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H2020 Research and Innovation

Deliverable D3.1
Set of specifications for the selected PGx assays

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Lead beneficiary: **P7 – bio.logis Center for Human Genetics**
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Introduction

An increasing number of scientific studies in the last decade showed the importance of pharmacogenomic (PGx) testing before medication intake begins and its impact on the improvement of health care. Nevertheless, the successful implementation of PGx testing into clinical practice is relatively slow. General challenges and barriers for incorporating PGx testing into clinical routine are missing guidelines, education, turnaround time, costs and reimbursement.
The first step towards implementation into clinical routine was the establishment of one standardized panel with clinically relevant genetic variants in selected genes (s. WP 2, deliverable D2.1). Successful realization of a standardized genotyping routine with a high throughput genotyping platform is depending on genotyping costs, turnaround time and result interpretation.

Set of specifications for the selected PGx assays and platform

In the selection process for the genotyping platform following criteria were considered:

- Genotyping costs per sample ≤ 50€
- Possibility to process several samples in one work process (batch production)
- Turnaround time: 2 days
- Assay design for platform fulfils diagnostic criteria: positions of primer have to be evaluated concerning polymorphisms and homologous sequences that could result in a wrong genotyping result
- Accuracy and reproducibility
- Genotyping technology fulfils QM criteria: work processes have to be transparently documented by the system with log files
- The typus of platform was already successfully implemented in at least one diagnostic laboratory
- Investment for seven sites fits into the budget of 1.19 Mio € (incl. VAT)

Results

As a first step six actually on the market available high throughput genotyping platforms were considered for an investigation concerning the set of specifications listed above. Platforms and respective prices are listed in table 1. Since the total costs for two platforms were announced to be more than 2 mio €, they were excluded after the first round of analyses from further negotiations processes (see table 1, entries marked in red).

	ThermoFisher Scientific		Affymterix	LGC Genomics	Douglas Scientific	Illumina
Platform	QuantStudio 12K OpenArray	QuantStudio 12K 384 well plates	Axiom DMET Plus	SNPLine	IntelliQube	MiniSeq
Costs H&S*	626,115 €	661,028 €	> 3 Mio €	782,880 €	> 2,5 Mio €	432,188 €
Costs C**	434,713 €	> 500,000 €		32,274 €		597,562 €

Table 1: Analysed high throughput genotyping platforms and respective costs
* = cost for hard- and software, incl. training and maintenance for 3 years
** = consumables for genotyping of 8,000 samples

Proof of the selection criteria batch size and total genotyping costs per sample revealed that the MiniSeq Platform from Illumina (see table 2, entry marked in red) has to be excluded for the project as well.

	ThermoFisher Scientific		LGC Genomics	Illumina
Platform	QuantStudio 12K OpenArray	QuantStudio 12K 384 well plates	SNPLine	MiniSeq
Costs H&S*	626,115 €	661,028 €	782,880 €	432,188 €
Costs C**	434,713 €	> 500,000 €	32,274 €	597,562 €
Batchsize	10	3	10 (up to 20)	fix 16
Price / sample (full Batch)	28.70 €	85.94 €	35.00 €	74.70 €
Price / sample (processing of single sample)	287 €	257,82 €	175 – 350 €	1195.20 €

Table 2: Analysed high throughput genotyping platforms and respective genotyping costs per sample

Purchase price, cost for consumables and maintenance for the three remaining platforms QuantStudio 12K OpenArray, QuantStudio 12K 384 well plates and SNPLine remained in the total budget.

However, QuantStudio 12K with 384-well plates was excluded from the selection, since it would not be possible to use controls within the genotyping costs range as it is possible with other platforms.

Besides the specifications described, other advantages and disadvantages of all four platforms were evaluated (for overview s. table 3).

	ThermoFisher Scientific		LGC Genomics	Illumina
Platform	QuantStudio 12K OpenArray	QuantStudio 12K 384 well plates	SNPLine	MiniSeq
Advantages	• use of synth. controls in each run • all samples measured in duplicate • **hands on time (~ 1d)**	• smaller batches	• **assays for all U-PGx targets successfully designed** • use of synth. controls in each run • all samples measured in duplicate • **rerun of single assays possible (e.g. drop-outs, outliners etc.)** • **flexible panel design** • **possible to run single /selected assays** • **highest flexibility**	• state of the art technology! • market leader
Disadvantages	• fixed panel design • rerun of single assays (e.g drop outs) not possible • two targets not measurable (CYP2B6*16 and rs61736512, included in the CYP2D6*29) • additional step for CYP2D6 xN and *5	• fixed panel design • rerun of single assays (e.g drop outs) not possible • not possible to use synth. controls in the same manner as with OA / LGC • High genot. costs / sample • two targets not measurable (s. OpenArray) • additional step for CYP2D6 xN and *5	• hands on time > than OA /Illumina (~ additional 4 h) • additional step (LR PCR) for CYP2D6 xN and *5	• Batchsize: fix 16 • to expensive for processing of small batches

Table 3: Advantages and disadvantages of analysed genotyping platforms.

Furthermore, the final feasibility analysis revealed that only LGC Genomics provided successful assay designs for all U-PGx targets.
Taken together all the results described, a final choice was made in favour of SNPLine (LGC Genomics).

Summary/Conclusions

Final analysis showed that beside the low genotyping costs, SNPLine (LGC Genomics) was the only high throughput genotyping platform which could fulfil all specifications listed above.