ALBERTA PRECISION LABORATORIES
Leaders in Laboratory Medicine

Next Generation Sequencing (NGS) Panels: Information for Ordering Providers

What is Next Generation Sequencing (NGS)?
NGS is a high-throughput DNA sequencing technology that allows sequencing of millions of fragments (massively parallel) at one time. This enables the simultaneous analysis of many genes known to be associated with a phenotype (ie. gene panels). Current methodologies allow for detection of sequence changes as well copy number changes (deletions or duplications) of one or more exons.

Since not all genes associated with a given phenotype / presentation are known or included in the panel, a pathogenic variant will not be identified for every patient. **The absence of a pathogenic variant does not necessarily exclude a diagnosis.**

My patient has a family history of a known pathogenic variant. Is an NGS panel the appropriate test for my patient?
No. Once a pathogenic variant has been identified in the family it is best to begin testing by looking for the variant that has already been identified in the family.

Is testing available for a single gene included on a NGS panel?
Yes, in some circumstances it may be appropriate to test only one gene instead of a panel of genes. Please contact the laboratory to discuss your request as they are approved on a case by case basis.

Is testing available for patients without Alberta health care coverage?
For patients without a valid Alberta PHN, please contact the laboratory genetic counsellor to discuss test availability, billing and sample requirements.

How do I order an NGS panel?

Consult the APL Test Directory (http://ahsweb.ca/lab/apl-td-lab-test-directory) for test indications and ordering restrictions. If all ordering criteria are met:

1. For Alberta Health Services (AHS) providers, NGS panels can be ordered through Connect Care
2. For non-AHS providers and AHS providers who do not currently have access to Connect Care, complete the appropriate Molecular Genetics Laboratory (MGL) requisition (information available from the test directory)
3. Provide all relevant clinical and family history information in your order. **Incomplete requisitions will not be accepted and will delay testing and results.**
4. Provide the fully completed Connect Care order or MGL requisition to your patient and **direct them to their local collection lab for a blood draw.**

Methods
Genomic DNA, usually isolated from a blood sample, is analyzed using next generation sequencing technology (NGS). NGS detects nucleotide substitutions, small insertions and deletions, and copy number variants. If a variant is clinically relevant or of uncertain significance and does not meet our validated analytic requirements it is confirmed by an appropriate molecular method. Sanger sequencing is used to analyze regions which do not meet requirements for depth of sequence coverage. The methods used to generate results are identified on each patient report.

Reporting results
Results are sent to the ordering provider and may take up to 4 months to report.

Can testing be expedited to facilitate medical management of a patient?
Rush testing (~1 month from the time the sample is received) is available if required for immediate surgical or therapeutic management. Expedited testing can also be requested if results are needed within 5-16 weeks. Please provide details on the requisition form regarding the reason for prioritizing testing as well as a target date for results.

What Types of Results Can I Expect?

Type of NGS result	Interpretation
Pathogenic Variant	A variant has been identified that is disease-causing.
Likely Pathogenic Variant	A variant has been identified and there is significant but not conclusive evidence that the variant is disease-causing.
Variant of Uncertain Significance	A variant has been identified and there is not sufficient evidence to classify the variant as pathogenic/likely pathogenic or benign/likely benign.
No pathogenic variant (Uninformative)	No variants of clinical or uncertain significance were detected. This is an uninformative result and no explanation has been identified for the patient's phenotype. There may be other genes or variants not assessed by the current NGS panel associated with the patient's phenotype. A genetic condition or genetic component to the phenotype has not been excluded.

NOTE: Benign, or likely benign variants (variants known not to be disease-causing) are not reported.

My patient has a pathogenic or likely pathogenic variant. What are the next steps?
Your patient should be managed based on their diagnosis and clinical presentation. If your patient has a pathogenic variant or a likely pathogenic variant, genetic counselling is recommended to discuss the implications for other family members.

My patient has a variant of uncertain significance. What are the next steps?
Variants of uncertain significance are generally not used to inform medical management decisions. If your patient has a variant of uncertain significance, a referral to Clinical Genetics may aid in understanding the implications of the variant.

My patient's results are uninformative. What are the next steps?
A referral to Clinical Genetics may still be appropriate for your patient if they have physical features and laboratory findings suggestive of an inherited disorder and / or desire additional counselling regarding their results.

Contact Information
Genetic Counsellors, Genetics & Genomics
Edmonton: 780-407-1015
Calgary: 403-955-3097

Requisition forms, contact information and other resources can be found at:
http://ahsweb.ca/lab/if-lab-genetics-and-genomics