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PROFESSIONAL ISSUES

Ancestry Testing and the Practice of Genetic Counseling

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Abstract Ancestry testing is a home DNA test with many dimensions; in some cases, the implications and outcomes of testing cross over into the health sphere. Common reasons for seeking ancestry testing include determining an estimate of customer's ethnic background, identifying genetic relatives, and securing a raw DNA data file that can be used for other purposes. As the ancestry test marketplace continues to grow, and third-party vendors empower the general public to analyze their own genetic material, the role of the genetic counselor is likely to evolve dramatically. Roles of the genetic counselor may include assisting clients with the interpretation of and adaptation to these results, as well as advising the companies involved in this sector on the ethical, legal, and social issues associated with testing. This paper reviews the history, fundamentals, intended uses, and unintended consequences of ancestry genetic testing. It also discusses the types of information in an ancestry testing result, situations that might involve a clinical genetic counselor, and the benefits, limitations, and functions that ancestry genetic testing can play in a clinical genetics setting.

Keywords Ancestry · Direct to consumer · Genetic counseling · Personal genomics · Third-party tool · Databases

Introduction and Background

As the home DNA test marketplace continues to grow, the role of the genetic counselor is likely to evolve dramatically to include assisting clients with the interpretation of and adaptation to these results, as well as advising the companies involved in this sector on the ethical, legal, and social issues associated with this testing. The value of having genetic counselors involved in the home DNA testing setting has been identified by a number of professional societies (NSGC 2015a; ACMG Board of Directors 2016). This paper reviews the history, fundamentals, intended uses, and unintended consequences of ancestry genetic testing, a sub-type of home DNA testing. It also discusses the types of information in an ancestry testing result, situations that might involve a clinical genetic counselor, and the benefits, limitations, and functions that ancestry genetic testing can play in a clinical genetics setting.

Ancestry testing lies at the intersection of genealogy and genetics. Genealogy, the tracking of familial lines through documentation of marriages, births, and adoptions, is the second most common hobby in the United States (Farnham 2012). The value of integrating genealogy studies for health and genetic studies is growing in recognition, as demonstrated by a growing list of scientific publications (Cannon-Albright et al. 2013; Carbone et al. 2015; Daya et al. 2013; Norton et al. 2013; Scholand et al. 2013; Stefansdottir et al. 2013; Zaitlen et al. 2013).

Ancestry genetic testing as it is often utilized in the home setting has many dimensions, and in some cases, the uses are beginning to cross over into the health sphere. A common purpose for seeking ancestry testing is to provide an estimate of an individual's ethnic or biogeographical origins. In other cases, the primary purpose for testing is to determine genetic relationships between people and enable contact between them. The ability of DNA testing to establish and determine a relationship between individuals is not a new idea. According to DNA Diagnostics Center, one of the leading suppliers of relationship DNA testing, DNA testing for

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purposes of close relationship establishment has been available since the 1980s with RFLP technology and the 1990s with PCR techniques; prior to that relationship testing was performed using different techniques including HLA typing, serological testing, and blood typing (DNA Diagnostics Center 2016). Traditional relationship testing compares a limited number of DNA markers and the results provide a binary answer (excluded/not excluded). Ancestry testing has provided a new option for relationship testing, providing a comparatively deeper, more comprehensive analysis of DNA shared between individuals. Access to the test's raw data is yet another use for ancestry testing. Customers can utilize online tools that are independent of the testing companies to explore their raw data in ways that go beyond ancestry or genealogical purposes, including further investigation of health-related SNPs or genetic indications of endogamy and consanguinity.

The first company to establish commercial DNA testing for ancestry purposes was Family Tree DNA, founded in 2000 by Bennett Greenspan, with a mission of confirming genealogical relationships between suspected, but unconfirmed, relatives (Aulicino 2013). Since 2000, the options for DNA testing for ancestry purposes has grown from Y and mitochondrial DNA analysis, to all human DNA including the full nuclear genome. Y-DNA testing continues to be available for specific genealogical purposes, namely for tracing direct patrilineal lines using Y DNA signatures. Identification of a haplogroup along the Y chromosome is also possible, which can provide biogeographical origins of the paternal line, and in some cases allows for the tracing of a surname for genealogical studies. Mitochondrial DNA testing also retains value for specific purposes in genealogical study by allowing for the tracing of direct matrilineal lines, and the establishment of a mitochondrial haplogroup, for both males and females. The 2005 launch of the Genographic Project, a partner project between the National Geographic Society and IBM, ushered in a new era of testing that included autosomal chromosomes (ISOGG 2016). Autosomal testing allows for deeper search through all of the nuclear chromosomes and all ancestral lineages, and is not restricted to either sex. The introduction of autosomal DNA testing is credited for the explosion of interest in ancestry testing and comprises the majority of ancestry tests ordered today which have grown to greater than 3 Million tests ordered as of early 2016 (see Fig. 1).

This data was compiled by a genetic genealogist from available information on history of edits to the isogg.org/wiki chart of autosomal DNA test information. Information present in the chart is based on company announcements of database growth.[1] This graph only includes autosomal tests, thus including mitochondrial and Y-DNA ancestry tests would further increase the numbers. Exact estimates are difficult due to factors identified by genetic genealogist Debbie Kennett (Kennett 2015). The factors include but are not limited to the following: not every kit ordered and paid for is returned by the customer, not every person who submits their kit chooses to be or remains in the database over time, and company press releases do not provide full transparency.

Three companies control the vast majority of the ancestry genetic testing market: Family Tree DNA, 23andMe, and AncestryDNA.[2] Family Tree DNA was the first company to hit the market, with Y and mitochondrial DNA testing first offered commercially in 2000. 23andMe launched its personal genomics screen in 2007 which included autosomal analysis; Family Tree DNA entered the autosomal DNA testing market in 2010, and AncestryDNA followed in 2012. At the time of publication, the combined total of ancestry tests ordered by customers of these three companies totaled over three million tests (ISOGG Wiki 2016). Some of these tests have provided limited health information with FDA-approved reports along with ancestry data (23andMe). AncestryDNA and Family Tree DNA do not provide health or trait data at this time, however some customers have taken their raw data files provided from these companies and transferred the files to third-party sites that are able to provide some degree of health information.

The original purpose for ancestry testing focused on genealogical exploration: tracing the inheritance of a surname using DNA evidence, proving familial connections, and enabling customers to get past dead ends (referred to as "brick walls") in a family tree by matching with newly identified biological relatives. Over time, the uses of ancestry testing have expanded tremendously. Increasingly, these tests are being used by individuals who are adopted, for example, as well as individuals conceived by egg or sperm donor assistance and individuals estranged or cut-off from a branch of their family tree for other reasons. Others are seeking out ancestry testing in an effort to "prove" kinship to a certain ethnic population for purposes such as application for indigenous tribal membership, or for programs with ethnicity-restrictions like minority scholarship.

