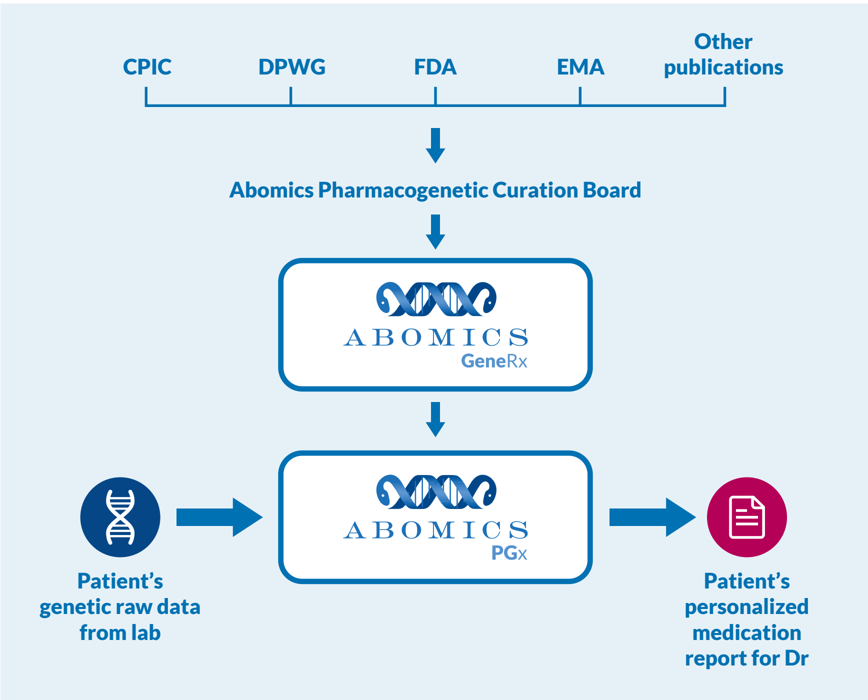
ABOMICS
Supporting medication decisions

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, thrombosis, and stroke. [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.

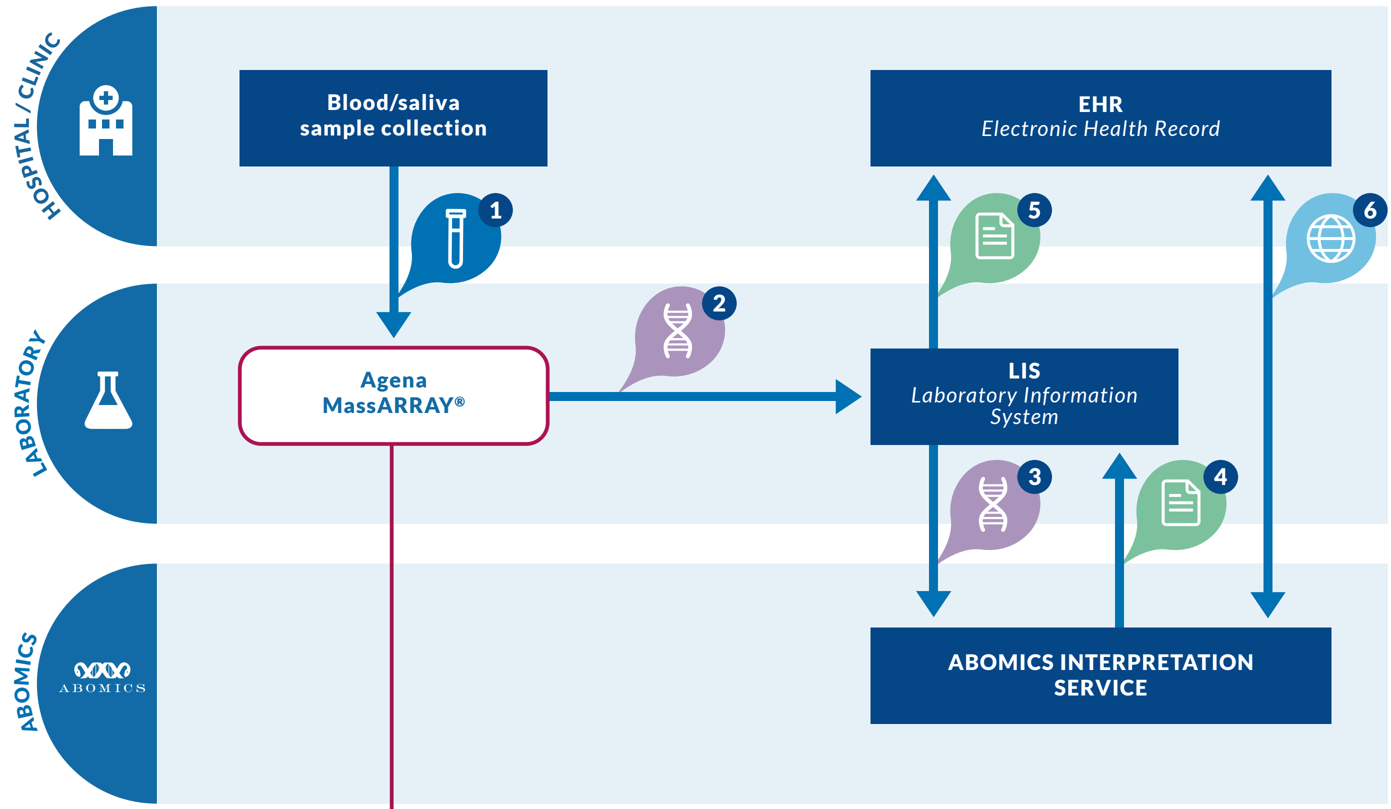
Tier 1 - Essential*	Tier 2 - Optional**
CYP2B6	BCHE
CYP2C19	F2
CYP2C9	NAT2
CYP2D6	
CYP3A5	
CYP4F2	
DPYD	
F5	
G6PD	
IFNL3	
NUDT15	
SLCO1B1	
TPMT	
UGT1A1	
VKORC1	

