GEC KO Point of Care
www.geneticseducation.ca
@GECKOgenetics

Tips for providers *after* ordering an Expanded Carrier Screening panel

www.geneticseducation.ca

After ordering an EXPANDED CARRIER SCREENING panel;

A Negative result: This is reassuring. Your patient is not a carrier of any of the conditions on the panel. But remember, an expanded carrier screening panel does not screen for all genetic conditions. Be sure that, in addition to the panel, your patient is also appropriately offered screening based on her/his ethnicity (e.g. alpha-thalassemia is not typically on expanded carrier screening panels, but is a condition for which certain ethnic populations have a higher carrier frequency) and family history. See www.geneticseducation.ca Reproductive Genetic Carrier Screening in Canada point of care tool for what should be considered standard of care.

When screening for over 100 disorders, you are likely to receive at least one positive result. A recent study found that about 24% of individuals were identified as a carrier of at least one disorder when screened by a panel containing 108 disorders and about 5% were identified to be a carrier of more than one disorder[1].

A Positive result:

1. Your patient is found to be a *carrier* of one or more recessive genetic disorders:

   There are usually no screening or medical management recommendations for an individual who is a carrier of a recessive condition as s/he is expected to be otherwise healthy. However, carrier status of recessive conditions is an important consideration for couples who are planning their family.

   If your patient or patient's partner is pregnant or planning to become pregnant, **consider suggesting your patient's partner have the same carrier screening panel**. If both members of the couple are carriers of the same recessive disorder, consider offering referral for genetic counselling.

   Remember:

   - Family history-based risk assessment is still the gold standard in the initial assessment for heritable conditions.
   - Genetic counselling is offered by many private genetic testing companies. Your patient may wish to have genetic counselling from the company where s/he purchased testing. This may require payment of an additional fee. Ideally counselling should be provided by a *board certified genetic counsellor* (designated as Certified Genetic Counselor (CGC) or Canadian Certified Genetic Counsellor (CCGC)).
   - Your patient inherited her/his carrier state(s) from one of her/his parents, who will also be a carrier of the recessive condition(s). Your patient's siblings are also at a 50% risk to be a carrier of the same recessive condition(s). **You may wish to advise your patient to share this information with her/his adult family members.**

2. Your patient is found to **have one or more gene mutations which may have** *health implications* e.g. familial hypercholesterolemia, hereditary hemochromatosis:

   Offer referral to an appropriate specialist (e.g. geneticist, lipid specialist, hematologist).

CHEO · Mount Sinai Hospital, Sinai Health System, Joseph & Wolf Lebovic Health Complex · Family & Community Medicine, University of Toronto · uOttawa

Updated March 2017

GEC KO Point of Care
www.geneticseducation.ca
@GECKOgenetics

Tips for providers *after* ordering an Expanded Carrier Screening panel

www.geneticseducation.ca

A Variant of Uncertain Significance (VUS) result:

Most Expanded Carrier Screening (ECS) panels use next-generation sequencing (NGS) to analyze patient samples. This testing method improves sensitivity of testing across ethnicities, however is limited in detecting some mutation types. NGS utilizes the human genome as a reference and compares that to a given patient sample to identify variation. Variations are then classified based on guidelines[2] into one of five categories:

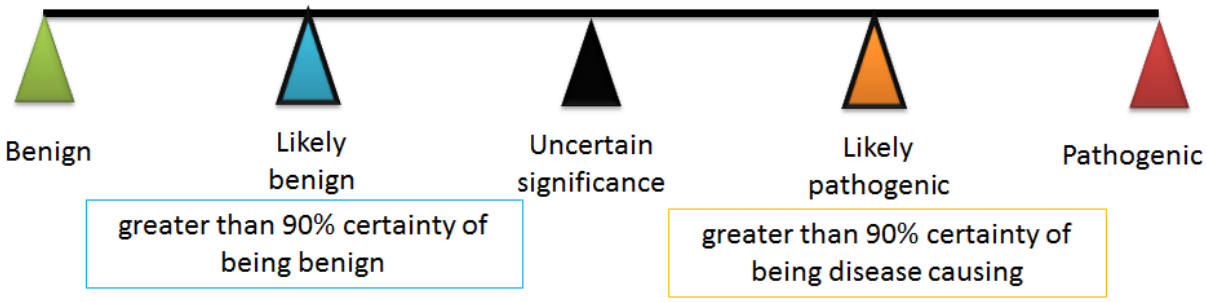

Figure 1. Classification of genetic variants.

Benign or likely benign variants are most often not reported (negative test result).

Pathogenic and likely pathogenic variants are known to or expected to cause disease (positive test result).

A variant of uncertain significance (VUS) is a genetic variation that has not yet been classified as either benign or pathogenic. Variant interpretation is challenging. While most laboratories use standardized guidelines[2] there is variability in which tools are used for interpretation[3]. Additionally, as more information about the human genome is discovered, variants will be reclassified. Some laboratories will re-contact the ordering provider with this new information and some leave the onus on the provider and/or patient to seek out new information.

Follow-up on a reported VUS is generally case-by-case. Factors that may be considered are the gene, the disorder, family history, additional literature review, clinical interpretation. Consultation with a genetics specialist may be required.

REFERENCES:

[1] Lazarin GA, Haque IS, Nazareth S, et al. An empirical estimate of carrier frequencies for 400+ causal Mendelian variants: results from an ethnically diverse clinical sample of 23,453 individuals. Genet Med 2013;15(3):178-86.

[2] Richards S, Aziz N, Bale S, et al. Standards and guidelines for the interpretation of sequence variants: a joint consensus recommendation of the American College of Medical Genetics and Genomics and the Association for Molecular Pathology. Genet Med 2015;17(5):405-24

[3] Facio FM, Lee K, O'Daniel JM. A genetic counselor's guide to using next-generation sequencing in clinical practice. J Genet Couns 2014;23(4):455-62

Resource on NGS: Evans M, [DocMikeEvans] (2016/Aug/10). *Genomic Sequencing 101: Pros, Cons, and Implications for You and Your Family* [Video file]. Retrieved from https://www.youtube.com/watch?v=w05tphqgnJo

See www.geneticseducation.ca for an Education Module on Expanded Carrier Screening in Prenatal and Preconception Genetics.

CHEO
Mount Sinai Hospital
Sinai Health System
Joseph & Wolf Lebovic Health Complex
Family & Community Medicine
UNIVERSITY OF TORONTO
uOttawa

Updated March 2017