What About DNA Testing?

A while ago, I authored a number of e-mails on Yahoo's *Ontariogenealogy* list in response to queries about DNA. Marie Spearman has since asked me to do a reprise of that exchange. After looking at it, and at subsequent e-mails from much more knowledgeable people, I decided to try to synthesize what I had to say with the new stuff.

I don't claim to have a deep understanding of DNA testing or the analysis thereof, but I do have a fairly decent grasp of the mechanics of inheritance. Anyone is free to correct/amend where I've written in error. (Note that I've amended the exchanges to eliminate erroneous information, ensure anonymity and provide clarity.)

Before I jump into that exchange though, I think it would be helpful to provide some background and define some terminology. Firstly, in any discussions of DNA typing we're talking about two completely different disciplines, genetics--the study of inheritance as well as the chemistry and mechanics that make it possible; and genotyping--the process of categorizing and testing organisms, including humans, by/for specific genetic characteristics. Some knowledge of genetics is useful in understanding who in a given family needs to be DNA-tested, as well as what kind of test to administer, while genotyping is the end goal of the DNA tests.

A brief background on genetics:

There is a hierarchy of structures within our genetic makeup:

1) At the lowest genetic level are the four "bases": adenine, guanine, thymine, and cytosine (represented by the letters A, G, T, and C, respectively, and are the basis for the genetic code).

2) These bases are then chemically (and electrically) bonded to "backbones" made of sugars, phosphate groups and esters--one base to each sugar molecule--that result in units called nucleotides.

3) Thousands of these nucleotides are joined to make one molecule of DNA or RNA.

4) DNA is then organized into longer chemical structures called chromosomes. These are the largest genetic units in the determination of genetic characteristics, such as gender. (Note: a subset of DNA, the gene, is simply a discrete chunk of DNA that regulates or performs specific functions within an organism.)

A brief background on genotyping:

Each of us inherits a mix of DNA from both parents. This DNA resides in two parts of the cell, the nucleus (the cell's core) and the mitochondria (the cell's engines). Our nuclear DNA is a 50/50 mix of parental DNA--half from Mom and half from Dad, but our mitochondrial DNA (aka mtDNA) comes only from Mom.

Over time, changes (mutations) in parts of the DNA occur--more quickly in nuclear DNA than in mtDNA. If these changes occur in our sexual cells (sperm and eggs) they will be passed on to our children. Now, if we belong to an isolated group (caused by distance, social mores, bigotry, etc.,), with cousins marrying cousins, etc., these mutations may become a prominent feature of that group, genetically distinguishing them from other such groups. This is the bread-and-butter of genotyping. By testing many people and then comparing and organizing the results, geneticists have developed a knowledge base that identifies patterns and relationships among groups of people; indicates migratory and cultural trends; and assigns individuals to groups based on their DNA signatures. This is what we call DNA testing.

In the process of developing this knowledge base, experts have come up with a number of testing procedures with which to relate an individual (you) to a given haplotype and/or haplogroup. Most prominent among these procedures are: Y-chromosome testing, which allows one to genetically relate a man (and by extension, his close relations) to his male ancestors; and mtDNA testing, which allows one to relate a person to his/her female ancestors. In the first case, the results should gibe with the history of the family surname as passed down from father to son (i.e., g-g-grampa Smith and g-g-grandson Smith should have essentially the same Y-chromosome.) In the second case, the DNA being tested will not be linked to a given surname but will be passed unchanged, from mother-to-daughter, over many generations. There are at least two other, less publicized, tests: the autosomal test, in which non-sexual chromosomes are tested--useful for finding distant cousins; and X-STR tests, which follow the X chromosome--useful for verifying a genetic relationship between siblings.

Some terminology used in genetics & genotyping:

- **Agnate** = the male side of your heritage (i.e., your father's side.)
- **Allele** = an variant form of a gene.
- **Autosomal test** = a method of testing DNA in chromosomes other than the sex chromosomes.
- **Autosome** = any chromosome that is not a sex chromosome (i.e., not X or Y.)
- **Bases** = primary sub-units of DNA, they come in 4 flavors adenine (A), guanine (G), cytosine (C) and thymine (T).
- **Base pairs** = a DNA building block consisting of a pair of.
- **Chromosome** = an organized structure of DNA & protein found in cells, the chromosome is a piece of coiled DNA containing genes & regulating elements.
- **Clade** = a group of people who share features inherited from a common ancestor.
- **Deep Clade test** = a test for SNPs to determine haplogroup.

