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Teaching Genomic Counseling: Preparing the Genetic Counseling Workforce for the Genomic Era

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Abstract

Genetic counselors have a long-standing history of working on the clinical forefront of implementing new genetic technology. Genomic sequencing is no exception. The rapid advancement of genomic sequencing technologies, including but not limited to next generation sequencing approaches, across all subspecialties of genetic counseling mandates attention to genetic counselor training at both the graduate and continuing education levels. The current era provides a tremendous opportunity for counselors to become actively involved in making genomics more accessible, engaging the population in decisions to undergo sequencing and effectively translating genomic information to promote health and well-being. In this commentary, we explore reasons why genomic sequencing warrants particular consideration and put forward strategies for training program curricula and continuing education programs to meet this need.

Keywords

Genomics; Next Generation Sequencing; Genetic Counseling Training; Continuing Education

Changing Paradigms

Large-scale, clinical genomic sequencing is challenging, and even up-ending, medical paradigms (e.g. (Ng et al., 2010; Sloan et al., 2011)). The traditional pathways to diagnosis of genetic disease are reversed, with mutations being identified early in disease course, often even before the development of canonical symptoms or identification of family risk. This paradigm shift blurs the lines between concepts of “affected”, “unaffected” and “at risk”. Single disease risk likelihoods and/or disease diagnoses will increasingly be interpreted in

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the context of other disease probabilities and risks competing with one another for salience and personal relevance. Furthermore, the range of genomic variants for which clinical relevance must be assessed is broadening, with limited but advancing evidence to inform these assessments. Significant questions remain about the ways genomic information will be received, understood and utilized by individuals, families and health care practitioners. Regardless, it presents a major change from the traditional manner in which medical genetics evaluations are conducted and information obtained.

In this issue, Profato et al, report the findings of a survey of genetic counseling training program directors on the integration of genomics into their curricula (Profato, 2011). Nearly all programs interviewed (15 out of 16) cited integration of genomics into curriculum as being important, and as of Fall 2011, most of these programs had started to integrate teaching objectives related to genomics into their curricula. Responding program directors ranked genomic technologies, complex disease genetics and genomic counseling techniques/strategies as most important to include when training genetic counselors. However there was significant variation in how this was operationalized. For example, the hours dedicated to genomics and related topics varied (from 2 to 35+ hours), as did the mode of teaching. Much of the content was addressed through 'informal' teaching (e.g. journal clubs or grand rounds, versus coursework), and topics traversed existing courses, making it hard to quantify. Despite this variability, the authors note that programs were consistently teaching a 'core skill set,' including; understanding genomic technology, interpreting variant data, translating it into clinically meaningful information, and communicating results to patients.

Similarly encouraging are the growing opportunities for practicing genetic counselors to learn more about genomic technologies and applications to clinical care and research. Over the last few years, there have been numerous and often overflowing plenary sessions, educational breakout sessions, presented papers and posters at the National Society of Genetic Counselors (NSGC) Annual Education Conference and its related short courses addressing genomics topics. In 2010, a new Personalized Medicine Special Interest Group was formed and has been instrumental in providing the NSGC membership with educational programs and resources, and in advancing exposure to genomic medicine. Nonetheless, integration of genomics into the training and education of genetic counseling students and practicing genetic counselors still poses ongoing and significant challenges. This commentary aims to address core areas we anticipate will change within genetic counseling practice as genomic medicine becomes increasingly implemented in clinical and research settings, and to propose educational approaches that can be incorporated into training programs and continuing education for the genetic counseling workforce.

Genomic Sequencing and the Practice of Genomic Medicine

In order to help clients and colleagues understand and adapt to the implications of specific genomic variants, genetic counselors will need both conceptual grounding and practical experience with the processes by which these variants are classified and interpreted. They will need to be prepared to actively participate in these processes whether employed in the laboratory or working in a clinical setting on the receiving end of sequencing reports, where they will translate the implications of results for colleagues and clients. Specifically,

students and practicing genetic counselors will need exposure to the techniques used to identify medically relevant variants from sequence data. This will include not only exposure to classic molecular concepts and the implications of various mutation types, but also exposure to analytic methods that predict and model conservation and splice variants and apply models of inheritance consistent with familial patterns of disease (Ng, Nickerson, Bamshad, & Shendure, 2010). For example, if a researcher analyzes genomic sequence data from a parent-child trio to identify a causal gene in a presumably autosomal recessive condition, they may filter out pathogenic variants that do not fit a recessive segregation pattern. To understand this process, learners must understand the bioinformatics filtering processes and the assumptions applied, while appreciating the dynamic nature of interrogation, and the still important role for manual annotation and interpretation of the existing literature.

