ACMG
American College of Medical Genetics and Genomics
Translating Genes into Health®

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Recent Activities of The American College of Medical Genetics and Genomics

The American College of Medical Genetic and Genomics (ACMG) is the professional home to over 1,600 board certified clinical and laboratory genetics professionals and is the only nationally recognized medical organization dedicated to improving health through the practice of medical genetics and genomics. The College's mission includes the following major goals: 1) to define and promote excellence in the practice of medical genetics and genomics and to facilitate the integration of new research discoveries into medical practice; 2) to provide medical genetics and genomics education to fellow professionals, other healthcare providers, and the public; 3) to improve access to medical genetics and genomics services and to promote their integration into all of medicine; and 4) to serve as advocates for providers of medical genetics and genomics services and their patients. This report summarizes key activities of the ACMG between May and August 2013.

ACMG Continues Follow-up Activities Related to its "Recommendations for Reporting Incidental Findings in Clinical Exome and Genome Sequencing"

When ACMG published its "Recommendations for Reporting of Incidental Findings (IFs) in Clinical Exome and Genome Sequencing," the authors stated that the report was intended to represent a starting point for discussions regarding the reporting of IFs. They went on to acknowledge that as additional evidence and expertise are gained the recommendations would require ongoing modification. Likewise, tools and resources to guide laboratorians and clinicians in the reporting of IFs would need to be created. This has already led to three new initiatives:

1) The ACMG Board of Directors recently released a Policy Statement, "Points to Consider for Informed Consent for Genome/Exome Sequencing" that focuses on the need for and content of the informed consent that should be obtained before genome sequencing and exome sequencing for germ-line testing are performed in a clinical setting. This document, which is appended to this report, cites eight specific aspects of the informed consent process. It is also available on the ACMG website and is published in the September issue of *Genetics in Medicine.*
2) A Working Group of the ACMG Laboratory Quality Assurance Committee developed clinical laboratory standards and guidelines for next-generation sequencing, which are now available on the ACMG website; they are also published in the September 2013 issue of *Genetics in Medicine.*
3) This fall, the Board of Directors will be surveying the ACMG membership regarding attitudes, experiences and perceived needs around the return of IFs. The survey data will be used in planning next steps in a number of areas including addressing: the development and maintenance of a list of IFs; the state of the evidence base; potential benefits and harms; costs, resources and workforce needs; and issues in shared-decision making and informed consent. Results and next actions will be shared with the ACMG membership.

ACMG Board Releases New Statement on Access to Reproductive Options After Prenatal Diagnosis

After a thoughtful discussion at its July meeting, the ACMG Board of Directors concluded that recent legislation in several states regarding access to reproductive options following prenatal diagnosis affects medical genetics practice to the extent that it would be appropriate to release a statement on this issue. Below is the statement that was drafted and approved by

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the Board. It has received strong support from the ACMG membership.

"The American College of Medical Genetics and Genomics (ACMG) is concerned with the enactment of laws in some states that prevent or restrict access to termination of pregnancy after prenatal diagnosis of genetic disorders or congenital anomalies. The practice of medical genetics is predicated on the principle of providing patients with accurate information on the genetic disorder or congenital anomaly that affects them, a member of their family, or an unborn fetus, and then discussing the management options that are available. The ACMG believes strongly that a balanced discussion of options, including termination of pregnancy, should be available to pregnant couples where their fetus has been diagnosed with a genetic disorder or congenital anomaly. This is accomplished on a case-by-case basis via discussions between the patient's care provider, a medical geneticist/genetic counselor, and the pregnant couple, with the goal of serving the medical needs of the couple to choose a safe and personally acceptable management plan. Access to safe and legal termination of pregnancy for genetic disorders or congenital anomalies that may be diagnosed prenatally is a critically important option for some pregnant couples and ACMG strongly opposes legislation that places limits on this access."

ACMG Takes a Multi-Pronged Approach to Tackle the Current Crisis in Molecular Pathology (MoPath) Test Reimbursement

In early June, ACMG hosted a two-part webinar series on the current crisis in molecular pathology (MoPath) reimbursement and what labs can do to optimize the chances of a favorable outcome from the current gap-filling process required by CMS to establish the National Limitation Amounts. The webinars were offered as an educational resource and provided laboratories with information and tools to effectively participate in the ongoing molecular pathology rate-setting process. It is expected that payers such as Medicare will drastically slash reimbursements for the new molecular pathology codes moving forward, unless laboratories take action now. The webinars attracted listeners in 425 sites, and were presented by an authority on the topic from Quorum Consulting, Inc. Part I addressed the background and current status of the rate-setting process, while Part II focused on what laboratories can and should be doing to advocate for sustainable reimbursement during this critical period.