- **DNA** = deoxyribonucleic acid, a nucleic acid containing genetic instructions for the development & functioning of all known living organisms & some viruses.
- **Enate** = the female side of your heritage (i.e., your mother's side.)
- **Gamete** = a sex cell, i.e., egg or sperm.
- **Gene** = a segment of DNA or RNA that is transmitted from one generation to the next, & that carries genetic information.
- **Genetic code** = a specific sequence of the four bases.
- **Genetics** = branch of biology concerned with heredity.
- **Genotype** = the genetic identity of an individual--often evident from physical characteristics.
- **Genotyping** = determination of one's genotype through genetic testing.
- **Haplogroup** = a genetic population grouping based on SNPs, is associated with early human migrations & which can be associated with a geographic region.
- **Haplotype** = aka haploid genotype, this is a subset of a haplogroup, & is a unique combination of alleles on the chromosome that are transmitted together to your offspring.
- **Maternal** = the female side of your heritage (i.e., your mother's side.)
- **Mitochondria** = compartments within a cell that act as the cell's engine, they make & supply energy for the cell.
- **MtDNA** = genetic material found in mitochondria & passed down from mothers to both sons & daughters, but inheritable only through the daughters.
- **Mutation** = a change in DNA.
- **Nucleotide** = a piece of DNA that contains one base, one phosphate group, and one sugar unit--thousands of nucleotides joined in sequence make up a molecule of DNA.
- **Nucleus** = the central cell unit, it contains our nuclear chromosomes.
- **Paternal** = the male side of your heritage (i.e., your father's side.)
- **Phenotype** = how an organism looks as a result of its genotype & environment.

- **RNA** = ribonucleic acid, genetic material found in cells, RNA contains the codes for protein synthesis.

- **SNP** = (short for Single Nucleotide Polymorphism) is a type of mutation in which just one base pair on the DNA changes. SNPs on the Y-chromosome are are passed down unchanged for literally hundreds of generations, & are used to define entire populations of men. Populations that have the same Y-SNPs are said to belong to the same haplogroup.

- **X-STR** test = a specific test of the X-chromosome to determine sibling relationships.

- **X-chromosome** = one of the two sex chromosomes, the X-chromosome is present in both genders: men have 1 X-chromosome while women have 2.

- **Y-chromosome** = one of the two sex chromosomes, the Y chromosome is normally present only in men.

- **Y-DNA** = DNA on the Y-chromosome.

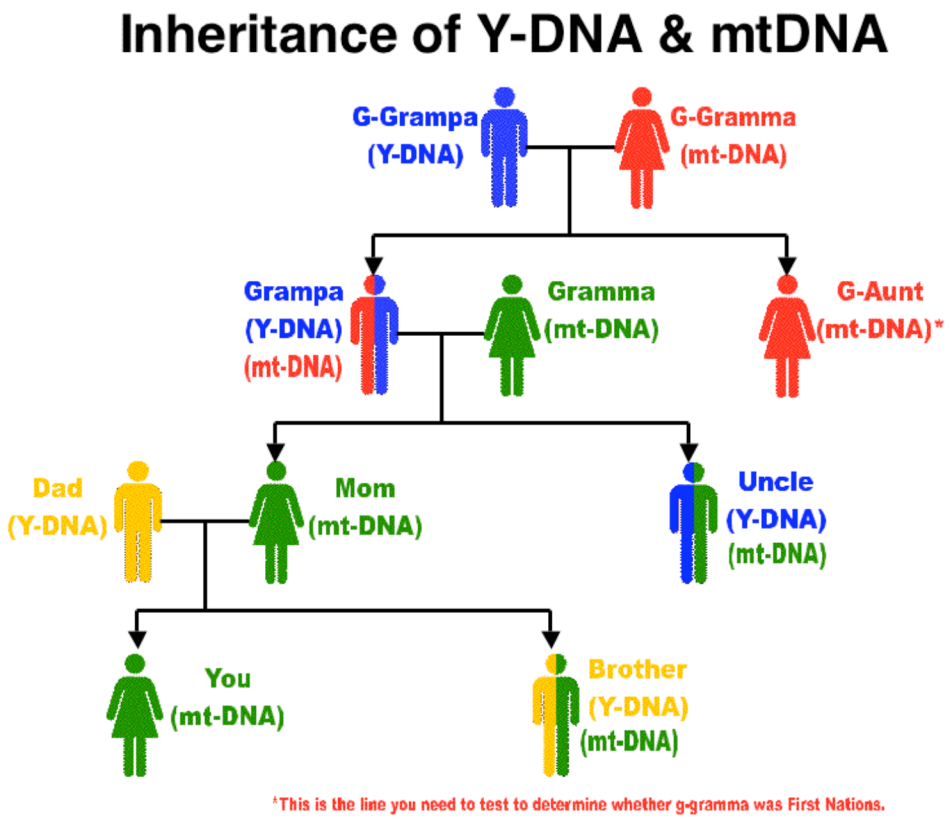
- **Zygote** = a cell formed by the union of two gametes.

