a genetic component to its origin. It is for this reason that I am a supporter of the $10M Archon X PRIZE for Genomics to drive rapid human genome sequencing. This prize and the resulting technology can help bring about an era of personalized medicine. It is my sincere hope that the Archon X PRIZE for Genomics can help drive breakthroughs in diseases like ALS at the same time that future X PRIZEs for space travel help humanity to become a galactic species."

Well there you have it! It is probably quite obvious that I have high hopes for efficient and inexpensive genome sequencing and subsequent interpretation. Although the necessary technology is still a few years away, it is important that we as a society address the many issues that will result from these technologies. As always, I would appreciate any comments that you many have on this topic, or any thoughts you may have had while reading this series.

P.S. - I just stumbled across an interesting article at In the Pipeline about the use of cheap(er) genomic sequencing to follow the development of antibiotic resistance in bacteria (*S. aureus*). I don't have access to the PNAS paper, but it appears that the genome (which is tiny compared to ours) was completely sequenced twice, once before treatment and once after treatment failed due to the development of resistance. The strain had developed a total of 35 mutations! The author makes a great statement at the end:

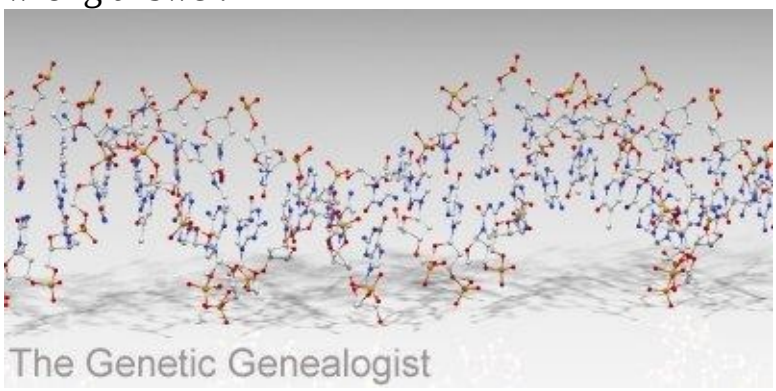
*"The technology involved here is worth thinking about. Even now, this was a rather costly experiment as these things go, and it's worth a paper in a good journal. But a few years ago, needless to say, it would have been a borderline-insane idea, and a few years before that it would have been flatly impossible. A few years from now it'll be routine, and a few years after that it probably won't be done at all, having been superseded by something more elegant that no one's come up with yet. But for now, we're entering the age where wildly sequence-intensive experiments, many of which no one even bothered to think about before, will start to run."*

# DNA From the Dead: DNA Banking is Legal, but is it Ethical? Part I

(Originally posted August 28, 2007)

The field of genomics is exploding. Every day, the mysteries of our genome are revealed and we learn more and more about the power of DNA. Soon, with affordable whole-genome sequencing, we will be able to analyze our own personal genome for clues about our ancestry, our propensity for disease, and insight into our body and our personality. In fact, this is already well underway.

Undoubtedly, each of us will be faced with a decision in our lifetime - do we want to learn the secrets of our genome, or do we want to live without that knowledge, as all of our ancestors have done for millions of years. This decision is a personal one, and at this point I don't think there's any right or wrong answer.




But what about those who are unable to make that decision? For example, an infant is unable to give consent for genetic testing, but many states in the US routinely test newborns for genetic disorders. Today and tomorrow we will be examining another group of individuals who are not able to consent to genetic testing – the recently deceased.

**DNA Banking**

There are number of companies in the US and throughout the world that offer DNA retrieval from recently deceased individuals. Kauber-Miller Funeral Home in Pataskala, Ohio has been using DNA Connections to offer storage service to bereaved families. In a 2004 interview, Mr. Miller stated that the service has been popular:

"About 30 percent of the families take advantage of it," he said. "It seems to be a generational thing, with younger people more in favor of it."