Ancestry testing is revealing relationships previously unsuspected and unknown. As the techniques of genealogy have expanded with technological innovation, so have the types of results customers receive and the conclusions they can intuit from their results and "matches." Individuals are matching with previously unknown genetic half-siblings or not matching with previously assumed biological relatives who have also tested with the same company. Only after approaching parents or other relatives with a puzzling match or

[1] Source: http://isogg.org/wiki/Autosomal_DNA_testing_comparison_chart

[2] This list does not include the Genographic Project, which provides testing for biogeographical analysis without a DNA relative-finding feature, an online community/network, or access to raw data.

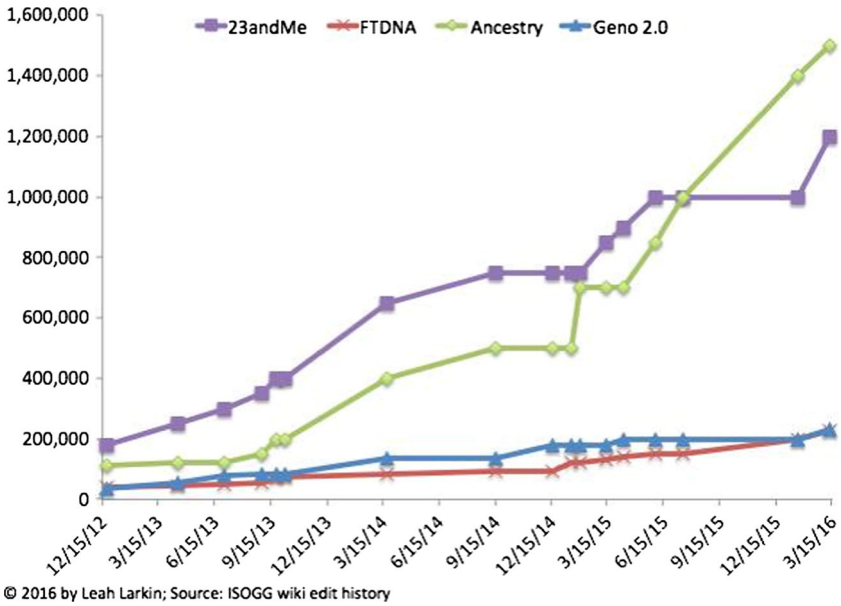

Fig. 1 Number of individuals/ kits in company-specific ancestry databases (2012–2016)

discovery do some of these individuals learn they were products of a donor-assisted pregnancy, or that infidelity on the part of one parent led to the revelation of an unknown half-sibling or altered the understanding of a genetic relationship between siblings raised in the same household. Identities, relationships, life plans, personal expectations, finances, housing, and countless other staples of an average person's existence can be affected.

Some discoveries are welcomed by customers as happy coincidences and surprise discoveries. An ancestry test that alters the understanding of relationships between parents, children, siblings, and other relatives also may affect the interpretation of that family's health history. An ethnic background uncovered via testing might raise concerns or uncover more information for assessing risk for ethnicity-based disease or carrier risks not previously known. An individual could learn, for instance, that their risk of Crohn's disease, although not monogenically determined, is increased based on known population data about his or her ethnic group. A married couple could learn that they have a shared ethnic heritage, and worry about the fact that heterozygous recessive and dominant pathogenic mutations common to that specific ethnic group have increased odds of being passed onto a child in a homozygous or compound heterozygous state. In a larger sense, these results can raise ethical and existential questions that trained genetic counselors may need to learn to explore with their clients. Discovery of unexpected parents, siblings, aunts, uncles, cousins, and grandparents is re-writing the family narrative, adding branches to (or subtracting branches from) the biological family. Individuals can discover that they are the product of incest and/or sexual assault. These revelations can happen at unexpected times, and sometimes in public ways.

What Is Ancestry Testing? The Basics

Three aspects to ancestry testing are important for genetic counselors (see Fig. 2). These are described in more detail below.

Overview of Admixture Tests

The first type of testing, for which an ever-growing number of television commercials are aired, is the testing that is able to identify the ancestral origin or "ethnicity estimation" of an individual. Referred to in the genealogy field as admixture testing or biogeographical analysis (BGA), this estimate of ethnic origins relies on a reference dataset of ancestry-informative markers (AIMs) from current, native populations and indigenous groups from around the world. Through an online private portal, customers are able to see their individual pie chart and/or geographical map of one's ethnic background

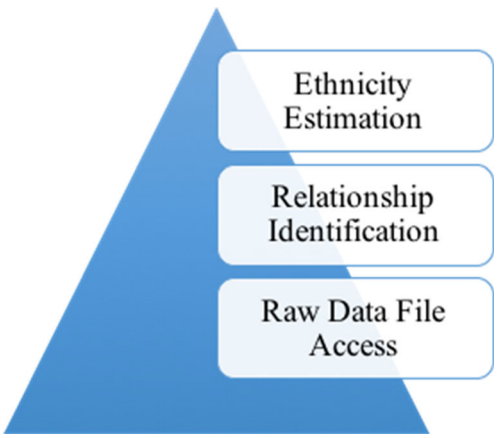

Fig. 2 Aspects of ancestry testing

developed for them by the particular company where they tested (see Fig. 3a and b). The company providing results makes conclusions by comparing an individual's DNA to a reference set of SNPs that represents ethnically and geographically diverse populations. The reference sets vary from one company to the next, and the algorithms used for calculating an estimate of ethnicity also are adapted and changed over time. Therefore, an individual's ancestry map or pie chart often varies from one company to the next, or from one year to the next. Additionally, because of the randomness of crossover events during genetic recombination, the inheritance of ancestry informative markers from each grandparent is not equivalent and therefore not proportionate for each ancestor. Thus, admixture analysis should be considered a rough estimate of an individual's ethnic background.

Of additional interest to genetic counselors is the implications of admixture analysis as it relates to health risks. Health-related results of ancestry testing could include the discovery of an increased likelihood for a medical concern given membership to a certain ethnic or biogeographical population, psychological issues due to a change in ethnic and/or racial identity, and reproductive concerns via an increased probability for a recessive or biallelic dominant condition.

Figure 3 exemplifies a pie chart and biogeographical map showing estimation of ancestor origins from two testing companies, AncestryDNA and 23andMe. The information is displayed in both map and pie chart format, allowing the customer to toggle between and adjust the level of information visible. Fig. 3b. is a similar display of results of the sample person from 23andMe. Additional information (percentage breakdowns) is available by scrolling down the screen, if a user is logged in through their personal portal account.