Adding to this, the parameters used to assign pathogenicity to any one particular variant may change with evolving data on penetrance, expressivity, non-genetic influences and genetic modifiers. For example, we know that initial estimates of penetrance derived from high risk families enrolled in research studies (e.g. sudden cardiac death or cancer syndromes) are often higher than those seen as testing becomes more broadly performed (Watkins, Ashrafian, & Redwood, 2011). Additionally, as more people receive these results outside of the context of primary testing, either through sequencing for other indications, or from a direct-to-consumer laboratory, we can expect that both laboratory and clinical interpretation of specific variants will continue to change (Berg, Khoury, & Evans, 2011; Green et al., 2013). It is also increasingly likely that we will work with variants which simultaneously confer diagnostic, prognostic, pharmacogenetic and/or risk information (Westbrook et al., 2013). Examples include variants in *NOD2*, associated with Crohn's disease risk and prognosis, or *GSTM1*, associated with susceptibility to a number of cancers and response to chemotherapy.

Beyond the core scientific knowledge, clinical genomic sequencing will need to be taught in the context of emerging paradigms in diagnosis, risk prediction and patient care. For instance, program curricula may need to accommodate shifts in the relevance and framing of classical principles of human genetics. Traditional genetic counseling training has focused on the application of family and medical history to identify a differential diagnosis, appropriately target the proper genetic test to the proper person, and provide accurate family risk information. In the future, rather than looking for variants to explain family history, the converse will apply as we use family and medical history to help better understand variants and their potential penetrance within a specific family or individual (Green, et al., 2013). An example of a "variant-first" diagnosis has been reported in a participant in the NIH ClinSeq® study where an individual previously reported to be healthy was found to carry two mutations in the *ACSF3* gene and subsequently shown to have the metabolic condition, combined malonic and methylmalonic aciduria (Sloan, et al., 2011). As the technological capabilities evolve, we will be increasingly able to account for and counsel about the combined effects of multiple genes (and the environment) to cause disease. For example, individuals with congenital Long QT (LQT) syndrome may be found to have mutations in more than one disease associated gene (biallelic digenic inheritance), or may be found to

have deleterious mutation in one gene (*KCNQ1*) and acquired LQT drug sensitivity in another gene (*KCNE1*), posing medical management challenges not only for the proband but also at risk family members (Schaffer, 2013; Tester, Will, Haglund, & Ackerman, 2005).

Genetic counselors are well positioned to help both the health care workforce and individual clients explore specific issues related to clinical and personal relevance of genomic sequencing and specific variants, and of the limitations in our knowledge about these variants. Speaking to the importance of this role, the recent recommendations from the American College of Medical Genetics and Genomics suggest that clinicians take responsibility for contextualizing sequencing findings to clinical circumstances (Green, et al., 2013). Individuals may learn about variants which bear little immediate relevance to their own personal health management decisions, but which may be highly relevant for other family members (e.g. an 80 year old man with end stage renal disease learning of a known pathogenic mutation in *BRCA2*). Conversely, individuals may learn about variants that are highly relevant to their health status, family history and/or health decision making, but be faced with uncertainty regarding the pathogenicity of a single specific variant. Though variants of unknown significance are not new to genetic counselors, the potential number of variants for any one individual will increase the magnitude of the associated complexity. In these situations, having the skills to assess, understand and apply clinical and personal relevance for the genetic counseling client is of critical importance.