In addition to the educational webinars, ACMG's Economics of Genetic Services Committee's MoPath CPT code rate-setting workgroup partnered with Quorum Consulting to produce a Molecular Pathology Rate-Setting Guide for Laboratories, available on the ACMG website, under Education/MoPath Rate Setting. A cost analysis survey of clinical laboratories was also conducted to gather data on high volume molecular tests. These data were collected, de-identified and analyzed by Quorum Consulting before being submitted to CMS by ACMG, with a letter stating that the current proposed reimbursement fees are well below the actual cost of performing these tests. It continues to be vitally important for every lab to appeal to both CMS and its regional Medicare MACs for both denials of coverage and any reimbursement rates below actual lab costs.

ACMG Looks Ahead to New Grant Opportunities

ACMG's Executive Director, Michael S. Watson, PhD, FACMG, as a co-PI on the University of North Carolina grant that partners with ACMG and Geisinger Health Plan, attended the introductory meeting requested by NHGRI of the Clinically Relevant Variant Resource grantees and the International Consortium for Clinical Genomics, held in Bethesda, MD on September 3-4. ACMG considers this project to be among the most important follow-up initiatives to the Human Genome Project for advancing our clinical understanding of the relationships between molecular markers and genetic diseases, and to apply this knowledge to improve clinical practice. Formal grant awards are pending final release by DHHS.

The ACMG Foundation for Genetic and Genomic Medicine has also received an unrestricted educational grant from the Illumina Corporation to develop and deliver a series of webinars for non-genetics trained health care providers that address the roles of genome/exome sequencing in patient care. One series focuses on carrier screening, including cystic fibrosis carrier screening, and another on preimplantation genetic diagnosis and screening.

Genetics in Medicine Updates

ACMG recently learned that the Thomson Reuters Impact Factor Journal Citation Reports has increased the impact factor of our peer-reviewed journal, *Genetics in Medicine* (*GIM*), to 5.560 for 2012, up from 4.762 in 2011. This places *GIM* in the top 20 of all Genetics journals and in the top few of those genetic journals that have a significant clinical focus. *GIM's* Editor-in-Chief James P. Evans, MD, PhD, FACMG reflects on the journal's climbing impact by saying, "…it suggests that more and more clinicians and scientists are finding *Genetics in Medicine* to be a useful resource as they care for patients and apply emerging genomic knowledge to clinical care. …The rising impact of

Genetics in Medicine is also a reflection of the growing general importance of genetics and genomics in patient care." *Genetics in Medicine* has been in existence since 1998; the Nature Publishing Group has published it since 2012.

The following Clinical and Laboratory Practice Guidelines and ACMG Policy Statements were published in *Genetics in Medicine* between May and August 2013:

Gregg AR, Gross SJ, Best RG, Monaghan KG, Bajaj K, Skotko BG, Thompson BH and Watson MS; are The Noninvasive Prenatal Screening Work Group of the American College of Medical Genetics and Genomics. **ACMG statement on noninvasive prenatal screening for fetal aneuploidy.** *Genet Med* 15(5):395-398 (May 2013)

Schaefer GB and Mendelsohn NJ; for the Professional Practice and Guidelines Committee. **Clinical genetics evaluation in identifying the etiology of autism spectrum disorders: 2013 guideline revisions**. *Genet Med* 15(5):399-407 (May 2013)

Cooley LD, Lebo M, Li MM, Slovak ML and Wolff DJ; A Working Group of the American College of Medical Genetics and Genomics (ACMG) Laboratory Quality Assurance Committee. **American College of Medical Genetics and Genomics technical standards and guidelines: microarray analysis for chromosome abnormalities in neoplastic disorders.** *Genet Med* 15(6):484-494 (June 2013)

Grody WW, Thompson BH, Gregg AR, Bean LH, Monaghan KG, Schneider A and Lebo RV. **ACMG position statement on prenatal/preconception expanded carrier screening.** *Genet Med* 15(6):482-483 (June 2013)

Green RC, Berg JS, Grody WW, Kalia SS, Korf BR, Martin CL, McGuire AL, Nussbaum RL, O'Daniel JM, Ormond KE, Rehm HL, Watson MS, Williams MS and Biesecker LG. **ACMG recommendations for reporting of incidental findings in clinical exome and genome sequencing.** *Genet Med* 15(7):565-574 (July 2013).