DNA Relative Matching

DNA relative matching allows customers to discover who else in a company's database has tested and is a genetic relative to themselves, typically within six generations (Aulicino 2013). Matches see one another when logged into their personal profile and are then able to connect with one another, using either an internal messaging system maintained by the testing company, or via direct email. Whether contact can be made with a

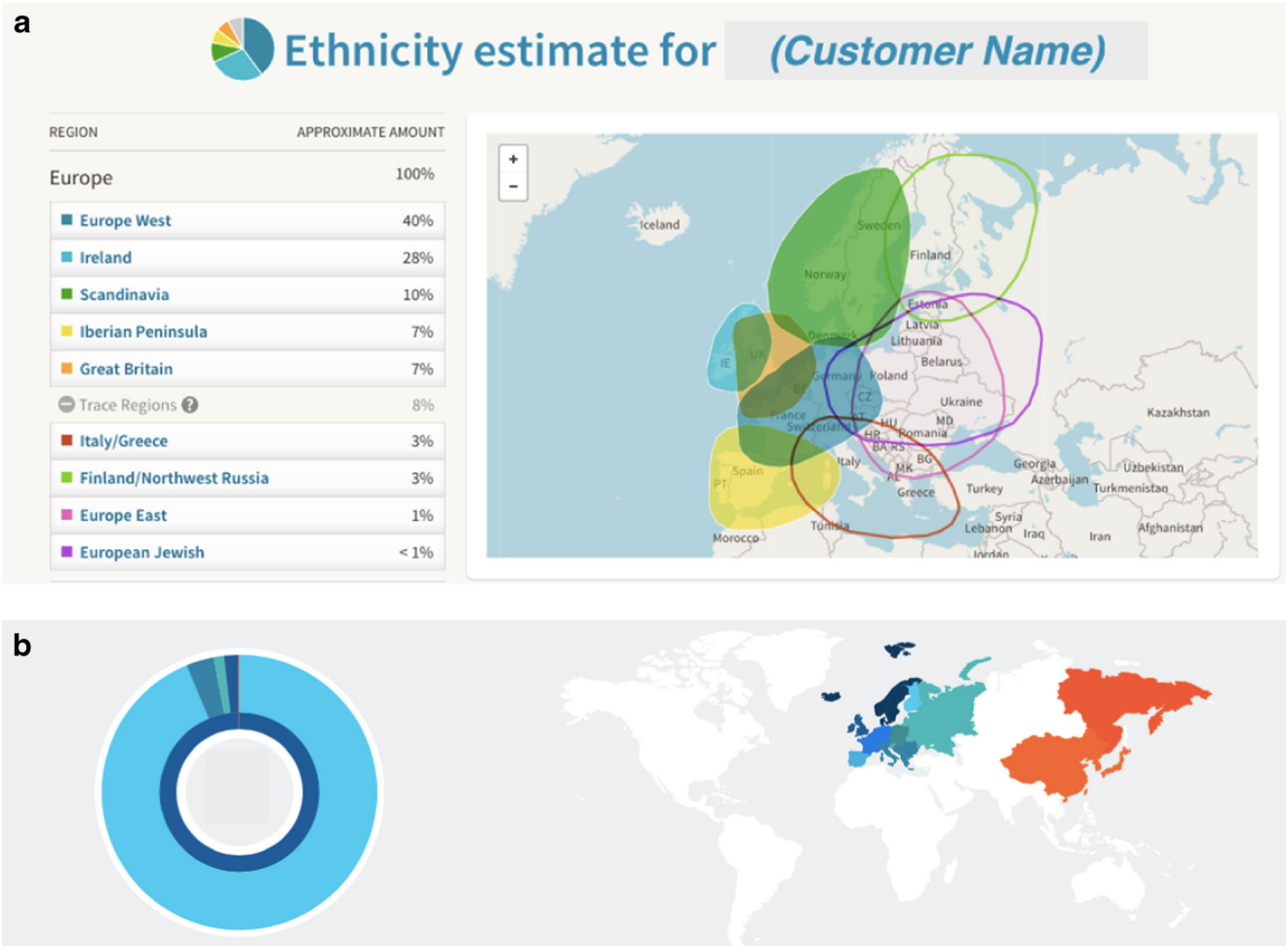

Fig. 3 **a** AncestryDNA display of one person's biogeographical estimate. **b** 23andMe display of biogeographical estimate from same individual represented in Fig. 3

match depends on the opt in/out settings chosen by each customer in the pair; whether a response to an email or inquiry within the system occurs depends on the recipient's interest in responding.

Companies are able to provide estimates of relatedness between pairs of customers by comparing the sequence of markers between all individuals within the database; comparing marker sequences side by side allows for the assessment of relatedness between individuals who have tested at the same company. Using centimorgans (cM) as the measurement, the total *length* of overlapping identical sections are compared between individuals. The total *number* of shared DNA segments is also documented. Using a length and number of shared DNA segments, companies create relationship estimates between individuals in the database. The relationships that are estimated range from close to distant; an exact match (e.g. monozygotic twins) would be listed as such, as would a first-degree relationship (parent, child, or full sibling). A second-degree relationship (half-sibling, niece/nephew, aunt/uncle, grandparent, etc.), third-degree relationship, and more distant "genetic cousin" relationships may also appear. The majority of matches that appear in an individual's account are generally composed of genetic cousin relationships, often provided as ranges (2nd-3rd cousin, 2-4th cousin, or 3-4th cousin, for example). A customer can enter or select the correct relationship from the list if they already know or are aware of the exact relationship between themselves and a match. Customers can further clarify their family tree by sharing genealogy information with one another (see Fig. 4).

This is a sample of the five top matches that appear in one customer's online profile at Family Tree DNA. Identifying information and images have been redacted for privacy. The appearance and level of information available about "matches" within a customer's profile differs from one company to the next and is based on levels of security chosen by the individual test recipients, who have some control over what information is available to others. Each company maintains its own database and does not share its customer information with others.

Raw Data Access

Ancestry testing also serves as a direct-to-consumer raw genomic data service. Customers who wish to download a raw file of SNP panel results are able to do so if they order a test from 23andMe, Family Tree DNA, or AncestryDNA (ISOGG Wiki 2016). The contents of a raw file differ between companies as each tests a different marker set, but access to the file holds the power to grant health information to customers who are willing to use a third-party analysis tool. This aspect of "ancestry genetic testing" is possibly the most significant for the genetic counseling profession, as well as regulators of this space, as the companies providing the data, as well as the third party analysis tools, are providing genetic information that can be interpreted to implicate health risks directly to the general public. Because a raw data file by itself is simply a series of characters and is of limited value, a number of third-party tools have been developed in attempts to decode the

