Sixth in an occasional series on genomic and genetic medicine

By Doug Scott

One thing that scientists learned from the mapping of the human genome was that as the word ‘normal’ can no longer be used to describe a person’s genetic makeup. People have their own unique genotype, just as they have their own personality and appearance.

“Virtually all disease that we know of has some hereditary contribution, and what we did not know until very recently was what those genes are,” said Francis Collins, M.D., who until August was director of the National Human Genome Research Institute (NHGRI) and also director of the Human Genome Project. “So looking at the human genome of an individual, what you will find is something that we might call ticking ‘time bombs’ or risks for common diseases.”

“Taking a family history is a good way to advise patients about what health risks might be lurking, but the real challenge for the project’s application to clinical practice at the present time is to uncover what those genetic components are, which will point health care providers such as PAs to better ways of prevention and treatment of common diseases,” Collins said.

Understanding exactly what those genetic components for an individual are falls under the category of genetic testing, which for certain levels of care is controversial. There is general agreement among the medical community that genetic testing holds great promise for diagnosis and treatment of many diseases, but determining who should get a genetics test, how to interpret results, and if it can accurately predict risk, is a big challenge facing clinicians today.

“It is incumbent upon us to dispel the myth that all genetics and genomics are extremely complicated,” explained Greg Feero, M.D., chief, Genomic Healthcare Branch at NHGRI. “It is true that certain types of genetic testing are in fact very complicated and best dealt with by a medical geneticist. But then there are other applications such as Factor V Leiden genetic testing that are not hard to order or interpret.

“And it is very likely in the near future, we will see more and more applications relevant to chronic common disease that fall into the category that are not complicated to order, understand, interpret, and apply to care.”

According to the NHGRI there are more than 1,200 genetic tests available on a clinical level and nearly 300 available for research. Currently, laboratory test results can probably determine if your child has cystic fibrosis or Fanconi anemia as well as predict the likelihood that one of your patients might develop Alzheimer’s or schizophrenia later in life. But most of these kinds of genetic tests relate to rare, or at least uncommon, single gene disorders. Testing for genetic susceptibility to more common diseases is not yet commonplace and only about a dozen genetic tests are used routinely and considered reliable — most prominently for BRCA1 and BRCA2 genetic testing for breast cancer and multiple endocrine neoplasia type 2.

L to R: Wylie Burke, M.D.; Muin Khoury, M.D.; Greg Feero, M.D.; and Francis Collins, M.D.

“The main problem with genetic testing now is that many tests emerging from research have unclear clinical utility; for example, a test to identify a person at moderately increased risk for diabetes, heart disease or prostate cancer,” said Wylie Burke, M.D., professor and chair of the Department of Medical History and Ethics at the University of Washington and principal investigator of the University of Washington Center for Genomics and Healthcare Equality. “It is not clear that such information offers the patient or the health care provider information that is useful in health care, or that the information about genetic risk is more clinically useful than non-genetic risk tests.

Still, make no mistake about it: the genetics business is just beginning to take off. Because most types of genetic testing go unregulated, and the development, methodologies, and test components don’t have to be disclosed, just about anybody can bring a test to market. Companies like 23andMe, deCODEme, and Navigenetics are offering personalized complete genome or multiple single-nucleotide polymorphisms (better known as SNPs) to people willing to plunk down as much as $2,500 for the service. Patients who do may expect PAs and other medical providers to give

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medical advice, based on this genomic test information.

“In medicine, any new technology is being looked at in the lens of what value does it bring to the practice,” said Feero.

“So it is incumbent upon us in the scientific community to demonstrate the utility of genetic application before approaching the potential genetic test consumer or health professional learner.”

So what exactly is the clinical utility today of a ordering genetic test when a PA suspects their patient may be suffering from a particular disease?

“That is the $64 million dollar question,” said Muin Khoury, M.D., director of the National Office of Public Health Genomics at the Centers for Disease Control and Prevention (CDC).

“The answer to that question depends on the intended use of the test and the situation because genetic tests range from diagnosing very rare conditions like Huntington’s Disease all the way to the kinds of tests that could be used on a wider population base for things like screening all newborns for metabolic diseases, etc.”

“The good news is that we are now developing methods for the evaluation of validity and utility of tests, and then applying it to different candidate applications that are coming down the pike.”

One of those methods, Khoury said, is called the Evaluation of Genomic Applications in Practice and Prevention (EGAPP). EGAPP is a pilot project initiated by the CDC National Office of Public Health Genomics, whose goal is to establish and evaluate a systematic, evidence-based process for assessing genetic tests and other applications of genomic technology in transition from research to clinical and public health practice.

EGAPP aims to integrate existing recommendations on implementation of genetic tests from professional organizations and advisory committees. This independent, multidisciplinary panel — which now includes a PA, Karen Clark — prioritizes and selects tests, reviews CDC-commisioned evidence reports and other contextual factors, highlights critical knowledge gaps, and provides guidance on appropriate use of genetic tests in specific clinical scenarios. Khoury, who also sits on the EGAPP Steering Committee, said the pilot project plans to release three new recommendations in January.

“The PA community needs to be aware and have the right genetic and genomic competencies so that they know what the right questions are and know where to go and find the answers,” explained Khoury.

“For PAs working in primary care settings, I think the tests to keep their eyes on are some of the emerging pharmacogenetic tests,” added Burke. “For example, testing for variants in the CYP2C9 and VKORC1 genes identify people who require lower doses for the blood-thinner Warfarin. Experts disagree as to whether these tests will improve health care, but clinical trials are in process, and better evidence on the appropriate use of such tests is likely to emerge soon.”

There is general agreement that in order to improve genetic testing and to release its diagnostic and treatment potential, industry reforms are needed. Several bills in Congress are being proposed to address these issues. The Laboratory Test Improvement Act (S. 736) would amend the Food, Drug, and Cosmetic Act to require prescriptions for all laboratory-developed, direct-to-consumer tests by classifying them as medical devices and put the under the control of the FDA. Another bill, The Genomics and Personalized Medicine Act (S. 3822) would require manufacturers of laboratory-developed genetic tests to submit analytical and clinical validity data to the Secretary of the U.S. Department of Health and Human Services, who in turn would make that information public.

“We need easily accessible, rapidly updated, and reliable guides to genetic tests and hopefully, this need will be addressed by agencies like the NIH [Institute of Health] and the CDC,” said Burke.

As a resource for PAs, the Gene Test website, at www.geneclinics.org, provides current, authoritative information on genetic testing and its use in diagnosis, management, and genetic counseling. Gene Test also promotes the appropriate use of genetic services in patient care and personal decision making. Additional information on genetic testing can be found in the Health Professionals section of the National Human Genome Research Institute Web site at, www.genome.gov/27527599. For more information about EGAPP, go to www.cdc.gov/genomics/gtesting/EGAPP/about.htm.