ABOMICS

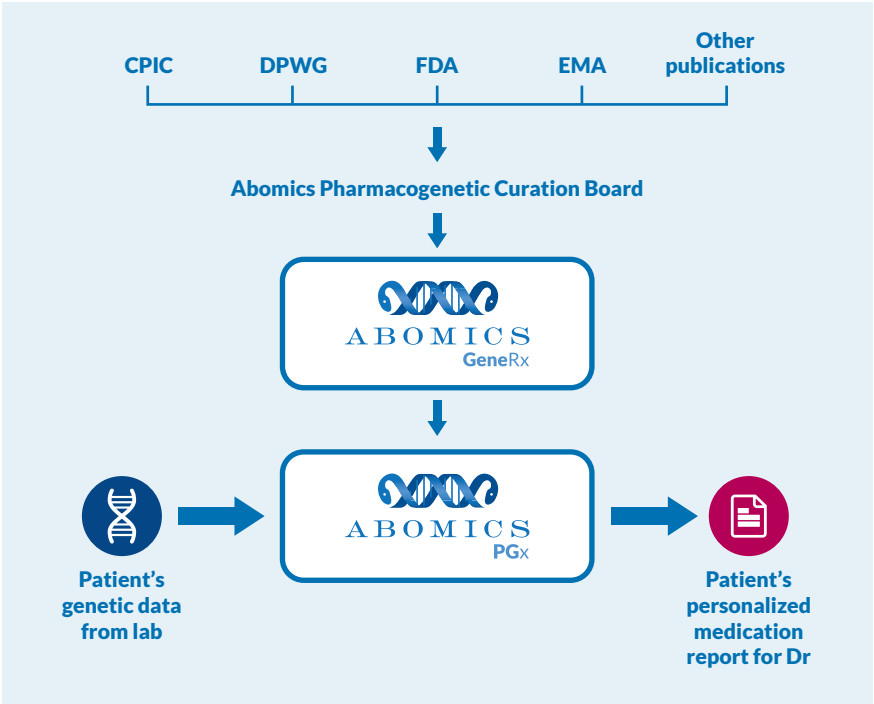
Supporting medication decisions

White Paper

Pharmacogenetics – precision medicine is available for your customers

Pharmacogenetics (PGx) is the science that combines genetics with pharmacology. Your genes impact how you react to a certain medicine. This is individual for all of us, and this science can be used to personalize the medication for patients as individuals.

Pharmacogenetics is disrupting medication decision-making as the cost of genetic testing has dropped from thousands of euros to hundreds of euros. Scientific evidence shows that pharmacogenetics gives better clinical outcomes for the patient and better cost efficiency for society, particularly in treatment of depression[1, 2] and geriatric polypharmacy[3, 4]. Evidence is strong also in the treatment of coronary heart disease and stroke patients. [5, 6]



About Abomics

Together with clinical laboratories, we at Abomics make pharmacogenetics an easy tool for doctors in their daily clinical work. Based on a blood test or a buccal swab sample, we provide doctors with a patient specific report that shows whether a specific medicine is suitable for the patient or not and how the dosage should be adjusted.

Abomics was founded in Finland in 2013 with the fundamental idea to translate research into personalized medication recommendations.

Abomics' Services

Abomics PGx
Pharmacogenetic interpretation service for clinical laboratories.

Abomics GeneRx
Pharmacogenetic database for integration with e.g. EHR, DSS, or Rx systems.

[1] Brown, Lisa C., Joseph D. Stanton, Kanika Bharthi, Abdullah Al Maruf, Daniel J. Müller, and Chad A. Bousman. "Pharmacogenomic Testing and Depressive Symptom Remission: A Systematic Review and Meta‐Analysis of Prospective, Controlled Clinical Trials." Clinical Pharmacology & Therapeutics (2022).