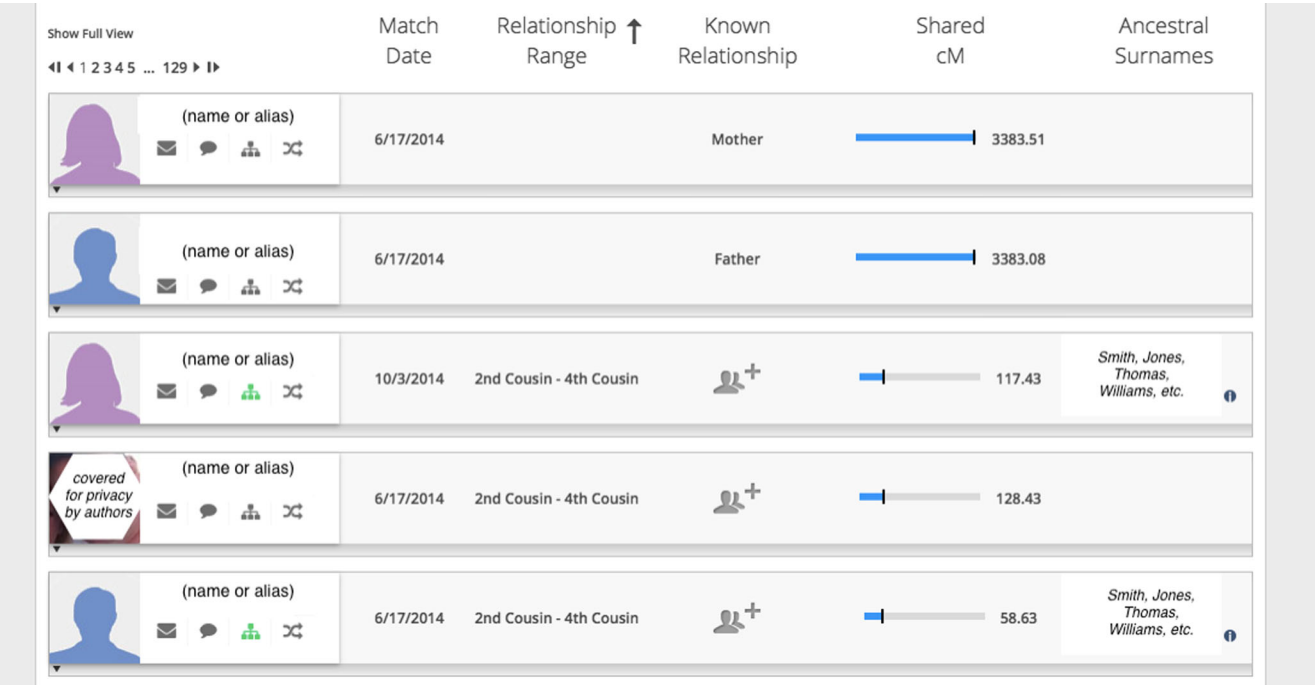

Fig. 4 Top five matches for one user of Family Tree DNA's "Family Finder" service

information stored in the computer-generated files of genomic data from ancestry testing (23andYou 2016). The raw data returned is from genotyping using a SNP panel (via microarray chip); the data is digitized and downloadable as a VCF file (or zip version of a .txt file). A VCF can be saved to one's computer desktop, external or cloud storage. Once saved, the file can be transferred between machines and systems and uploaded to external sites. The security of such a file depends on the intended use and the individual who owns or possesses the file.

One of the most common tools used by members of the genetic genealogy community is GEDMatch, an online resource with a diverse set of analysis tools including highly-refined biogeographical analyses, eye color prediction, and investigations into the possibility of incestuous or consanguineous origins with a tool that analyzes runs of homozygosity. Genetic counselors are more likely to have heard of analysis tools related to health, such as Promethease, Interpretome, Livewello, and Genetic Genie. These third-party tools aim to provide various types of medically-relevant information from raw data.

Promethease is a system that builds personalized DNA reports based on markers in a DNA raw file that are also represented in the SNPedia database. Customers of a variety of home DNA services that include raw data provision are able to pay a fee of $5–10 to upload a raw data file and receive back a report highlighting the information known on given genotypes based on current SNPedia information. There are limitations to the genetic analysis provided: health and family history are not incorporated into risk assessment, the quality of the various entries for genotypes stored in SNPedia and reported on a Promethease summary vary, and the genotypes returned are from a limited list of markers and therefore not representative of a person's entire genome. Additionally, analyzing, investigating and understanding the classifications of genotypes (listed often as "good" or "bad") requires advanced understanding of how genomic interpretations are made and the various factors important to consider, such as limitations of making pan-ethnic interpretations on genes or variants only studied in one group, or incomplete penetrance of dominant traits. SNPedia entries can be openly edited by users, making this a crowd-sourced genotype information database (SNPedia 2016a, b).

Interpretome describes itself as an interpretation engine for utilizing raw data obtained from certain testing companies, including 23andMe. The website describes that the tool is able to help a user explore his or her genome but with "little to no" interpretations of health significance returned (Interpretome 2016). A review of the website reveals sections for exploring one's genome, divided into tabs including a "Clinical," "Ancestry," and "Explore." The Clinical tab lists categories for Diabetes, Disease, Warfarin, Pharmacogenomics, which raises obvious questions about the website's health interpretation disclaimer, a concern about third-party tools not limited only to the Interpretome tool. Interpretome allows potential users to first download and see a sample genotype file before deciding whether to use the tool, a feature that not all third-party tools supply to potential users.

LiveWello is similar to Promethease in its provision of custom reports based on raw SNP data analysis. LiveWello provides users with a permanent portal account that acts as a repository for health documents for interested individuals. In addition, LiveWello markets a growing community of apps, provides an emergency contact web address for users which can be imprinted on medical jewelry, and an online network of active users. More of an online central repository for health-related communications, LiveWello has developed more options than its SNP-based genetic health report (LiveWello 2016).

Genetic Genie is a tool which provides a methylation analysis and detox profile from a 23andMe raw data file (Genetic Genie 2016). The results explain how a user's genetic profile causes them to process substances like folate differently than others. Access to the analysis is free, and the website states support for the tool is provided by donations made to the site. A section of the website promotes lab testing and the purchase of specific supplements; the commercial enterprise may also provide support for the free accessibility of the Genetic Genie tool, although this not explicitly stated on the site. Although it is possible that researchers may be able to consistently retrieve usable information from methylation and detox profiles via SNP testing in the future, at this time, it does not appear that firm conclusions can be drawn from an individual's genetically-determined methylation profile.

These are five examples known to the authors from the growing list of third-party tools which have taken raw data provided from an "ancestry" testing company and provided additional information of potential medical significance. Also, the way customers use the information from these third-party companies is unknown.

