



Clinical Pharmacology & Toxicology Pearl of the Week

Pharmacogenomics: How and Where?

- ✓ Pharmacogenomic testing is usually done on whole blood samples or oral mucosal samples.
- ✓ Pharmacogenomic testing availability is variable. Currently, most testing is performed by private laboratories.
- ✓ In Alberta, HLA testing for abacavir, carbamazepine, oxcarbazepine, and allopurinol hypersensitivity is available through Alberta Precision Labs.
- ✓ At present, most pharmacogenomic testing is not covered by Alberta Health Services.

How is the test performed?

- ✓ A whole blood sample or buccal mucosa swab is collected by the patient or a phlebotomist.
- ✓ DNA is extracted from the sample tissue.
- ✓ The DNA is then genotyped using assays that are designed to detect specific variants in a gene or a panel of genes.
 - Unfortunately, assays may not be able to detect rare genotypes. If a patient has one of these rare genotypes the assays will report them as normal (false-negative).
- ✓ The genotype report is interpreted by a clinical biochemist, physician, geneticist, or pharmacist working in the lab. A clinical interpretation of the phenotype is often included.
 - Phenotypic interpretation is based off of known effects of genotype on gene product activity.
 - Ex: CYP2D6 *4 is known to be a non-functional enzymatic mutation. A patient who is homozygous for CYP2D6*4 is reported as a poor metabolizer.
- ✓ The report, with clinical interpretation, is provided to the requesting physician. This information can then be used to make rational medication choices and dose adjustments.

Where is pharmacogenomics testing done?

- ✓ Pharmacogenomic testing for many cancer phenotypes is provided by Alberta Health Services and is typically performed at a single site.
 - Ex: KRAS gene mutation is performed at University of Alberta Hospital.
 - Ex: Breast Cancer phenotyping is performed at University of Alberta Hospital and Alberta Children's Hospital.
- ✓ Pharmacogenomic testing for genotypes at high risk for a severe adverse drug reaction.
 - Ex: HLA testing for allopurinol, [carbamazepine](#), oxcarbazepine, and abacavir genotypes at high risk for [DRESS](#) are performed in Calgary at the Diagnostic and Scientific Centre.
- ✓ Currently, pharmacogenomics testing related to medication pharmacokinetics (CYP-enzymes) and pharmacodynamics (drug targets and associated genes) are mainly performed at independent (private) labs.
 - These carry a cost of between 200-1800\$, and are not currently covered by Canadian public health care
 - Ex: [CYP2D6](#), [CYP2C19](#), VKORC1 testing.

What does the future look like?

- ✓ Many institutions in the United States have begun to implement pharmacogenomics testing on a wider scale to incorporate into their medication prescribing decision algorithms.
 - These testing protocols impact prescribing decisions by highlighting high risk medications, as well as appropriate dose adjustment based on a patient's ability to metabolise a drug based on their genetics.
 - Institutions include: Vanderbilt University Medical Centre, St. Jude Children's Research Hospital, University of Florida and Shands Hospital, Mayo Clinic, and Mount Sinai Medical Centre
- ✓ June 11th, 2020, The Centers for Medicare and Medicaid Services have announced coverage for pharmacogenomic testing of actionable gene-drug combinations
- ✓ Pharmacogenomic testing is [incorporated into a patient's profile](#), similar to drug allergies and past medical history. Once performed, testing does not need to be repeated unless new gene targets or actionable mutations are identified.
- ✓ The University of Calgary, University of Alberta, and Alberta Precision Labs are currently working together to design, evaluate, and implement pharmacogenomic testing in Alberta.



The Calgary Clinical Pharmacology physician consultation service is available Mon-Fri, 9am-5pm. The on-call physician is listed in ROCA. Click [HERE](#) for clinical issues the CP service can assist with.



The Poison and Drug Information Service ([PADIS](#)) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414, and select option 1.

References:

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3. Dunnenberger HM, Crews KR, Hoffman JM, et al. Preemptive clinical pharmacogenetics implementation: current programs in five US medical centers. *Annu Rev Pharmacol Toxicol.* 2015;55:89-106. doi:10.1146/annurev-pharmtox-010814-124835
4. Peck RW. Precision Medicine Is Not Just Genomics: The Right Dose for Every Patient. *Annu Rev Pharmacol Toxicol.* 2018;58:105-122. doi:10.1146/annurev-pharmtox-010617-052446
5. Maruf AA, Fan M, Arnold PD, Müller DJ, Aitchison KJ, Bousman CA. Pharmacogenetic Testing Options Relevant to Psychiatry in Canada [published online ahead of print, 2020 Feb 17]. *Can J Psychiatry.* 2020;706743720904820. doi:10.1177/0706743720904820