Consent to Genome Sequencing

Facilitating informed consent for clinical and research genetic testing is a long-standing core competency for genetic counselors. Traditional informed consent for genetic testing has included a set of fairly specific details including the procedures to be performed, possible risks, and, in research, expected duration of one's participation (OHRP, 1998). In contrast, the evolving consent process for genome or exome sequencing involves the potential not only for a focused genetic test result for a particular indication, but also for incidental or secondary findings. These findings encompass a wide range of both medically actionable and non-actionable conditions with varied penetrance, age of onset and symptoms, and come with the possibility of updated or new variant results over time (Berg, et al., 2011). As such, the informed consent process has expanded to include agreeing to a vague notion of uncertainty about the type of results to be returned, when they will be returned, and how they will be returned. Individuals undergoing testing will be increasingly faced with variants predicting increased risk for conditions not predicted by their personal or family history, and therefore the informed consent process will be inherently different from the 'traditional' genetic testing consent process, which often taps into the personal and family experience with disease, and where individuals often have strong feelings about whether or not they desire information regarding their own personal risks.

Ideally, clinicians will find a way to provide sufficient information without providing so much information that the most salient points are lost. Available evidence would suggest that information-giving strategies involving less verbal dominance on the part of the genetic counselor and active exchange between counselor and client promote deeper understanding and are more highly valued by clients (Bernhardt, Biesecker, & Mastromarino, 2000; Roter,

Ellington, Erby, Larson, & Dudley, 2006). Some have proposed consideration of a more ‘generic consent’ process, whereby individuals are informed of a broad range of results they may receive, with the potential for deeper discussion based on individual preference or resultant needs (Elias & Annas, 1994; Wolf, Annas, & Elias, 2013). To support an evidence-based approach to the practice of genomic counseling, future research should assess various consent models and their outcomes.

Early studies of clinical research populations and representative samples of the general population have reported enthusiasm towards genomic sequencing and optimism regarding use of genomic information to improve health (Facio et al., 2011; Platt, Bollinger, Dvoskin, Kardia, & Kaufman, 2013). Genetic counselors will be instrumental in helping to mitigate these high expectations and to facilitate a more tempered perspective that acknowledges the time it will take to learn how to interpret and use genomic information to improve health or disease outcomes. Related to this, the ongoing re-annotation of variants and discovery of new disease gene variants require that clinicians and researchers confront many aspects of “duty to re-contact” (Wolf et al., 2012). These challenges to the informed consent process warrant further consideration into how genetic counselors are trained to promote informed choice in the presence of uncertainty and to manage expectations. It is increasingly important that students be exposed to evidence-based models of decision making and embrace a conceptual understanding of uncertainty (Han, Klein, & Arora, 2011). Specifically, emerging evidence suggests that research participants may hold perceptions about uncertainty which are different than those held by the clinicians and researchers with whom they interact (Biesecker et al, manuscript in preparation). This has important implications for facilitating informed choice about undergoing and receiving results from genomic sequencing.

Return of Genomic Sequencing Results

There is growing evidence that individuals receiving high penetrance variant results are often motivated take action to reduce risks and screen for disease. Women who learn they carry deleterious *BRCA* variants show significantly greater uptake of screening and risk-reducing surgery (Schwartz et al., 2012), individuals who carry Lynch syndrome mutations undergo more colonoscopies than those who are not found to have mutations (Hadley et al., 2011) and families with a range of genetic diagnoses communicate to a majority of their first degree relatives about their conditions (Wiens, Wilson, Honeywell, & Etchegary, 2013). However, these behaviors are not universally adopted; there are significant modifying factors, some of which include personal and family experience with the condition, perceptions of susceptibility to and severity of the condition and encouragement by health care providers. Additionally, there is some data to suggest that when faced with lower predictive results (e.g. low penetrance genetic risk associations for common complex diseases such as diabetes or heart disease), individuals may have intent towards behavior change, though limited long term change occurs (Bloss, Schork, & Topol, 2011; McBride, Wade, & Kaphingst, 2010). Since most of these studies are also biased by variables likely unique to “early adopters” (James et al., 2011; Kaphingst et al., 2012; McBride et al., 2010), this concept of how individuals who receive predictive risk information through genomic sequencing will act on their results is an open question that warrants research, particularly

when we consider that they will include diverse populations who have had limited or no exposure to genetic and genomic testing and who are likely to differ in a number of ways from those previously studied