Monaghan KG, Lyon E and Spector EB. **ACMG Standards and Guidelines for fragile X testing: a revision to the disease-specific supplements to the Standards and Guidelines for Clinical Genetics Laboratories of the American College of Medical Genetics and Genomics.** *Genet Med* 15 (7): 575-586 (July 2013)

American College of Medical Genetics and Genomics. **Incidental findings in clinical genomics: a clarification.** *Genet Med* 15(8): 664-666 (August 2013)

ACMG's Visibility Grows in Washington, DC and Beyond

ACMG is becoming more visible to the public on nearly a daily basis:

- Our YouTube channel has surpassed 15,000 views of our videos on genetics topics; the most popular video is "Medical Genetics is Transforming Medicine," which encourages students to consider residency training in medical genetics.
- From NPR and the Today Show to *Scientific American* and the blogosphere, ACMG's members and publications are being quoted widely and with more frequency than ever before.
- In Washington, the ACMG Foundation is proud to be a sponsor of the major exhibit at the Smithsonian's National Museum of Natural History, co-sponsored with NHGRI, "Genome: Unlocking Life's Code." This interactive exhibit is designed to engage the public in an exploration of how genomic science is impacting people's lives and influencing medicine and health care.
- Also in Washington, as the Supreme Court announced its unanimous decision on June 13th that natural isolated DNA is not patentable, the ACMG applauded this important victory for patients. ACMG, a plaintiff in this case, believes, however, that the decision did not go far enough. Our preferred outcome contends that any form of a gene is not patentable because it is the information content that is naturally occurring regardless of whether it is genomic or cDNA. It is ACMG's long-standing position that genes and their mutations are naturally occurring substances that should not be patented, and we hope that this will eventually include cDNA as well.

2014 Annual Clinical Genetics Meeting is Only Six Months Away!

Planning is well on the way for the 2014 ACMG Annual Clinical Genetics Meeting, to be held in Nashville, TN, March 25-29. Meeting and hotel information, online registration, and abstract submission materials are available on the ACMG meeting website, www.acmgmeeting.net, with new information about the program added each week. Abstract submission opens in October and remains open through December 6, 2013. Program highlights include: Two Short Courses, "Interpretation and Reporting of Sequence Variants" and "Recent Advances in Clinical Neurogenetics;" a Workshop on "Transition to Evidence-Based Clinical Guidelines: Understanding Systematic Review and Translation of Evidence to Recommendations;" the annual R. Rodney Howell Symposium in Public Health Genomics, "Care Models for the Delivery of Clinical Genetics and Genomics Services:" and the 45th Annual March of Dimes Clinical Genetics Conference, "Vascular Anomalies: Classifications, Etiologies and Therapies."

2013 ACMG Genetics and Genomics Review Course Materials are Now Available

The popular ACMG Genetics and Genomics Review Course was held in Tampa FL, June 20-23. Since its inception, this course has been built around exam preparation lectures covering a broad range of genetics and genomics topics, presented by recognized experts in the field. This year's course was highlighted by a newly updated syllabus, dynamic exam practice sessions, breakout group discussions focusing on the specialty exams, and the option to participate on-site, via live streaming webinar, or through archived video that will be available for up to 24 months. The archived webinar includes synchronized audio, PowerPoint slides, speaker video and all embedded mouse movements and video clips seen on the streaming video. Audio recordings that can be downloaded in MP3 format are also available with PDF files of all speakers' slide sets. Finally, the syllabus is available in both printed and digital formats. To learn more about purchasing these educational products, visit http://www.prolibraries.com/acmg/?select=conference&conferenceID=2.

Further information about all ACMG activities and a full listing of our press releases and clinical genetics laboratory and practice guidelines can be found on our website at www.acmg.net. The ACMG website now houses an Online Learning Center, as well. ACMG uses Facebook, LinkedIn, YouTube, and Twitter to augment its educational and advocacy missions, provide news and resources related to medical genetics, and improve communication with and among its members and stakeholders.

