



## 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 being performed by private laboratories
- ✓ In Alberta, HLA testing for abacavir, carbamazepine, oxcarbazepine, and allopurinol hypersensitivity is available through Alberta Precision Labs, as is DYPD testing
- ✓ Additional pharmacogenomics testing is available for send out to labs throughout North America.

#### 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 on an array assay that is designed to detect specific variants in a gene or a panel of genes.
  - Unfortunately, array assays may not be able to detect some of the rarest genotypes and may report results 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 on 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 (i.e., \*4/\*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?

- ✓ Somatic (tumor) 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.
- ✓ 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
- ✓ Pharmacogenomic testing can be incorporated into a patient's profile, similar to drug allergies and past medical history.

## **References:**

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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. Can J Psychiatry. 2020;706743720904820. doi:10.1177/0706743720904820

The Clinical Pharmacology (CP) physician consultation service is available Mon-Fri, 8am-5pm. The on-call physician is listed in ROCA on the AHS Insite page. CP consultations are also available through Netcare e-referral and Specialist Link. You can also find us in the [Alberta Referral Directory](#) (ARD) by searching "Pharmacology" from the ARD home page. Click [HERE](#) for more details about the service.

The Poison and Drug Information Service (PADIS) is available 24/7 for questions related to poisonings. Please call 1-800-332-1414 (AB and NWT) or 1-866-454-1212 (SK). Information about our outpatient Medical Toxicology Clinic can be found in [Alberta Referral Directory](#) (ARD) by searching "Toxicology" from the ARD home page.

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