Clinical and Analytical Validity

Clinical and analytic validity are common and understandable concerns of genetic counselors and other medical genetics professionals (Royal et al. 2010). To understand these aspects of ancestry testing, it is important to understand the major scientific fields involved in the foundation of the testing: molecular anthropology, population genetics, and genetic epidemiology. Scientific publications in all of these fields have enabled the growth of understanding about the value of DNA studies in understanding human history (Brown and Pasaniuc 2014; Kumagai and Uyenoyama 2015; Larmuseau et al. 2013; Ma and Amos 2012; Ralph and Coop 2013;

Shriner et al. 2014; Tofanelli et al. 2014; Wang and Li 2013; van Oven et al. 2014; Zhang et al. 2013; Xu et al. 2015)

Molecular anthropology is a field of evolutionary biology investigating the links between modern and ancient humans, and between contemporary groups (Destro-Bisol et al. 2010). In this area of anthropology, DNA and protein sequences are analyzed at the molecular level, and inferences can be made about the relationship and history of evolution between groups. The work of population geneticists focuses on the application of Darwinian and Mendelian genetic principles to human groups: natural selection, gene frequency change, and variation; developments in this field have allowed for a deeper understanding of the genetic variation within and between human populations. Epidemiology is a field of medicine focused on the incidence, distribution, and spread or control of human disease and factors related to human health. Genetic epidemiology focuses on the study of human variation viewed through a genomics lens (Destro-Bisol et al. 2010). Work of researchers in these various areas has allowed for the identification of genetic variants within groups that protect or predispose for human disease, variants that are seen solely in one or a few human populations that may or may not be related to health, and estimates of human migrations and eras when human groups become isolated and/or merged with other groups. In a sense, the DNA of any given person contains a historical record of the movement his or her ancestors, and the history is beginning to be uncovered by scientific discoveries of today, some of which may have health implications.

In spite of all that is known about the biogeographical history of human populations, some have pointed out certain limitations of assigning "race" or "ethnicity," whether assessed by DNA test or other method (Jackson 2014). Some issues of significance related to conclusions of ethnicity made by ancestry testing companies are highlighted here:

1. Human migrations have occurred over thousands of years, yet current analyses use contemporary populations. Human populations have seen repeated series of bottlenecks, migration, and admixture due to famine, epidemics, war, colonialization, enslavement. The speed and ease of human movement world-wide, improved by transportation advances in the past few centuries, have also impacted gene flow in populations around the globe.
2. Each company uses its own available data, algorithms, and estimates of time (estimating populations from 200 years ago versus 500 years ago versus 1000 years ago, etc.). This causes ethnicity estimates to vary from company to company, as described in more detail above in the section regarding admixture analysis.
3. In general, ethnicity estimates can identify the continental level, but the finer details (sub-regions of Europe, or indigenous tribal groups in the Western Hemisphere, for example) are less reliable at this time. Yet this is often the information customers seeking the test desire: *From which indigenous North American tribe did I descend? In which country of Europe did my ancestor live?* Television commercials and other forms of marketing for commercial ancestry testing often insinuate that this level of detail is possible, however the outcomes of testing often fall short of the expectations of the customer.

Finally, it can be difficult to determine the validity of testing from home DNA test companies; companies providing ancestry testing make information on the methodologies of the testing available on their websites (Ball et al. 2013; Khan and Rui 2014; 23andMe 2014) however without publication in peer-reviewed journals, these white papers and information made public must be considered as un-reviewed by sources external to the companies. Since this is a competitive marketplace, this information is likely to stay proprietary for the long term.

Clinical Utility of Ancestry Testing

Although some studies have suggested high ratings of perceived personal utility for home DNA testing and, in some cases, the subsequent sharing of this information with physicians (23andMe 2014), research is limited specifically on the subtype of home DNA testing that is our focus in this paper, ancestry testing and its relation to the health/medical sphere. The clinical utility of ancestry testing is therefore unclear at this time. Because the testing is focused on identifying relationships and ethnicity and not directly health concerns, standards and recommendations for potential medical aspects of ancestry testing have not been established by any professional body to date (as far as authors are aware); some groups, such as Association of Molecular Pathology, have chosen to remain neutral on the testing (AMP 2015) or have not taken a stance (NSGC). Reasons provided for the testing are listed in Table 1.

Family health history depends on an accurate representation of genetic relationships between relatives in a family, and for a full assessment, acquiring accurate and reliable health information on three full generations of a family is suggested (NSGC 2015b). The feasibility of acquiring a full family health history is called into question for many people. One recent study demonstrated that the difficulty of completing a questionnaire on family health history was not due to the tool itself, but rather due to the difficulty of accessing one's family history (Armel et al. 2015). In some cases, ancestry testing is being used to rule in or rule out genetic relatedness between individuals in a family and is being ordered as a replacement for information missing due to adoption and lack of access to family health history (Royal et al. 2010; Baptista et al. 2016).

Table 1 Reasons cited for ancestry testing[1]

Various reasons for pursuing ancestry testing
Getting past dead ends ("brick walls") in family history research
Matching or comparing genealogical and biological family trees
Solving mysteries and investigating family lore
Tracing migration of surnames
Filling in missing information (particularly common in cases of adoption and donor conception)
Locating unknown genetic relatives
Proving group membership (indigenous or native tribe, minority group, etc.)
Immigration/citizenship purposes
Interest in personal genomics, including health and trait data that may be provided
Access to raw data
Generalized curiosity

[1] These reasons were listed by customers of the testing and obtained from a review of social media posts, blogs, articles, and personal communications with the authors

In one case reported in the literature, an ancestry test was used to infer a genetic marker for health based on whether a segment of DNA was inherited from the relative known to carry the marker (Roberts et al. 2011). And seeking out explanations for health conditions, in addition to predicting risks for them, have been identified as purposes for customer interest in personal genomics (Meisel et al. 2015).

Genetic testing has also allowed identification of types of endogamy, incest, consanguinity, and "founder" populations (Ten Kate et al. 2010; Halim-Fikri et al. 2015; Ceballos and Alvarez 2013; Ben Halim et al. 2005; Bittles and Black 2010). Recommendations for incidental discovery of consanguinity when discovered in the clinical setting have been developed by the American College of Medical Genetics and Genomics (Rehder et al. 2013). Some unpublished cases exist of individuals found to have been products of incest via analysis of ancestry testing results; discovery of the information about incestuous origins led to genetic counseling for concerns about increased risks of recessive conditions. Ancestry testing has also been used to investigate and confirm suspected incestuous origins for an adult adoptee in at least one documented case (Bedard 2015). This and other case reports are beginning to raise the awareness and affirm the clinical utility of ancestry testing, raise recognition of potential psychosocial implications, and increase the potential relevance in the healthcare setting.