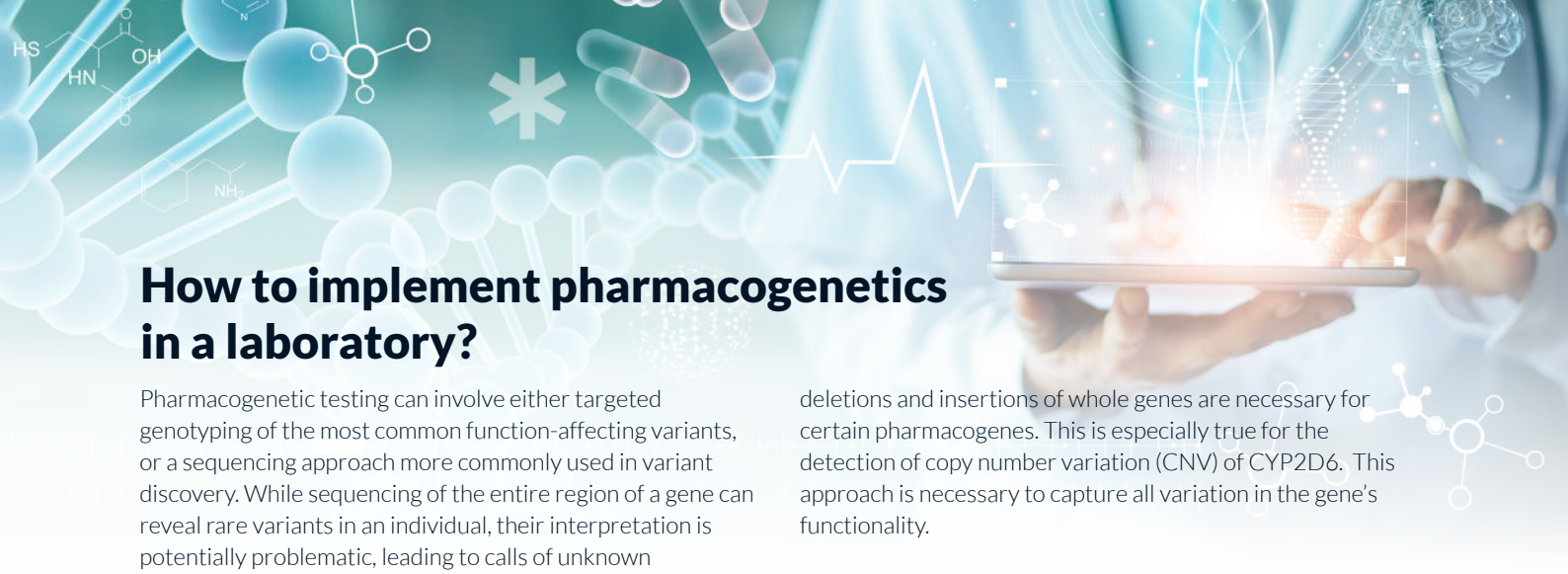
[2] Perlis, Roy H., et al. "Pharmacogenetic testing among patients with mood and anxiety disorders is associated with decreased utilization and cost: A propensity-score matched study." Depression and anxiety 35.10 (2018): 946-952.

[3] Elliott, Lindsay S., et al. "Clinical impact of pharmacogenetic profiling with a clinical decision support tool in polypharmacy home health patients: A prospective pilot randomized controlled trial." PloS one 12.2 (2017): e0170905.

[4] Brixner, D., et al. "The effect of pharmacogenetic profiling with a clinical decision support tool on healthcare resource utilization and estimated costs in the elderly exposed to polypharmacy." Journal of medical economics 19.3 (2016): 213-228.

[5] Magavern, Emma Forton, et al. "The role of pharmacogenomics in contemporary cardiovascular therapy: A position statement from the European Society of Cardiology Working Group on Cardiovascular Pharmacotherapy." European Heart Journal-Cardiovascular Pharmacotherapy 8.1 (2022): 85-99.

[6] Wang, Yongjun, et al. "Ticagrelor versus clopidogrel in CYP2C19 loss-of-function carriers with stroke or TIA." New England Journal of Medicine 385.27 (2021): 2520-2530.



How to implement pharmacogenetics in a laboratory?

Pharmacogenetic testing can involve either targeted genotyping of the most common function-affecting variants, or a sequencing approach more commonly used in variant discovery. While sequencing of the entire region of a gene can reveal rare variants in an individual, their interpretation is potentially problematic, leading to calls of unknown significance. Further, sequencing remains more expensive than genotyping. Targeted genotyping is commonly seen as the preferred approach for commercial pharmacogenetic testing.