From a training standpoint, a key teaching objective is that students and genetic counselors learn to assess and understand the ways individuals engage cognitively and emotionally with genomic information, how they cope with the information, and how they make decisions about how to use it. As discussed above, with sequencing comes the likely possibility that individuals and families may receive information for which they have no prior personal experience (Green, et al., 2013; Johnston et al., 2012). Client-centered, tailored counseling approaches and, where appropriate, attention to client intentions and readiness for change may promote engagement with genomic information potentially resulting in choices that reduce health risk and promote well-being (Glanz, Rimer, & Viswanath, 2008). Genetic counselors should also apply skills in providing clinical information about natural history and potential ‘actionability’ in a manner that includes assessing the clients’ response, addressing concepts such as perceived susceptibility, controllability, cause and emotion, and recognizing the ways these concepts may differ widely among individuals lacking a personal frame of reference for the information.

Finally, it is important to recognize that uncertainty is not a concept that is unique to the informed consent phase of sequencing. Many of the results stemming from sequencing may also bear a significant amount of scientific (prognostic, diagnostic, treatment) and personal (existential and relational) uncertainty, around which genetic counseling may be poised to help clients process and cope (Han, et al., 2011). Genomic sequencing adds new dimensions to traditional views of medical uncertainty, with the possibility of multiple risks for any number of disease-related outcomes being presented in concert with one another (Dorschner et al., 2013). Compounding this is the common misperception that more information should provide more certainty and control, rather than less (e.g. Hamilton et al., 2013). Uncertainty has been a part of genetics clinics since the advent of predictive testing, and genetic counselors are well trained to assess perceptions of risk and uncertainty, but may need to adapt their skills to the scope and scale of genomic information.

How can training keep up with these changes?

Overall, it is apparent that large-scale sequencing poses new challenges across the core competencies of genetic counseling, from the principles of human genetics to the counseling concepts that help clients adapt to genomic information. To address these new challenges, both new information and new teaching strategies should be integrated into current curricula in diverse ways, maximizing graduate level learning and continuing education opportunities.

- 1. Human and Medical Genetics Instruction:** Courses, seminars and clinical training (‘rotations’) should build critical thinking skills related specifically to the conceptual processes and bioinformatics approaches towards variant identification and annotation, to allow for evaluation of the strengths, weaknesses and limitations of different technologies and approaches. This includes not only familiarity with the specific genomics concepts discussed earlier, but also conceptual and practical experience with websites and resources for variant annotation. While these will

certainly change over time, current examples include: dbSNP, 1000 genomes, UCSC browser, HGMD and other variant databases (recently reviewed in detail in Johnston & Biesecker, 2013), and analysis programs such as Polyphen and SIFT (Jaffe et al., 2011; Yu, 2009). Further, students and counselors should have exposure to current standards for analysis of genome sequence information, in order to effectively integrate into practice the interpretations received from the testing lab (Rehm et al., 2013).