E-mails:

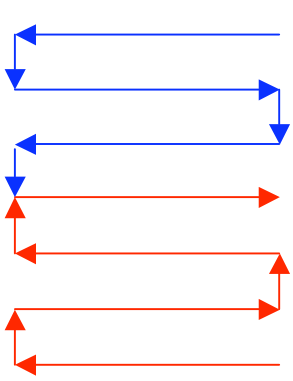
Having laid the groundwork, we can now lay out the series of e-mails, as follows:
Message 1: Original Question)
"*My mom has mentioned that she believes her father's mother was a Native Indian. Chippewa I think, anyway, if my mom or one of her brothers does the DNA test would that show the Indian heritage? I have her marriage registration that has both parents' names and unless she was adopted I don't think she's Native. I don't know how else to find out if my mom's right or not.*"

I responded with:
Message 2: response to message 1)
"*In this case you want to check the mitochondrial DNA (mtDNA) of a descendant of your granddad's sister. Male descendancy is done using the Y-chromosome, this chromosome being the primary one determining male gender.*

DNA follows the family line as follows:
In the following diagram we start with the g-gramma in question whose mtDNA is red. She gives birth to your maternal grampa who has his mom's mtDNA and his dad's Y-chromosome, as well as to your g-aunt, who has her mom's mtDNA, but <u>not</u> her dad's Y-chromosome.) He and your gramma give birth to your mom who has her mom's mtDNA (who has <u>neither</u> your grampa's Y-chromosome <u>nor</u> his mom's mtDNA). She and your dad give birth to you who also has your maternal gramma's mtDNA (but not your dad's Y-chromosome).*



One member of the list found my explanation confusing and responded with:
Message 3: response to messages 1 and 2)
"*There were some confusing information posted--at least to me.*
So I would like to rephrase in a way that when told to me, helped me understand DNA testing. If you make a family tree that branches from left to right horizontally.



(G-grampa, Y-DNA)
(Grampa, Y-DNA)
(Dad, Y-DNA)
(You, mtDNA)
(Mom, mtDNA)
(Gramma, mtDNA)
(G-Gramma, mtDNA)

where the top line is your father, then his father, then his father and the bottom line is your mother, then her mother, etc. The Y-DNA test goes along the top line, the paternal, father line. The mtDNA follows that maternal, mother line. Y-DNA is only passed to a son. mtDNA is passed to all children. If the person whose ancestry you are interested in is not in one of those lines, you have to find someone else who's tree has that line.

I think most companies now do both kinds of testing. I used FamilyTree DNA because they had a surname project related to one of my dead-ends and gave a discount. Found out there was not match to the surname, but a really good match 66 of 67 for a different surname. We now need to do more tests from more male lines to verify that the mis-match was our brick wall, and not a "non-paternal" event in a later generation.

Google has a relatively new company that also looks for medically related genes that do not follow the outside lines mentioned above.

The Y-DNA tests with levels below 35 seem to give us too many unrelated matches. Most companies will let you upgrade, but give you a price break if you do all the tests at once. Shop around."