Submitted by Michael S. Watson, PhD, FACMG
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Genetics inMedicine | ACMG POLICY STATEMENT

Points to consider for informed consent for genome/exome sequencing

ACMG Board of Directors

In its recently released report, "ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing," the American College of Medical Genetics and Genomics (ACMG) created a set of recommendations addressing incidental findings and a minimum list of conditions, genes, and variants that are recommended to be returned whenever clinical sequencing is performed. The ACMG recommended that, for the conditions on the list, the laboratory should return the incidental findings to the doctor ordering the sequencing, and those doctors should manage this information with the patient in the context of that patient's clinical presentation and family history. This document, "Points to Consider for Informed Consent for Genome/Exome Sequencing," focuses on the need for and content of the informed consent that should be obtained before clinical applications of genome sequencing and exome sequencing (GS/ES) for germ-line testing.

GS/ES are rapidly transitioning into clinical practice. Initial applications include testing based on clinical indications that permit the targeting of specific and multiple genes/variants. Consent issues for such applications differ little from those already in use in genetics. However, many unique issues arise when testing platforms are used that provide information that extends beyond the specific genes of interest.[1] These include issues of informed consent that are the focus of this "points to consider" document.

The types of information derived from genome sequencing will be both health (current and future) and non–health related. In addition to information specific to clinical indications for testing on a GS/ES platform, they include: gene-variant carrier status that may have implications for reproductive decision making; information about disease susceptibility or predisposition; information about ancestry, which is currently mostly informational but that may in time have clinical utility; and diagnosis of unsuspected disorders. Some phenotypes may allow narrow targeting, and others (e.g., intellectual disability or autism spectrum disorder) may leave the majority of the exome open for testing. Current technologies are being applied in both the postnatal and prenatal settings as well as to somatic and germ-line conditions. In some cases, incidental findings can be as important to a family as they are to the individual.

The following are recommendations regarding the informed consent that should be obtained before clinical applications of GS/ES for germ-line testing. Particular focus is placed on situations in which the laboratory and physician may be presented with information apparently unrelated to genes known to be associated with the phenotype that led to testing. These points reiterate some prior ACMG positions on this topic.

1. Before initiating GS/ES, counseling should be performed by a medical geneticist or an affiliated genetic counselor and should include written documentation of consent from the patient.
2. Incidental/secondary findings revealed in either children or adults may have high clinical significance for which interventions exist to prevent or ameliorate disease severity. Patients should be informed of this possibility as a part of the informed consent process.
3. Pretest counseling should include a discussion of the expected outcomes of testing, the likelihood and type of incidental results that may be generated, and the types of results that will or will not be returned. Patients should know if and what type of incidental findings may be returned to their referring physician by the laboratory performing the test.
4. Patients should be counseled regarding the potential benefits and risks of GS/ES, the limitations of such testing, potential implications for family members, and alternatives to such testing.
5. GS/ES is not recommended before the legal age of majority except for:
   a. Phenotype-driven clinical diagnostic uses;
   b. Circumstances in which early monitoring or interventions are available and effective; or
   c. Institutional review board–approved research.
6. As part of the pretest counseling, a clear distinction should be made between clinical and research-based testing.
7. Patients should be informed as to whether individually identifiable results may be provided to databases, and they should be permitted to opt out of such disclosure.

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8. Patients should be informed of policies regarding re-contact of referring physicians as new knowledge is gained about the significance of particular results.

These points to consider were designed primarily as an educational resource for clinical geneticists and genetic counselors to help them provide quality clinical genetic services. Adherence to these points to consider is completely voluntary and does not necessarily ensure a successful clinical outcome. These points to consider should not be considered inclusive of all proper procedures or exclusive of other procedures that are reasonably directed to obtaining the same results. In determining the propriety of any specific procedure, the clinician should apply his or her own professional judgment to the specific clinical circumstances presented by the individual patient or specimen.

Clinicians are encouraged to document the reasons for the use of a particular procedure, whether or not it is in conformance with these points to consider. Clinicians also are advised to take notice of the date this guideline was adopted and to consider other medical and scientific information that becomes available after that date.

REFERENCE

1. ACMG Board of Directors. Points to consider in the clinical application of whole-genome sequencing. *Genet Med* 2012;14:759–761.