2. **Teaching Client Education:** With increasing amounts of information available, genetic counselors must increasingly learn to discriminate which information is of highest relevance to their clients (and their health care providers) and to help clients of all backgrounds to assimilate this information in a context specific manner into their own knowledge base. More than ever, counselors will need to tailor information to meet client needs and background understanding, and recognize that more information conveyed does not always translate to more information learned (Glanz, et al., 2008). With time and research, evidence-based strategies can be developed for effectively consenting clients to sequencing, focusing on the details most relevant to clients, and for returning findings from genome sequencing in such a way as to maximize client engagement and adaptation. Consideration may also be given to the implementation of genomics educational tools. Online genetic and genomic educational resources are also becoming more readily available, and increasingly easier for our clients to use to further explore and evaluate concepts related to genomics. Some examples include the Genetic Science Learning Center: <http://learn.genetics.utah.edu/> and “DNA From the Beginning”: <http://www.dnafb.org/>. Available tools are also becoming more customizable to allow clients to examine their own sequence information (e.g. <http://www.my46.org>).
3. **Ethics:** As in the past, genetic counselors should have strong grounding in medical ethics principles such as autonomy, privacy and confidentiality, discrimination and justice. Placing a genomic lens on these concepts, we suggest that genetic counselors have exposure to: approaches to informed consent, particularly in the face of uncertainty; patient preference; duty to warn of medically actionable variants; confidentiality in the context of research studies (including concepts of de-identification and anonymity, and data-sharing requirements); ownership of genetic data; equitable distribution of scarce resources; and duty to re-contact and/or re-annotate (Wolf, et al., 2012). Familiarity with general concepts and approaches, as well as relevant laws and position papers will be important.
4. **Counseling Skills:** As described above, genomic sequencing has the potential to exacerbate some very difficult genetic counseling issues related to uncertainty, client engagement and decision making, warranting augmentations to counseling training to promote client adaptation to genomic information. Counselors may benefit from more extensive training around the psychology of uncertainty and evidence-based methods of facilitated decision making. In working towards the goal of client adaptation, counselors should be familiar with the growing literature regarding the many diverse behavioral and emotional responses clients exhibit in response to receiving genetic and genomic information (Claassen et al., 2010;

Collins, Wright, & Marteau, 2011; McBride, Koehly, Sanderson, & Kaphingst, 2010).

Beyond curriculum content, strategies for teaching this content to students and genetic counselors are also important to consider. Evidence from studies of graduate and adult education favors student-centered didactics, in which learners take a more active role in the learning process (Knowles, 1980). These models would predict that teaching strategies promoting discussion, hands-on experiences and independent exploration will be received with more success than digital slide shows or other didactic presentations (Glanz, et al., 2008). Teaching genomics, this might involve discussions of specific clinical cases and the genetic, educational, ethical and counseling issues which arise, exposure to individuals undergoing genome sequencing and hands-on exposure to sequence data with time spent exploring available bioinformatics tools. Rather than presenting screen shots of available databases, a “computer lab” approach might be considered in which students are given mock data and asked to work through the databases themselves, with guidance. Similarly, students rotating in laboratory settings might learn more from being asked to physically work through laboratory protocols and processes, rather than being shown demonstrations or examples. Though this approach may seem resource intensive, many bioinformatics tools have been made freely available for download. On a national level, consideration may also be given to the development of online interactive training modules or courses to serve the genetic counseling community at large.

Several recent publications have studied and commented on the method of teaching genomics by allowing students to explore their own genomic sequences (Boguski, Boguski, & Berman, 2013; Callier, 2012; Salari, Karczewski, Hudgins, & Ormond, 2013; Salari, Pizzo, & Prober, 2011; Vernez, Salari, Ormond, & Lee, 2013; Walt et al., 2011). Early qualitative evidence would suggest that this process could, with some specific populations, enhance student engagement with genomics curriculum. However, it is critical to realize that these early studies included a self-selected population of learners with potentially significant biases and were conducted with significant cautions into the curricular and testing process. As such, broader implementation of this process needs to be carefully considered, given the inherent power differential between faculty and students, and the potential need for clinical follow up on some subset of variants identified. Similar processes initiated at other institutions have been subsequently halted in favor of models which posed fewer risks to learners and still allowed for genomic exploration (Walt, et al., 2011).

It is becoming increasingly apparent that education can be maximized with a diversity of approaches drawing on issues of immediate relevance to learners, learning with specific and pragmatic goals, experiential learning and problem-solving approaches. As a field, our goal must be to prepare our workforce to be active leaders in the thoughtful implementation of this technology, maximizing its benefits to our clients and reducing any potential harms. With a more prepared workforce we can better engage our many client populations, making them partners in the translation of genomics by empowering them to use the information they gain to promote their health and well-being. Our existing skills are at the core of these new paradigms. Throughout our field’s history, we have shown remarkable dexterity in our ability to adapt to advancing genetic technologies (Stern, 2012). In the present era, a

concerted and deliberate effort to integrate genomics across the curriculum is warranted and will undoubtedly bring further attention to the important role genetic counselors can play in the ever changing and evolving health care system.

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