I responded to this message with:
Message 4: response to message 3)
"*You are correct, but we must remember that it is Mom's mitochondrial DNA (aka mtDNA), though passed on to all her children, that dead-ends at her sons--they cannot pass it on to their children. This is because although the male gamete (the sperm cell) carries half the normal complement of nuclear DNA, the DNA in its mitochondria (the engines of the cell) is not expressed in the zygote (the fertilized egg). On the other hand, the egg has both half the normal complement of nuclear DNA plus the mother's mtDNA. Thus, once the egg and sperm join, the resulting zygote has a full complement of nuclear DNA (half from each parent) and the original egg's mitochondria. (Yes guys, this means that we get more total DNA from Mom than from Dad). Compared to the nuclear DNA, mtDNA is much less likely to mutate, thus making it a very good tool for tracking female lineage. Using mtDNA, a woman can theoretically track her maternal lineage back to Eve.*

Among mammals, the Y-chromosome is one of two sex-determinants that are part of the nuclear DNA, the other being the X-chromosome. Each zygote receives one of these chromosomes from each parent. Two X chromosomes usually results in a girl, while one X and one Y usually results in a boy (there are exceptions but its not necessary to get into that here). This makes the Y-chromosome a very handy tool for tracing male lineage, but, as you said, it only works for male heirs.

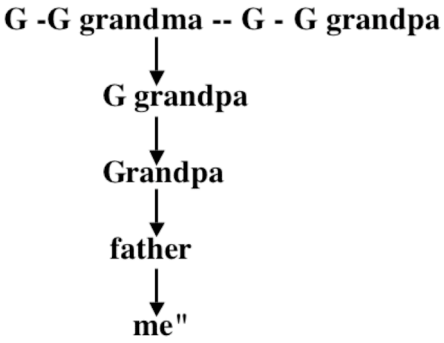
So, when you look to have a DNA test done, you have to work with the family tree a bit to determine which test will give you what your looking for."

Another member responded to question 1 with:
Message 5: response to message 1)
"*There is mtDNA testing, which traces the female line. In order to test that, tho, you'd need to get a female line descendant of your supposedly Native ancestor. You won't do because there's a man (your mother's father) between you and her. Ditto for your mom and her brothers.*

Note that a man can take the test (same as a woman) -- there just has to be an unbroken line of women back from the test-taker to the supposed Native woman.

Starting from your great grandma -
- any of her children would do.
- any of her daughters' children would do.
- any of her daughters' daughters' children would do.
and so on.... So you need to look into your grand-father's sisters and their descendants."

Yet another member of the list asked:
Message 6: response to message 2)
"*So in my case where it's my gg grandmother who was believed to be First Nations, who would have to be checked?*



My response was:
Message 7: response to message 6)
"*For mtDNA it would be any of her female descendants. As soon as a male appears it will be his wife's mtDNA that will be inherited by all their children. Thus, your g-grampa would have had her mtDNA but all of his female descendants would have his wife's mtDNA; your grampa would have his mother's mtDNA but all of his descendants would have your gramma's mtDNA; your father would have your gramma's mtDNA but you have your mother's mtDNA. Your brother, however, would carry your dad's Y-chromosome, which was also his paternal grampa's Y-chromosome, and his dad's Y-chromosome in turn.*

So, bottom-line, unless your mom is descended through the female-line (female to female to female) of your dad's g-g-gramma (not impossible), you don't have that particular g-g-gramma's mtDNA. The closest you could come to her line would be a female-line descendant of one her daughters (your g-grampa's sisters)."

Just recently, another question was asked in re the value/validity of DNA testing,
Message 8: New Question)
"*Has anyone done DNA testing for genealogy? Is it worth it? Who is best company or group to use?"*

I responded with:
Message 9: response to message 8)
"*One thing you have to know in advance is that male ancestry is typed by the genes on the Y-chromosome, while female ancestry is typed by the DNA in the mitochondria. Thus, if you want to trace your agnate (i.e., paternal) ancestry then you need to have a father, brother, paternal uncle, etc. tested for his Y-DNA. If you want to trace your enate (maternal line) then you yourself can be tested for your mitochondrial DNA (Note: in this last case the DNA won't be tied to a given surname.)*

The value of the tests is two-fold: 1) you can compare your DNA results against general haplotypes such as the Y-DNA R1b1b2 haplotype; and 2) if a number of Y-DNA tests for a given surname, such as Smith, have been done, compiled and documented, then you can compare your test results against those to determine whether you're related to anybody else who has been tested. In the latter case, you first want to do an on-line search for a database of Smith Y-DNA test results as a basis for comparison.

Knowing this, you'll have to decide for yourself whether it'd be worthwhile to you."

A very knowledgeable member responded with:
Message 10: response to message 8)
"*It very much depends on your specific aims, and on who is available to be tested.*

Wayne has already explained how yDNA can help trace your surname line. For that I would also suggest Family Tree DNA, and ordering no fewer than 37 markers, and depending on the circumstances possibly a deep clade test.

