Clinical Pharmacology & Toxicology Pearl of the Week

Introduction to Pharmacogenomics

- ✓ Pharmacogenomics is the study of how genes affect a patient's response to drugs.
- ✓ Pharmacogenetic testing seeks to identify patients who are at risk for clinical significant differences in their genome that can result in altered pharmacokinetic, pharmacodynamics, or immune responses to a medication.
- ✓ Ultimately, pharmacogenomics seeks to improve patient responses to therapeutics, while further minimizing the risks of adverse effects.

Pharmaco-what? Is this a new concept?

- ✓ The field of pharmacogenomics is relatively new, though you are likely already familiar with common testing that is done:
  - Estrogen Receptor testing in breast cancer to determine a response to tamoxifen or other SERMs / aromatase inhibitors.
  - HLA-B testing to determine risk of DRESS/TEN/SJS induced by abacavir or allopurinol
  - TPMT testing prior to azathioprine exposure to detect risk for myelosuppression.
  - BRCA testing in ovarian cancer for response to olaparib.
  - KRAS gene mutations in colon cancer to predict failure to respond to cetuximab and panitunumab.

How is pharmacogenomics testing done?

- ✓ Pharmacogenomic testing is performed using DNA extracted from a variety of tissue (e.g., whole blood, saliva, buccal swabs, or tumor).
- ✓ DNA is genotyped using assays designed to detect specific variants in a single gene or panel of genes.
- ✓ A report with the genotyping results and clinical interpretation are made by a clinical biochemist, physician, geneticist or pharmacist working in the lab.

How can pharmacogenomics affect my practice?

- ✓ Currently, pharmacogenomics has four main uses in clinical practice:
  1. To predict a patient's response/non-response to a treatment option.
     - Ex: ER+ breast cancer and tamoxifen, KRAS gene mutations in colon cancer.
  2. To determine a high risk genotype for a severe adverse drug reaction.
     - Ex: HLA testing for allopurinol, carbamazepine and abacavir for high risk genotypes for DRESS.
  3. To predict a patient's pharmacokinetics when exposed to a particular medication.
     - Ex: CYP2D6 genotyping for codeine and tramadol ultra-rapid metabolizers and non-responders, CYP2C19 genotyping for clopidogrel non-responders.
  4. To predict a patient's pharmacodynamics when exposed to a particular medication.
     - Ex: VKORC1 genotyping for absent or reduced vitamin K epoxide reductase activity prior to dosing warfarin.
- ✓ These clinical uses may result in changing the medication used to treat the individual patient, adjusting the dose to better match the patient's pharmacokinetic and pharmacodynamics profile, or monitoring the patient more closely for efficacy/adverse effects.
  - This can be thought of in the same way as we interpret eGFRs and other aspects of personalized medicine when deciding on therapeutics for our patients.

What does the future hold for pharmacogenomics?

- ✓ Multiple groups are working on identifying drug-gene pairs where pharmacogenomics testing can make a patient-centered clinical significant difference, while accounting for cost.
  - These include: Clinical Pharmacogenetics Implementation Consortium (CPIC) and PharmGKB.
  - Nationally, this includes The Canadian Pharmacogenomics Network for Drug Safety.
  - Locally, this includes the Psychiatric Pharmacogenetics Labs at the University of Calgary

- ✓ As availability of testing improves, and costs come down, pharmacogenomic testing will become routine and used to improve patient outcomes, patient response, and decrease adverse effect to medications prescribed regularly.

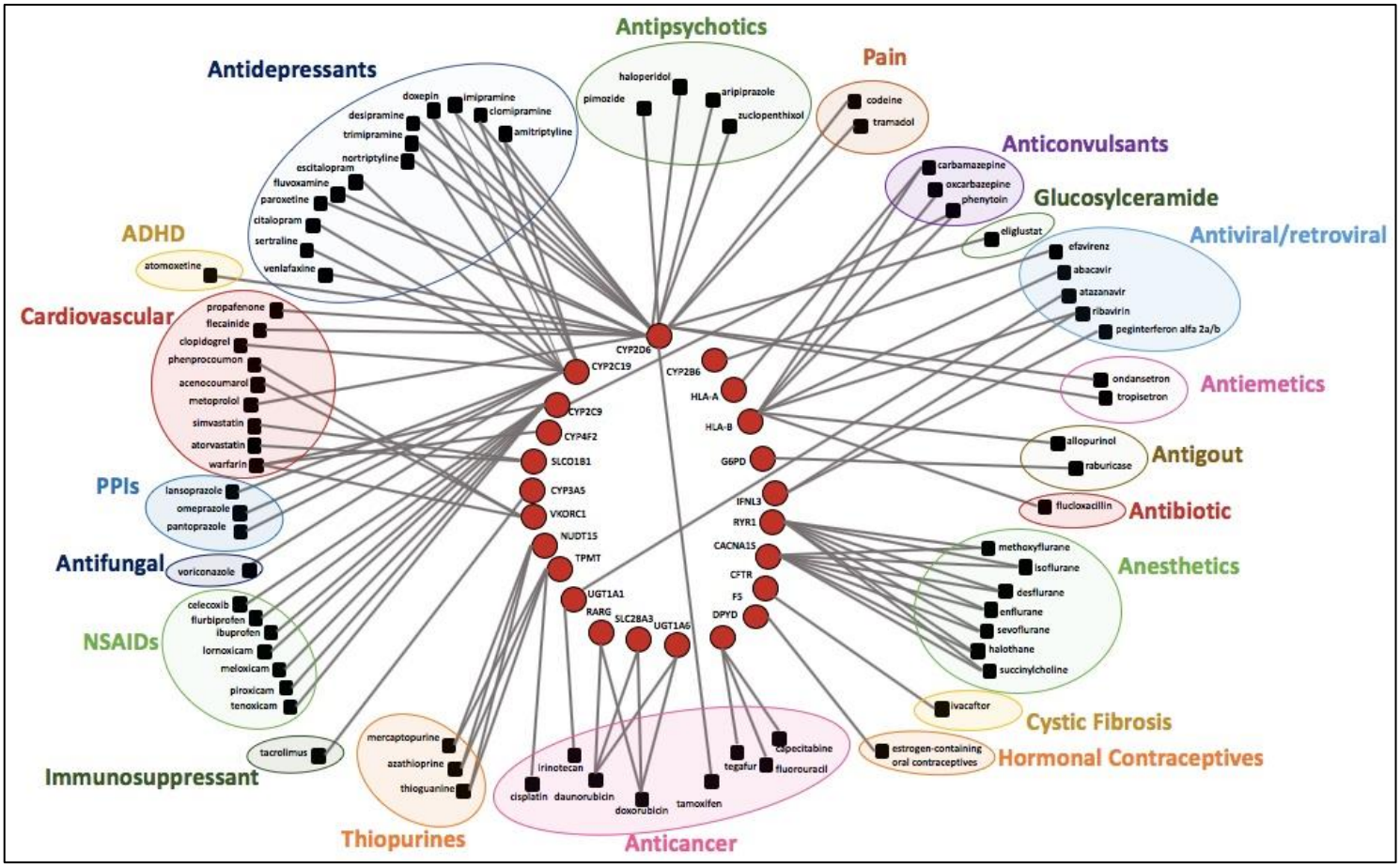

Figure 1: Currently documented gene-drug pairs with pharmamcogenetic-based prescribing guidelines. (adapted from: Bousman et al 2019)

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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