In addition to detecting single nucleotide polymorphisms (SNP) and short insertion and deletion (indel) variants, testing for deletions and insertions of whole genes are necessary for certain pharmacogenes. This is especially true for the detection of copy number variation (CNV) of CYP2D6. This approach is necessary to capture all variation in the gene's functionality.

Abomics PGx Interpretation Service can accommodate data from any genetic test, however, here we describe the most commonly used testing platforms and minimal technical requirements in order to help laboratories to initiate pharmacogenetic testing.

When you partner with us, you gain access to a wide range of PGx solutions and the vast expertise acquired from a decade of driving advancements in PGx.

List of recommended relevant genes

The following genes are deemed as highly relevant, either due to having a published dosing guideline or being mentioned in a drug label as a significant predictor of drug response or as a possible contraindication (for certain genotype carriers). Testing for these genes with genotyping (i.e. not sequencing) is appropriate (see information below concerning HLA genes).

Please refer to the document "Minimum allele selection for PGx panels" for a list of minimally required variants (variants with priority level 2 are the absolute minimum for each gene). Variant selection and prioritization are based on global and population-level allele frequencies, CPIC (Clinical Pharmacogenetics Implementation Consortium) guidelines, and on allele selection guidelines by the Association for Molecular Pathology for CYP2C19, CYP2C9 and CYP2D6.

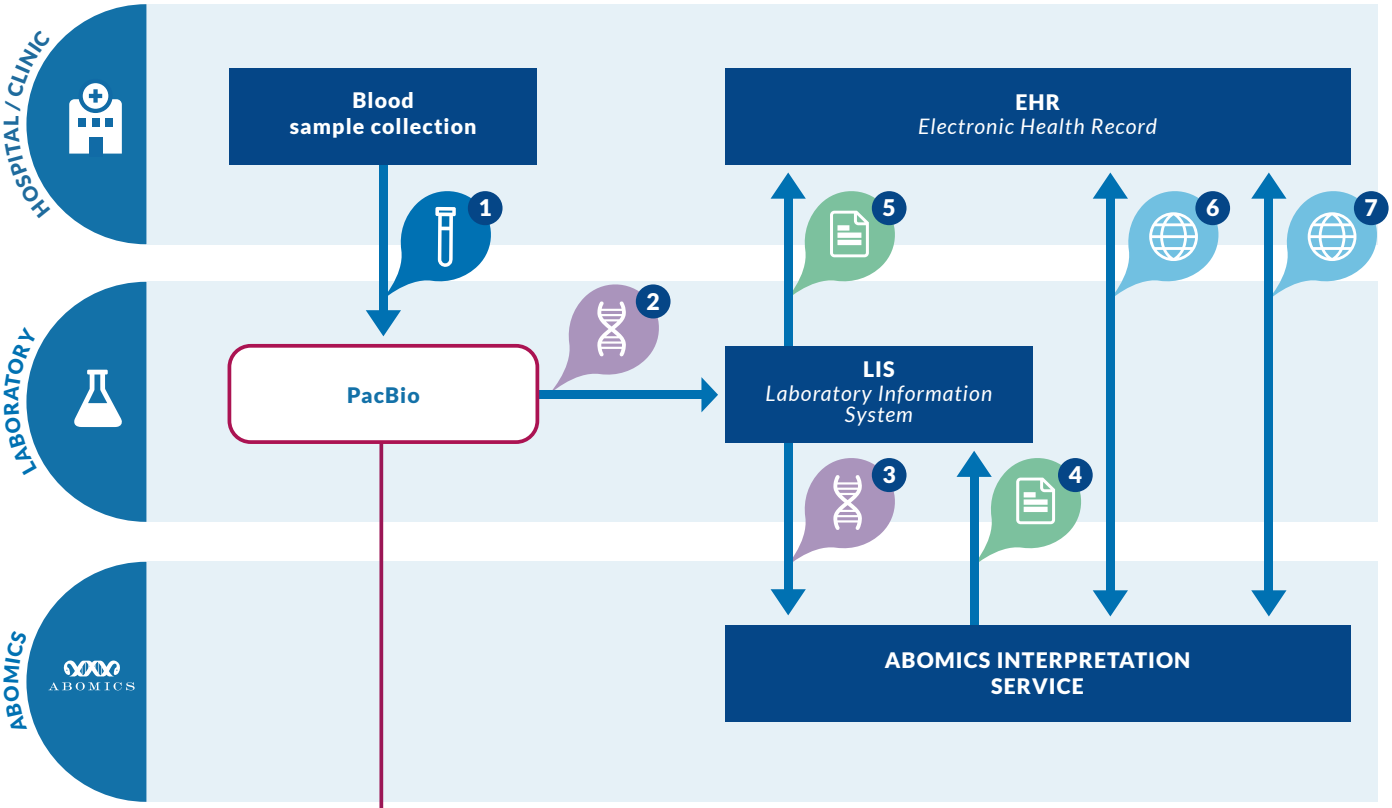
Tier 1 - Essential*	Tier 2 - Optional**
CYP2B6	BCHE
CYP2C19	F2
CYP2C9	NAT2
CYP2D6	
CYP3A5	
CYP4F2	
DPYD	
F5	
G6PD	
IFNL3	
NUDT15	
SLCO1B1	
TPMT	
UGT1A1	
VKORC1	