In 2004, the cost was $295 before embalming and $459 after embalming. Before embalming, a blood sample is dried on specially coated cards and stored inside a vault at DNA Connections' headquarters. After embalming, a skin sample must be taken to retrieve the DNA.

Perhaps surprisingly, the ability to store a deceased person's DNA has been around for more than ten years. In 1998, an article in the Huntington's Disease Lighthouse newsletter described a DNA storage service from Cincinnati-based DNA Analysis, Inc. For $350, the company would take hair, blood, and cheek swab samples for long-term storage. The family would also receive a "genetic fingerprint", although it is unclear exactly what that phrase means.

The ability to store DNA from both the living and the recently deceased is increasing every day. The City of San Bruno in California recently posted online instructions for banking the DNA of children in your own freezer. Although the instructions were provided to assist in finding or identifying lost relatives, it could be used for anyone. Even retailers have entered the market, offering a home DNA storage kit for only $29.99.

In 2006, the New England Historic Genealogical Society published an article by Edwin M. Knights, M.D. entitled "DNA Banking for Medical Information." In the article, Dr. Knights makes the following comment:

“For an increasing number of disorders there is urgent need to store DNA from elderly members of the family or affected persons whose life expectancy is reduced. We would go much further, as we feel strongly that DNA information is becoming so important that DNA should be banked from every elderly adult who has had children. This is particularly true because so many are now choosing cremation rather than traditional methods of burial, in which case DNA evidence is lost forever. It is becoming increasingly important for descendants to know what DNA they have inherited in order to modify or prevent subsequent serious medical conditions in future generations. Of course DNA also provides a priceless resource for genealogical pedigree studies. This objective can be achieved easily if we enlist the cooperation of funeral directors.”

**DNA Storage in Other Countries:**

Storage of a deceased person’s DNA is also being offered in the UK. According to Avi Lasarow, founder and director of DNA Bioscience Today, “in the UK the cremation rate is 73%, and the public need to be aware that there is a real need to store this vital piece of medical information.”

Interestingly, Mr. Lasarow also suggested that Funeral Homes might be liable for NOT offering DNA storage. “Given the importance of DNA preservation and knowing that upon cremation and most likely embalming that there will be no possibility of getting samples, we are beginning to wonder if there is an implied responsibility among funeral directors to make families aware of this service,” Lasarow said.

So it appears that DNA storage is being offered by funeral directors and retailers around the world. But it raises a few important questions – how necessary or useful is a dead person’s DNA, and is the retrieval of DNA from someone who has not given consent ethical? We’ll look into this tomorrow.

**Companies that Offer DNA Retrieval and/or Banking:**

1. DNA Safe Storage
2. DNA Connections
3. DNA Analysis
4. Genetic Identity
5. GeneSaver
6. PRO-DNA
7. DNA Diagnostics Center
8. DNA Products
9. Heritage DNA
10. DNA Genetic Connections 11. Legacy Biogenetics
12. Beta Genetics
13. Affiliated Genetics
14. GeneTree
15. GeneLink
16. DNA Bioscience

**For More Information:**

**1.** Genethics.ca
**2.** NEJM
**3.** National Society of Genetic Counselors

# DNA From the Dead: DNA Banking is Legal, but is it Ethical? Part II

(Originally posted August 29, 2007)

In the previous article we saw that many funeral directors offer DNA retrieval and storage as one of their services. Here, we'll look into the WHY of DNA storage, and bring up some of the ethical questions it raises.

**Why store DNA from the recently deceased?**

Undoubtedly, someone who has never heard of DNA retrieval and storage will probably ask WHY we should store a dead relative's DNA.

The reason most commonly quoted is that the DNA can be used in the future to identify inherited traits such as genetic disorders and other phenotypic characteristics. In 2006, the New England Historic Genealogical Society published an article by Edwin M. Knights, M.D. entitled "DNA Banking for Medical Information." In the article, Dr. Knights gives a number of reasons for banking DNA from both living and deceased individuals, many of which he gleaned from the Human Genetic Society of Australasia. He states:

o "To allow for molecular diagnosis and characterization of the mutation should this become available in the future, DNA needs to be stored from affected individuals. If none of the affected individuals in the family are available, it may be appropriate to store DNA from a fetus after termination of a pregnancy at risk, or from a stillbirth or neonatal death at risk for the disorder, especially in the case of X-linked recessive conditions.