*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/saliva sample
2. Genetic raw data
3. Genetic raw Data
4. Interpretation report
5. Interpretation report
6. Dr access to online up-to-date report (optional)

A Closer Look at Agena MassARRAY® PGx Workflow

AGENA BIOSCIENCE

MassARRAY® PGx Workflow*

*Workflow time may vary depending on chemistry and acquisition settings.

PCR/SAP/Extension

Multiplex end-point PCR followed by a single base extension reacion

Target Sequence Detection

Automated analyte transfer and data acquisition

Data Analysis

Data display and report generation

96 FORMAT

Run Time: 7 Hrs* Hands-on Time: 23 Min	Run Time: 90 Mins* Hands-on Time: 5 Min	Hands-on Time: 5-10 Min

384 FORMAT

Run Time: 7 Hrs* Hands-on Time: 23 Min	Run Time: 160 Mins* Hands-on Time: 5 Min	Hands-on Time: 5-10 Min

MassARRAY® PGx Workflow Overview from Agena Bioscience

The Agena MassARRAY® PGx Workflow takes approx 9-10 hours to be completed depending whether a 96 or 384 system has been used.

First, samples collected using approved methods (buccal swabs, saliva and/or blood), need to have the sample DNA isolated. This is performed by loading the samples onto a 96-well plate, before DNA extraction on the KingFisher Flex with MagMAX DNA Multi-Sample Ultra Kit. After less than two hours, the extracted DNA sample is then transferred to a 96 or 384-well plate and PCR reagents are added to the plate. Each individual PCR reaction can contain up to 32 unique SNP assays. The plates are sealed before cycling and PCR is performed on the SensoQuest PCR instrument. In 2:30 hours, the run is complete.

Thereafter, an SAP reaction is performed to render leftover dNTPs inactive, and an extension reaction is initiated in which an extend primer is added that lays down on the PCR product next to the SNP of interest and the reaction will incorporate the complimentary base (A, G, C, or T). No separate reactions are needed for tri- or quad-allelic SNPs. The SAP and Extension steps take about 3 hr total.

The 96 or 384 plate with the Extend product is then put on the Chip Prep Module (CPM) and this will transfer the product onto a SpectroChip and automatically feed the chip into the MassARRAY® for analysis. The results can be reviewed, and further analysis performed with integrated genotyping application software, available on the system.

Total workflow time is about 7-9 hours per run, but time from sample-to-first results is as low as 7 hours. Up to 8 runs can be completed per day with the 384 system – the complete workflow, using VeriDose Core (68 SNPs) and VeriDose CYP2D6 CNV (22 assays in 7 gene regions), enables up to 768 samples to be performed per day. If only a smaller single well panel (32 SNP assays) was required, the throughput of the system is actually approx. 3000 samples/day.

Agena Bioscience also offers solutions for oncology, sample identification, and clinical genetics that can be run concurrently with the Pharmacogenetics portfolio on the same PCR plates and MassARRAY® runs if needed.

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