PHARMACOGENOMICS (PGx)

- PGx = The study of the relationship between genetic variations and how our body responds to medications
- Alleles in certain genes determine how an individual responds to certain drugs
- The PGx field has been around for over 20 years; HLA testing can be informative (e.g., for adverse drug reactions) and has been around the longest, since 1960's
- Star (*) alleles are reported for certain PGx genes; star alleles describe a variant or string of variants (i.e., haplotype)
- Star allele nomenclature is unique to the PGx field and is historic in nature
- Challenges in PGx field include:
    - Deciding which genes and alleles should be included in clinical PGx tests
    - Ensuring representation of data from diverse populations (e.g., alleles relevant to underrepresented populations may not be included in PGx assays, and some alleles relevant to white populations may not be informative for other populations)
    - Physicians who are not PGx experts must be able to understand PGx reports, allowing for proper drug dosing
    - Drug-gene associations that were previously reported may not be accurate
    - *CYP2D6* testing is complex due to nearby pseudogenes, making it difficult to report alleles correctly (e.g., copy number of analysis of *CYP2D6*)
    - It is important to determine if variants are in cis or in trans when reporting star allele haplotypes

IMPORTANT RESOURCES USED BY PGx EXPERTS

Pharmacogene Variation Consortium (PharmVar)

- A central repository for pharmacogene (PGx) variation that focuses on haplotype structure and star allele definitions
- PharmVar works to unify and standardize PGx nomenclature
- The information in this resource facilitates basic and clinical research as well as the interpretation of pharmacogenetic test results to guide precision medicine
- Tutorial on *CYP2D6* copy number analysis that is highly recommended: click here

Clinical Pharmacogenetics Implementation Consortium (CPIC)

- International consortium of individual volunteers and a small, dedicated staff who are interested in facilitating the use of pharmacogenetic tests for patient care
- CPIC provides curated, evidence-based guidelines that provide prescription recommendations for gene-drug pairs
- Useful resource for physicians and laboratorians
- Sign up for CPIC email updates here: CPIC (list-manage.com)

Pharmacogenomic Knowledgebase (PharmGKB)

- Comprehensive resource that curates knowledge about the impact of genetic variation on drug response for clinicians and researchers
- Gene-specific Information Tables are available for download, allowing for automation of PGx laboratory reports: https://www.pharmgkb.org/page/pgxGeneRef
- Catalog of drug dosing guidelines and drug labels with PGx information
- Sign up for PharmGKB email updates here: PharmGKB (list-manage.com)

Pharmacogenetics Working Group of the KNMP a.k.a. Dutch Pharmacogenetics Working Group (DPWG)

- Produce PGx recommendations that are used in the Netherlands and around the world
- DPWG website provides general background information on PGx genes and variants

Association for Molecular Pathology (AMP)

- AMP publishes recommendations for minimum sets of genes and/or alleles to include on clinical PGx tests, thereby guiding the standardization of clinical PGx assays

Author Information and Affiliations:

Casey Brewer, PhD, FACMG

Cincinnati Children's Hospital

Division of Human Genetics

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