The National Society of Genetic Counselors, on the other hand, has stated that there are only two occasions when DNA banking is appropriate (the Society has a brochure available here (pdf)).

1. When current technology has failed to find a genetic cause for what appears to be an inherited disease in a family, or
2. When genetic testing is not feasible or available to an affected individual, but may be available in the future.

From a medical standpoint, it is unclear how useful stored DNA might be. According to Eric Juengst, an associate professor of biomedical ethics in MetroHealth Medical Center in Cleveland, until recently testing multiple generations for a hereditary disease like Huntington's chorea was not unusual. But scientific advances have allowed the same information to be gathered by testing just one individual. "The way that genetic tests are being sold to the public as prevention tools are no more powerful than the tools we use today like cholesterol tests," Juengst said. "This is a very minimal service."

Do we really need our parents' DNA for information? As far as we know, almost everything we need to know about our propensity for genetic disease is contained in our own genome. For me, the reason I would save my ancestor's DNA is to learn about their genealogy, not about any predisposition I might have towards disease.

"The DNA samples also could be used to determine paternity, which might reveal a few unexpected and unwanted surprises, Juengst said."You might find out your dad really wasn't your father," he said. "Maybe that secret was supposed to go to the grave. We're supposed to respect the dead and we need to respect their genetic secrets as well."

If I save my great-grandmother's DNA and analyze it for genealogical information, am I showing disrespect?

**Ethical Questions Associated with DNA Banking**:

Banking DNA from the deceased raises many ethical dilemmas and forces us to ask difficult questions. The American Society of Human Genetics (ASHG) has issued a "DNA Banking and Analysis" statement that offers a number of interesting questions surrounding DNA Banking:

1. Who Owns the DNA in a Bank?
2. Under What Circumstances, if Any, Should the DNA Diagnostic Laboratory Release Results or Deposited DNA to Anyone Other than the Patient?
3. Should DNA Banks and/or DNA Diagnostic Laboratories Be Certified?
A recent article available at New England Ancestors, "DNA Banking for Medical Information", suggests the obvious, that DNA should be stored today for tests that will only be available tomorrow. The article also lists some of the most important questions facing companies that offer DNA banking and consumers that plan to partake of these services: 1. Why is the DNA being banked?
2. Who owns the banked DNA?
3. Who controls the bank, and how secure is it?
Although both of the above studies were about DNA banking in general, the questions also apply to DNA retrieval from the dead.
I also wonder whether offering DNA retrieval and storage to someone who is grieving is unethical. In a way, the service is offering the bereaved the ability to retain a piece of the deceased and to store that piece for an indefinite period of time. Someone who is grieving might jump at this chance to prolong their ability to hold onto the deceased. On the other hand, perhaps it might help the healing process.
The most important concern about DNA retrieval from the deceased is the question of consent. Unless the deceased was asked before death, retrieval is without consent. Currently, however, you can obtain and analyze anyone's DNA without consent, so perhaps this isn't as radical as it seems. As a recent article in the New York Times discussed, some people have gone to great lengths to obtain a distant relative's DNA against their wishes. In most cases, at least the DNA retrieval from the dead won't be against their written or vocal wishes. But it will still be taken without consent.
In conclusion, I'm not completely against DNA retrieval and storage, especially when consent is given. Who knows what that DNA might be good for in the future. My analysis is just meant to look at some of the potential problems with DNA storage, and to foster thought and conversation. **Our genomes are able to hold many secrets**. Only recently have we had the technology to reveal these secrets.

# Conclusion

I hope you've enjoyed reading some of my favorite posts at The Genetic Genealogist. If you're interested in learning more about DNA, genetic genealogy, and personalized genomics, you can subscribe to my feed.