

Software for the clinical implementation of pharmacogenomic testing

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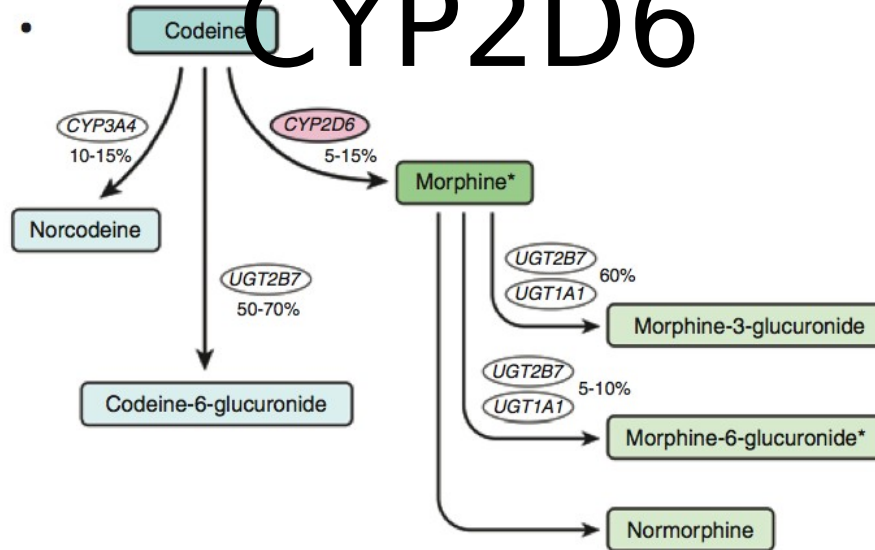
Big Data for Health Summer Workshop
July 2014

Pharmacogenomics

“The study of how genetics influence patient response to pharmacotherapies.”

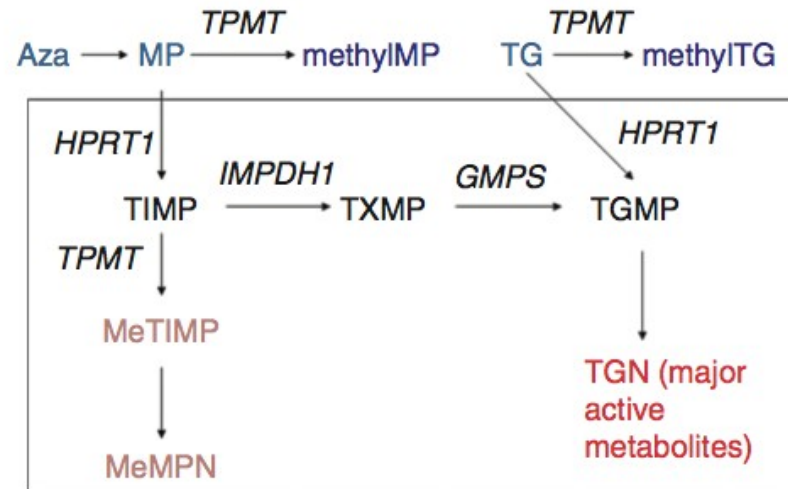
“The study of how genetic factors influence interindividual variability of drug response.”

Example: codeine and CYP2D6



<i>Ultrarapid metabolizer</i>	Increased formation of morphine following codeine administration, leading to higher risk of toxicity
<i>Extensive metabolizer</i>	Normal morphine formation
<i>Intermediate metabolizer</i>	Reduced morphine formation
<i>Poor metabolizer</i>	Greatly reduced morphine formation following codeine administration, leading to insufficient pain relief

Example: mercaptopurine



<i>Extensive metabolizer</i>	Lower concentrations of TGN metabolites, higher methylTIMP, this is the “normal” pattern
<i>Intermediate metabolizer</i>	Moderate to high concentrations of TGN metabolites; low concentrations of methylTIMP
<i>Poor metabolizer</i>	Extremely high concentrations of TGN metabolites; <u>fatal toxicity possible</u> without dose decrease; no methylTIMP metabolites

PGx app for MedSavant

The screenshot displays the PharmacoGx application interface. On the left, a light blue sidebar contains the sample ID 'NA12878-Seqenom', a note that results are based on CPIC guidelines, a disclaimer that the app is for research purposes only, and a confirmation that 'Analysis complete.' Below this are 'Refresh' and 'Export to PDF' buttons, and a 'Disclaimer' link at the bottom.

The main content area features a navigation bar with tabs for various genes: Summary, CTR, CYP2C19, CYP2C9, **CYP2D6**, DPYD, IFNL3, SLC01B1, TPMT, and VKORC1. The CYP2D6 tab is active, showing the following details:

- Gene:** CYP2D6
- Diplotype:** *3/*4
- Therapeutic class:** Poor
- Publications:** [Guidelines #1](#) [Guidelines #2](#)
- Genotypes are phased.

Below this is a **Haplotype summary** section:

- Haplotype #1:** *4
- Haplotype #2:** *3
- Haplotype #1 activity:** no activity
- Haplotype #2 activity:** no activity

Next is a **Genotype summary** table:

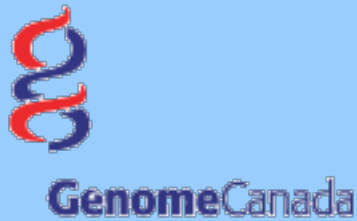
Marker ID	Haplotype #1	Haplotype #2	Observed/Inferred genotype	Chr	Position	Ref	Alt
rs1065852	A	G	observed	chr22	42526694	G	A
rs1135840	G	C	observed	chr22	42522613	G	C
rs16947	G	G	observed	chr22	42523943	A	G
rs28371706	G	G	observed	chr22	42525772	G	A
rs28371725	C	C	observed	chr22	42523805	C	T
rs35742686	T	-	observed	chr22	42524244	T	-
rs3892097	T	C	observed	chr22	42524947	C	T
rs5030655	A	A	observed	chr22	42525086	A	-
rs5030656	CTT	CTT	observed	chr22	42524176	CTT	-

Below the table is a **Novel variants (not part of guidelines)** section, which includes a brief definition and a table of variants:

Novel variants are non-synonymous mutations with allele frequencies <= 0.05 (or N/A) across all available AF databases

Chrom	Position	Effect	Zygosity	esp6500_all, Score	cg69, Score	1000g2012apr_all, Score	dbSNP
chr22	42523843	SPLICING	HomoAlt	N/A	N/A	N/A	rs72549349
chr22	42525035	STOPGAIN	Missing	0.000078	N/A	N/A	rs5030865
chr22	42525035	STOPGAIN	Missing	N/A	N/A	0.0009	
chr22	42526670	MISSENSE	Missing	0.000231	N/A	N/A	rs5030862

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Sick Kids PGx

Team

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