Ancestry Testing in the Health/Medical and Research Contexts

Participation in genetic research has been made available to interested 23andMe customers through partnerships with other companies and with researchers and research institutions. Participation in online genetic research has expanded and speed of discoveries increased as a result of these partnerships. Additionally, the increasing number of individuals who have possession of their own genomic data file due to ancestry testing is mobilizing additional participants in genetic research. The transferability of the raw data from ancestry testing has made participation possible for customers, via other projects such as DNA.Land and Genes for Good. DNA.Land allows for the sharing of existing raw genomic data files; Genes for Good also offers ancestry testing and raw data to individuals within a research setting, providing an alternative to ancestry testing in the for-profit marketplace. Genes for Good participants provide responses to online health surveys in addition to a DNA saliva sample with the understanding that the combination of health survey responses and genomic data will enable genetic health discoveries in the future. At the time of the writing of this paper, 23andMe is the only company providing FDA-approved health reports alongside trait and ancestry reports. There are rapid changes taking place in the ancestry testing sphere, including a 2016 update to the SNP chip used for testing at AncestryDNA and the 2015 launch of the personal genomics company Helix. Thus, the growth of the research and health markets - as well as competition among the companies aiming to offer both health and ancestry testing - is expected to grow and evolve.

Ancestry Markers and the Technology

Ancestry testing is performed via genotyping, using a set of markers that varies in number from approximately 500,000 to 700,000 depending on the company and its chip. According to the International Society of Genetic Genealogy, all of the major ancestry testing companies use an Illumina chip platform (ISOGG Wiki 2016). The types of markers evaluated by an ancestry test depends on the type of DNA testing available at a given company and the testing chosen by the customer. The options include mitochondrial, Y DNA, and "autosomal" testing (which also includes the X chromosome).

Y DNA Analysis

Y DNA analysis includes options for STR and SNP testing, and each of these types of analyses returns a specific type of information. Comparison of STR markers on the Y allows for determination of recent descent of two males from a common ancestor (in other words, a personal haplotype). SNP analysis reveals the deeper ancestry, the Y haplogroup to which that male belongs and into which part of the phylogenetic tree of male human history that male's paternal lineage falls (ISOGG Wiki 2016). The Y markers studied for genealogical purpose are in the non-coding regions of the Y chromosome, meaning

that as of this writing Y results are unrelated to medical conditions. However, medically significant findings have been deduced from Y testing including Y-related male infertility (King et al. 2005).

Mitochondrial DNA Analysis

Analysis of mitochondrial DNA (mtDNA) for purposes of ancestry testing is performed using the mitochondrial genome. Options for mtDNA testing include SNP testing, sequencing of the hypervariable regions 1 and 2 (HVR1 and HVR2), and sequencing of the full mitochondrial genome. Because of the value of the mtDNA to health research, some projects like mtDNA Community and NCBI's GenBank have been developed that allow customers of mtDNA testing to contribute their raw file to further human evolutionary studies and health-related genetics research (NCBI. GenBank Overview 2016; mtDNA Community 2016).

Autosomal and X DNA

In spite of the fact that X (and sometimes Y) is included as part of the testing of the numerical chromosomes, for simplicity sake ancestry testing on the autosomes and sex chromosome are referred to collectively as "autosomal DNA" testing. Rather than connecting the customer to the matrilineal or patrilineal lines only, autosomal testing allows for the investigation of genetic relationships of all genealogical lines. The tremendous value of this expansion of ancestry testing in genealogical research has been an important factor in the growth and popularity of ancestry testing as a whole.

Raw Genomic Data

Raw genomic data (via downloadable VCF file) is provided to customers at the top three ancestry testing companies (23andMe, AncestryDNA, Family Tree DNA), but the contents of each VCF file vary. The original set of markers included in a raw data file depends on the microarray chip used, and also whether the company does any editing to the data before making it available. Some companies like Family Tree DNA, for example, remove some health-related markers from the file before providing it to a customer.

Raw data can be transferred and analyzed by third-party tools. Ancestry testing companies themselves are not the developers of analysis tools, rather unaffiliated, individual developers. Although the testing companies often enable an easy process to share raw data with a third-party site, the ancestry testing companies have not been involved in developing the more common analysis tool (GEDMatch, Promethease, etc.). The concern with lack of oversight and regulation of home DNA testing which is highlighted in the next section is extended to third-party tools as well; as for the testing companies themselves, the oversight and regulation by regulatory bodies for third party sites and tools is either limited or non-existent at this time.

Protections and Oversight

Privacy and Security Concerns

Michael Cole v. Gene by Gene (2016) is, to the authors, the first known lawsuit filed against a company as a result of data from ancestry testing being shared without knowledge and explicit permission of the tested customer. As of this writing, the case is moving through the legal system. This is not the only incident involving publicly-accessible online genomic information having been possible to identify an individual (Bohannon 2013; Gymrek et al. 2013). With the exception of these cases, the privacy and security concerns discussed to this point focus on what is *possible* to do with open- and restricted-access genealogical databases, raw data, and analysis tools, rather than actual, identified harm to individuals. How common breaches are, and the consequences of such situations to individuals, is undetermined at this time. Some ethicists have argued the benefits of advancing genomic knowledge – i.e. beneficence to the public – must be considered and weighed against personal privacies (Gutmann and Wagner 2013). As the perception of risks and benefits shift over time, it is possible that policy and public opinion will as well.

Advocates of ancestry testing often highlight the Genetic Information Nondiscrimination Act of 2008 (GINA) as providing privacy protections to customers of home DNA testing (SNPedia 2016a, b; Wikipedia 2016), however investigations have pointed out the limitations of GINA and gaps in protection left behind (McGuire and Majumder 2009). It is unclear how this law may or may not protect customers of home DNA testing.

Regulating Bodies: CLIA, CAP, FDA, and More

There is a lack of oversight of the ancestry testing companies (ACOG 2008; Hawkins and Ho 2012; McGuire et al. 2010) and whereas discussions often focus on the regulation of the testing provided by genetic testing companies, the more concerning and less-discussed issue is the lack of oversight and regulation of third-party tools. This and additional concerns about the transfer and use of raw data, and of third-party tools, will be discussed in more detail in a following section.

A regulating body is a public authority or government agency that supervises or regulates a particular activity for the protection of the public. A number of different advisory

and regulatory agencies are involved in certifying and overseeing genetic testing laboratories (see Table 2). The specific roles and activities of each of these regulators is outside the scope of this paper, however we will briefly highlight the importance of these in the home DNA testing field.

In the home DNA testing arena, Clinical Lab Improvement Amendments (CLIA) certification (overseen by a regulating body, CLIAC) plays an important role by ensuring that genetic laboratory practices provide high clinical validity of test results (in short, that laboratories follow best practices for testing and that the results they provide are accurate and reliable). The recent involvement of the Food and Drug Administration (FDA) in asserting regulatory rights over home DNA testing has led to increasingly stringent rules by which home DNA test companies must abide (Mezher 2015).

Determining which regulatory bodies are involved and which certifications an individual home DNA test company is challenging. Firstly, there is no easily identifiable resource for checking on which companies' testing platforms have regulatory approval. It also requires extra investigation into the limits and protections provided by certain certifications to understand what they mean in terms of the results being valid and useful. Secondly, as we have seen with FDA's assertion of its role in home DNA testing sphere, changes and developments are ongoing. Understanding which of home DNA testing companies are in operation, the tests they offer, the certifications and regulations they meet, and what this means for the use of test results for the client would require much time and attention. Dedicating time is not reasonable to the typical clinical genetic counselor whose time demands are divided between other important tasks, such as understanding nuances of clinical testing and insurance coverage, meeting with clients, and managing various clinic operations.