*Dosing guidelines published.

** Gene mentioned in a drug label with significant implications.

The following genes are highly relevant but are more disease-specific, have extremely rare variants or require special testing procedures and might not be usable in non-targeted testing. Noteworthy, the HLA genes are highly useful in pharmacogenetically guided drug prescribing but not currently recommended by Abomics to be interpreted with SNP genotyping only. Accurate testing of HLA genes requires a sequencing-based approach.

CFTR
CACNA1S
HLA-A (genotype *3101)
HLA-B (genotypes *1502, *5701, *5801)
MT-RNR1
RYR1



1. Blood sample
2. Genetic data
3. Genetic data
4. Interpretation report
5. Interpretation report
6. Dr access to online up-to-date report (optional)
7. Patient access to up-to-date report (optional)

A Closer Look at PacBio Workflow*

High Quality DNA Extraction
e.g. Nanobind HT CBB kit

WGS library

Target Enrichment
PCR Amplicons or Hyb Capture

PacBio Library
SMRTbell prep kit 3.0

HiFi Sequencing on PacBio
Revio or Sequel II or IIe Systems

* Research use only. Not for use in diagnostic procedures.

Pharmacogenomics with SMRT® sequencing is smart business*

PacBio Sequel® II, IIe, and Revio systems are powered by Single Molecule, Real-Time (SMRT®) sequencing, a technology proven to produce highly accurate long reads, known as HiFi reads, for sequencing data you and your customers can trust. PacBio is the only sequencing technology to offer highly accurate long reads, resulting in comprehensive variant calling of SNPs, SVs, and indels on a single platform. This results in reliable, high confidence variant calling for reportable pharmacogenomic variants, as well as the ability to identify novel and rare variants, future-proofing your assays. Additionally, with direct haplotyping across pharmacogenes, HiFi sequencing offers direct phasing to enable unambiguous star allele assignment and accurate phenotype predictions. With PacBio, you can comprehensively capture important variation that may be missed with biased methods for genotyping, such as arrays or short-read sequencing, that may have gaps in coverage or rely on computational imputation for phasing.

With targeted sequencing methods, such as amplicon and hybrid capture, long-read HiFi sequencing is now cost-effective and high-throughput. For an off-the-shelf option to quick start your assay development, we designed the *Twist Long-Read Pharmacogenomics Panel*, in collaboration with Twist Bioscience and researchers from a leading institution. This 2 Mb panel includes 50 pharmacogenes, including major genes with CPIC and DPWG guidelines, with 39 genes covered full-length. A panel of this size can be run 24plex on a SMRT Cell 8M, or 72plex on a Revio SMRT Cell. Alternatively, custom designs can be quickly designed and produced through Twist. All PacBio products are backed by a global team of scientists, bioinformaticians, and engineers, and PacBio partners with leading automation providers to enable HiFi sequencing at scale.

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ABOMICS1003D 4/2023