Mitochondrial DNA tests are rarely useful unless you have the whole genomic sequence done, because a single mutation's difference with someone else could still be 500 years old. Also, because the surname changes every generation (it follows the direct maternal line), and because maiden names are often not recorded, it is less likely to be useful for genealogy, though at times it has been.

A third type of test nobody has mentioned is an autosomal test. The autosomes are your non-sex chromosomes (not X or Y), so they come from both your parents. This can be useful at finding distant cousins along non-direct lines, although you will not inherit genes from all your ancestors beyond about 4 or 5 generations. This sort of test will soon be available at Family Tree DNA as well, but in the meantime is only offered by another company called 23andme.

There is a fourth type of test, X-STRs, which follow the X chromosome. These can be very useful under limited circumstances, e.g. to determine siblingship of a boy and girl.

Most of these tests are not especially cheap, but if you have specific aims they can be very useful. Please feel free to send me an email off-list if you are interested, since I know a fair deal about this and would prefer not to tie up list resources unless others are also interested in hearing more."

After some to-ing and fro-ing among members, several other responses from this same knowledgeable source followed:

Message 11:

"*It's true that the mitochondrial test is hit-and-miss, but in some cases it can focus the search. For example, I was dead-ended in New Jersey, and I have only three mitochondrial matches, all in Germany and Austria.*

Part of the reason mitochondrial testing has proven less useful is the database is much smaller. People have tended to focus on the yDNA test to the exclusion of others because of an obsession among some family researchers (which I don't myself understand) with the surname/agnatic line."

Message 12:

"*Yes, Family Tree DNA is soon to introduce a new feature called Family Finder, which is not yet available. My understanding is it may be able to find people up to roughly 6th cousins, and will allow you to download your raw data, but it will lack the features of placing your ancestry on a map and describing how well your genes fit with three sample sets (African, European, and Asian/First Nations). However, it will also cost less.*"

Message 13:

"*Well, I'm knowledgeable about this one thing, anyway! I've been using DNA for genealogical research both directly and indirectly for a few years. This field has grown tremendously in a very little time.*

Is your ancestor along your direct maternal line (i.e. your mother's mother' mother's ... mother)? If so, you could take a mitochondrial test, which would tell you about her maternal origins. However, even one male between her and you will mean you are not testing her line. In that case you would need to test a direct female-line descendant of her, or even of her maternal aunt, say.

If you are of a certain few haplogroups--these are ways to group together descendants of maternal "family mothers," as it were -- that would suggest Jewish ancestry. However, in most cases the groups are so old they predate religion or ethnicity, so it's very hard to prove or disprove specific ancestry by haplogroup. Some can point very specifically to descent from a continent, region, or even country, while others can occur from Portugal to Russia to Africa. One group, X, is even found dotted across all Europe, most of Asia, and among First Nations such as Ojibwe.

If you had a Jewish link within the past few hundred years, the surest way to find this out would be by testing with 23andme and making use of their Relative Finder feature."

Message 14:

"*....several types of test could be useful. Your budget will largely determine which ones you want to pursue. At the lower end, a basic mitochondrial test would be enough to assign your mother a maternal-line haplogroup, which could point to regional ancestry*

(e.g. haplogroup H is very common in France, while X might suggest First Nations ancestry). The downside of this is she might have no matches, or thousands.

Another option in the higher range is 23andme (https://www.23andme.com/). This has the useful feature of placing the test-taker in a global context with features called the Global Similarity Tool and the Ancezstry painting. There is a basic mitochondrial scan included, but this is usually not enough to find relatives on the direct line. However, a recently introduced feature, Relative Finder, can be of tremendous use in this case. It can find first, second, etc., up until perhaps 8th or 10th cousins based on common inherited "chunks" of DNA. What it can't do is say on what line they are related, but you might be able to fill that in with some detective work.

I can't promise this would work for your mother, but if you do get the kit I would be happy to help analyze your results. If you do invest in this kit I suggest the full version. It is $100 more than the ancestry version, but it allows you to learn of possible health risks, and to download the raw data, which can be useful for analyzing ancestry.

What I would not suggest is a low-level autosomal test such as DNA Tribes. These are based on 20-odd markers, while for a little more money the 23andme test tests 550,000. In terms of accuracy, the difference is a bit like asking several of your friends what they think on a topic as opposed to a nationwide poll."