This is an important issue and raises the need for clearer explanations and transparency by the home DNA test companies about what guidelines they follow and certifications they have, and what this means for the customers of testing.

Genetic Counseling and Ancestry Testing

Pre- and Post-Test Counseling and Home DNA Tests

Prior reports have raised concerns about home DNA customers being able to make informed decisions based on potentially unbalanced information presented on company websites (Singleton et al. 2012). For home DNA testing, both pre-test and post-test counseling consists of information available on the website where a testing kit is ordered. Some information is available prior to testing, and some additional information becomes available after having already ordered and submitted the sample, while logged into through a personal portal account. Because testing from these home DNA test companies has primarily focused on information that is not directly medically relevant, this web-based informed consent structure has not come under significant scrutiny. However, as the menu of options increases, and spreads into medically relevant information, that will likely change for both pre- and post-test counseling. As the menu adjusts and expands, counselors will need to think critically about which type of test requires which modality, and amount of effort, in a client-centered process. Partnering with the home DNA companies will likely be a necessary piece of this process.

The value of genetic counseling services is being increasingly recognized, and some companies provide information on their websites for how to locate a genetic counselor. For example, as of the time of this writing, a link to the NSGC genetic counselor finder tool is listed on the 23andMe website.

Other than online groups and social networks, what support is available for consumers of ancestry testing who receive unexpected information? Pre-test counseling is not common or part of the routine services of testing, and studies have shown clients of home DNA testing are unlikely to seek out genetic counseling services (Levin et al. 2012) even though the benefits in terms of decisional conflict, knowledge, and psychosocial adaption, are significant (Bernhardt et al. 2000;

Table 2 U.S. advisory and regulating bodies of the medical genetic testing sphere

Regulating bodies	Current role in home DNA testing oversight
AABB (formerly referred to as American Association of Blood Banks)	Provides oversight for paternity, maternity, and other traditional relationship tests; does not currently provide oversight for ancestry testing
College of American Pathologists (CAP)	Professional group that offers certification for laboratories that perform clinical testing and meet quality control criteria
Clinical Laboratory Improvement Advisory Committee (CLIAC)	Committee that oversees the FDA and the CLIA program for the promotion of laboratory quality control practices
Food and Drug Administration (FDA)	U.S. federal agency newly participating in oversight of laboratory-developed testing, including home DNA tests
Federal Trade Commission (FTC)	U.S. federal agency that issues alerts and information for protection of consumers; has published a consumer alert regarding home DNA testing
Secretary's Advisory Committee on Genetic Testing (SACGT)	A committee of the U.S. National Institute's of Health offering recommendations regarding oversight of genetic tests

Davey et al. 2005). Unintended consequences/outcomes from testing will in some cases require extra support, information, and expertise (misattributed parentage, chimeras, undisclosed adoption affecting accurate family health history, incest/consanguinity, unexpected ethnicity). Knowing where to refer such cases would be a valuable part of the toolbox of genetic counselors if they are being cited as referral sources for customers of ancestry and other home DNA tests. Customers of ancestry testing are notified by email when results are "in" and the information can be learned at any time or location, whether at home, work, or out in public. The information can be confusing at first, and the first time a person interacts with an online ancestry test result is often the same time that an unexpected close match or other unanticipated information can be seen. The network of genetic genealogists that operates online has been an important resource for helping individuals dealing with outcomes of an incidental or unexpected outcome to find support and information. This group has been requesting support from genetic counselors and other genomic health professionals with limited response [personal communications, 2014].

Relevance of Ancestry Testing to Genetic Counselors

Whose responsibility is it to counsel on ancestry test results? Although there is a lack of studies specifically about ancestry genetic testing, there have been many studies about home DNA testing, which encompasses ancestry testing. Prior publications have discussed the psychological distress possible in the setting of home DNA testing and the emerging roles of genetic counselors in the home DNA testing market (Dohany et al. 2012; Harris et al. 2013). A study published in 2011 by Hock, et al. investigated genetic counselors' knowledge and beliefs about home DNA testing. Outcomes revealed a gap in knowledge about home DNA testing for a large minority of genetic counselors and widespread concern amongst genetic counselors about the possibility of misinformation and a false sense of security provided to consumers of a home DNA test (Hock et al. 2011). The survey also revealed findings that genetic counselors are varied in their beliefs about home DNA tests but generally take a nuanced approach rather than a black-and-white stance on the testing, considering factors such as geographical location and privacy desires of potential customers of home DNA testing as important to the decision-making process and contents of the discussion with the client.

A common theme seen in multiple publications on the topic has been a call to action for genetic counselors to learn about and become educated on home DNA testing; some have pointed out the foundational skills developed by genetic counselors can be adapted and applied to counseling for home DNA tests with positive benefits to customers, (Hawkins and Ho 2012; Hock et al. 2011; Sturm and Manickam 2012; O'Daniel 2010; Uhlmann and Sharp 2012; Middleton 2012; Weaver and Pollin 2012; Khoury 2016; Predham et al. 2016). The benefits of genetic counseling for helping assist in family communication about genetic results and to meet client's psychological adjustment have been explored by others in the past (Bernhardt et al. 2000; Davey et al. 2005; Corpas 2012; Middleton 2012).

With growing cases of ancestry results affecting identity, psychosocial assimilation of information, and health-related factors, the value of genetic counseling services are beginning to be recognized for this sub-type of home DNA test (Moore 2014). What role do genetic counselors in different settings have in assisting customers of ancestry testing to interpret and adapt to their results? An obvious first question is which specialty of genetic counselor should see these clients – prenatal, pediatric, personalized medicine – or should an entirely new specialty be created? Secondarily, are genetic counselors prepared to counsel clients who have questions and if not, how do they become prepared?

Although no genetic counselors are currently employed in a clinical or tele-counseling role at an ancestry testing company, some companies and third-party tool developers seem to expect genetic counselors to be able to support and answer questions for customers who have them. Additionally, the National Society of Genetic Counselors encourages such referrals in its position statement on Direct Access to Genetic Testing (Hock et al. 2011).

In one 2012 article in the Journal of Genetic Counseling, specific guidance was provided in the request for genetic counseling graduate curriculum to include material on home DNA testing (Weaver and Pollin 2012). The source of ongoing training for genetic counselors on home DNA tests including ancestry testing is unclear, however. As far as the authors are aware, training on ancestry testing is not covered or an emphasis in the graduate curriculum. There have been modest efforts to educate genetic counselors on ancestry testing via professional learning opportunities and continuing education (Moore 2014; Kirkpatrick et al. 2015). These presentations were well-received and additional training was requested from within the community following the webinar and in the session feedback [personal communications, 2015]. We argue in favor for an extension of this call to action. Heightened awareness and preparedness amongst genetic counselors involved in the personalized medicine area should be viewed as an extension of genomic counseling.

The results of ancestry testing might be considered by some as benign, interesting, or irrelevant to health and thus not subject to the provision of genetic counseling services; however, the case prevailing against the use of ancestry testing as purely "recreational" is growing. Results of some ancestry tests cross over into the sphere of health implications as will be explored below. As mentioned earlier in the paper, the understanding of the value between genealogical research, family tree building, and health research is increasingly recognized.

Aside from health implications, ancestry testing and the analysis of raw data have provided unexpected and incidental information to customers (Moore 2014). The support after unexpected test outcomes is a special area of expertise for genetic counselors that could be applied in these situations. Customers of ancestry tests have learned they were products of incest, and that a parent/child relationship was not as they had believed or expected (infidelity, non-paternity, undisclosed adoption, donor-conceived origins, and chimerism) (Baird et al. 2015; Hercher and Jamal 2016). Some individuals have been able to determine the presences of a pathogenic variant in BRCA either from direct reports by a home DNA test or by interrogating raw data (Francke et al. 2014). In some cases, ethnicity estimates from biogeographical analysis have not been consistent with a customer's sense of identity prior to the testing, or the story of ethnic origins revealed from DNA testing does not match the family history they were raised to believe. Finding out an expected ethnic background that is present can be as upsetting to a sense of identity as finding one that is not present and is "supposed" to be. Grappling with new information that must be integrated into a sense of identity and rewrites a family narrative is more difficult for some people than others. Genetic counselors who have worked with individuals struggling to integrate a discovered genetic variant or a new diagnosis will be familiar with the challenges these individuals face and the varied responses that can be seen from one individual to the next. The value of a genetic counselor's perspective on typical responses to DNA test results, and the value of a post-test genetic counseling session for exploring the psychosocial impact of information from a DNA test, are clear.

Guidance for Genetic Counseling in Scenarios Involving Ancestry Testing

Practice guidelines for genetic counselors do not yet exist for ancestry testing. Until guidelines are available, we offer some thoughts for best practices.

A. Support and validate the client's desire to understand more about genetics and the implications of DNA discoveries for themselves and their family members.
B. Consider your responsibility as the Genetic Counselor – determine is this inside of my specialty or not? Recall that discussing the benefits, limitations, and residual risk associated with genetic testing is within the competencies of all counselors.
C. Ancestry testing is a significant part of the home DNA testing market and as such, genetic counselors have a responsibility to learn about the testing; when someone has questions, listen, validate, support them, and seek additional resources and information.
D. Acknowledge the value of ancestry testing as a tool for exploring identity, ethnicity, family, relationships, and how they can connect to health. Do not fall into the trap of seeming dismissive of someone's choice to pursue testing.
E. Briefly inquire into the goals of the person - could the information be obtained another way? Is the answer they are seeking available from ancestry or other DNA testing?
F. Ask, will you know where to go if you have questions or need support after testing?
G. Answer the questions you can, and refer if the client desires additional genetic counseling beyond your scope of practice; search the "Find a Genetic Counselor" tool for GCs who list Personalized Medicine and/or ancestry testing as a specialty.
H. Understand and point out benefits of genetic counseling services, such as the provision of information, supporting improved communication between family members, and enhancing psychological well-being.

Future Directions of Ancestry Testing and Paths for Genetic Counselors

The value of large databases of genomic data from customers for medical research purposes is significant, enabling cohorts of participants that is precedent setting, at a pace that is never-before-seen in biomedical research. As a result, some groups are beginning to get involved in attempts to marry genealogy and genetics. If recent developments are an indication of future trends, the next few years are likely to present growing opportunities for the integration of genealogical research and ancestry testing, genetics research, and healthcare. What this means for the variety of stake-holders, including individuals, researchers, for-profit companies, healthcare providers, and genetics professionals is still to be determined. The current healthcare payer systems and their effects on access to testing and care in the United States is also making this a more complicated situation for potential and existing customers in the United States.

There are many possible roles for genetic counselors in an expanded future of genetic genealogy. Genetic counselors have already begun to serve in roles for research groups in this niche. Projects such as Genes for Good and DNA.Land could likely benefit from increased engagement of genetic counselors and the skills that research genetic counselors bring to research projects in the form of project coordination, management, patient/client engagement, ethics consultation, writing, and education. Just as genetic counselors are employed at increasing numbers by commercial laboratories, a future with genetic counselors employed at genealogy firms, ancestry companies or startups entering this sphere is likely. The value of the genetic counselor's skills are clearly evident. Communication of complex information for a variety of audiences is a core feature of the successful graduate from a

genetic counseling training program. Project management and leadership, provision of psychosocial support, research and writing skills, case development and follow-through, and resource identification for customers are a few of the many other skills of a genetic counselor that fit with the needs of companies in this market.

The market for startups in the genomics and genealogy worlds also looms large. Every year, entrepreneurs and startups in the genealogy industry meet at conferences such as RootsTech and Genomics Fest to learn, network, and compete for prizes. The startup company is a type of setting some genetic counselors have already explored and report having found satisfaction and professional skill development (Rabideau et al. 2016).

Another path that may attract some genetic counselors is that of private consulting. There is precedent for this in both the genetic genealogy profession and the genetic counseling profession. Other ideas for genetic counselors include consulting for or direct employment by testing companies and third-party tool developers. Which of these opportunities will be of interest to genetic counselors? Which opportunities hold the greatest value for the greatest number of clients? Finally, as we consider genetic counselors moving into this area of work, will practice guidelines be an important part of genetic counselors entering this area, and if so, who will write them, and what might they say?

Conclusion

Ancestry testing has evolved since the early 2000s and shows no signs of waning. The role of the genetic counselor in the sphere of this type of home DNA test will continue to evolve with the growth and development of the ancestry testing market and projects involved in making the data collected from the testing relevant to genetics and health. The benefits of the genetic counselor perspective are growing in recognition among those involved in the genetic genealogy world and genetics research. Opportunities have presented themselves; genetic counselors have the choice to decide how, when, and in what capacity to be involved. How the integration of genetic counseling services in situations involving ancestry testing will be used to the improved understanding by and support for customers of ancestry testing will depend on how it is leveraged by those in the profession.

Compliance with Ethical Standards

Conflict of Interest Author Brianne Kirkpatrick is founder and owner of WatershedDNA, LLC a company which provides consultations on ancestry testing and raw data.

Author Misha Rashkin declares no conflict of interest.

Human Studies and Informed Consent No human studies were carried out by the authors for this article.

Animal Studies No animal studies were carried out by the authors for this article.

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