Poster # 01

Performance Analysis of a Comprehensive Clinically Focused Pharmacogenetic Assay

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- Axiom™ PharmacoFocus™ array offers a **highly accurate clinically focused** pharmacogenetic genotyping assay.
- It also **contains HLA typing and copy number calling** for highly actionable genes.
- Samples from **different biological specimen types like blood and saliva** generate high quality results.

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Introduction and Goal

- Genotyping of relevant pharmacogenetic (PGx) genes and HLA typing for known associations with drug metabolism and hypersensitivity allows for personalized drug selection and dosing prior to administration.
- The accuracy and reproducibility of testing methodologies are critical to ensure accurate phenotype assignment. We have previously demonstrated the quality and relevance of the PharmacoScan™ (pScan) assay for clinical PGx testing.
- While pScan offers the most comprehensive genotyping platform (4,627 ADME markers in 1,191 genes + copy number analysis) there continues to be a need for a more targeted, higher throughput and more cost-effective platforms. In this study, we tested the Axiom™ PharmacoFocus™ (pFocus) assay, a targeted assay (2,000+ ADME markers in 150 genes + copy number analysis) that includes highly relevant PGx genes and markers and offers the potential for routine and reliable clinical PGx testing.

Results

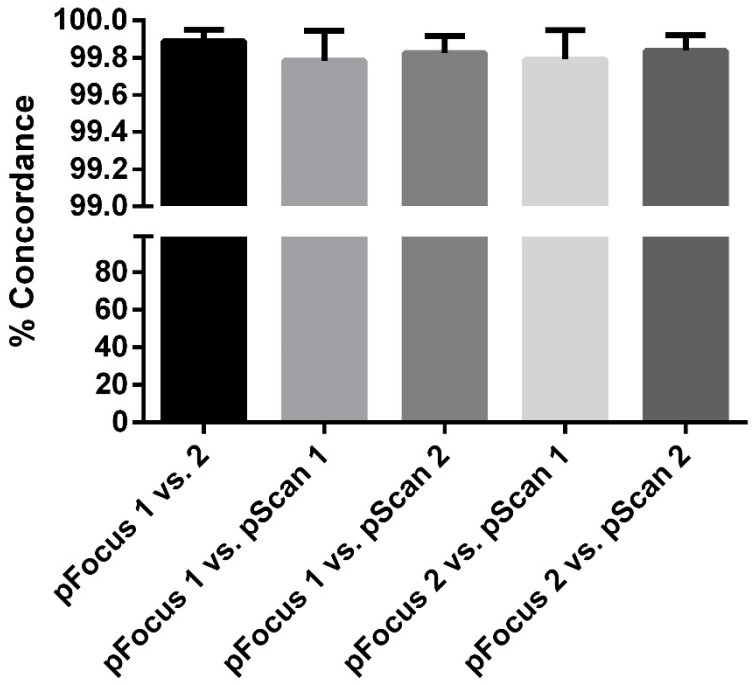

Figure 1. Probe level concordance between different pFocus and pScan batches. A median inter-run concordance of 99.6% was observed between the two pFocus plates. A median concordance of 99.5% was observed between the pFocus and pScan data.

Methods

- Genomic DNA (gDNA) was acquired from Coriell (isolated from LCL cell lines) or isolated from blood and saliva.
- Samples were batched (including mixed sample types per plate) and run using the PharmacoScan™ Assay Kit (pScan), 24-Format and the Applied Biosystems™ Axiom™ PharmacoFocus™ Assay Mini 96.
- Array analysis was done using the Axiom™ Analysis Suite 5.0 and performance was measured in terms of genotyped probe and actionable pharmacogene star allele haplotype level.
- Comprehensive content in one assay (96 or 384 array formats)
  - 2000+ variants in 150+ genes
  - ~ 88% variants referenced in CPIC guidelines (1A/1B, 2A/2B)
  - Copy number calling for genes like CYP2D6
  - HLA typing including PGx relevant HLA-A and HLA-B alleles
  - 900+ unique star alleles/haplotypes across 66 PGx genes

CPIC Genes	Haplotype Calling Genes			Copy Number Genes
CFTR	CDA	POR	UGT2B17	CYP2A6
CYP2B6	CYP1A1	PTGIS	COMT	CYP2D6
CYP2C9	CYP1B1	SLC15A2	CYP1A2	GSTM1
CYP2C19	CYP2A13	SLC22A2	CYP2A6	GSTT1
CYP2D6	CYP2F1	SLCO2B1	CYP2C8	UGT2B17
CYP3A5	CYP2J2	SULT1A1	CYP2E1	
DPYD	CYP2S1	TBXAS1	CYP3A4	
G6PD	CYP3A43	UGT1A3	CYP3A7	
IFNL3	CYP4B1	UGT1A4	GSTM1	
SLCO1B1	CYP4F2	UGT1A6	GSTP1	
TPMT	CYP19A1	UGT1A7	NAT1	
UGT1A1	F5	UGT1A8	NAT2	
VKORC1	FMO1	UGT1A9	UGT2B7	
CACNA1S*	FMO2	UGT1A10		
NUDT15				
RYR1*				

Table 1. A subset of PGx genes genotyped on the PharmacoFocus™ array. *ACMG genes

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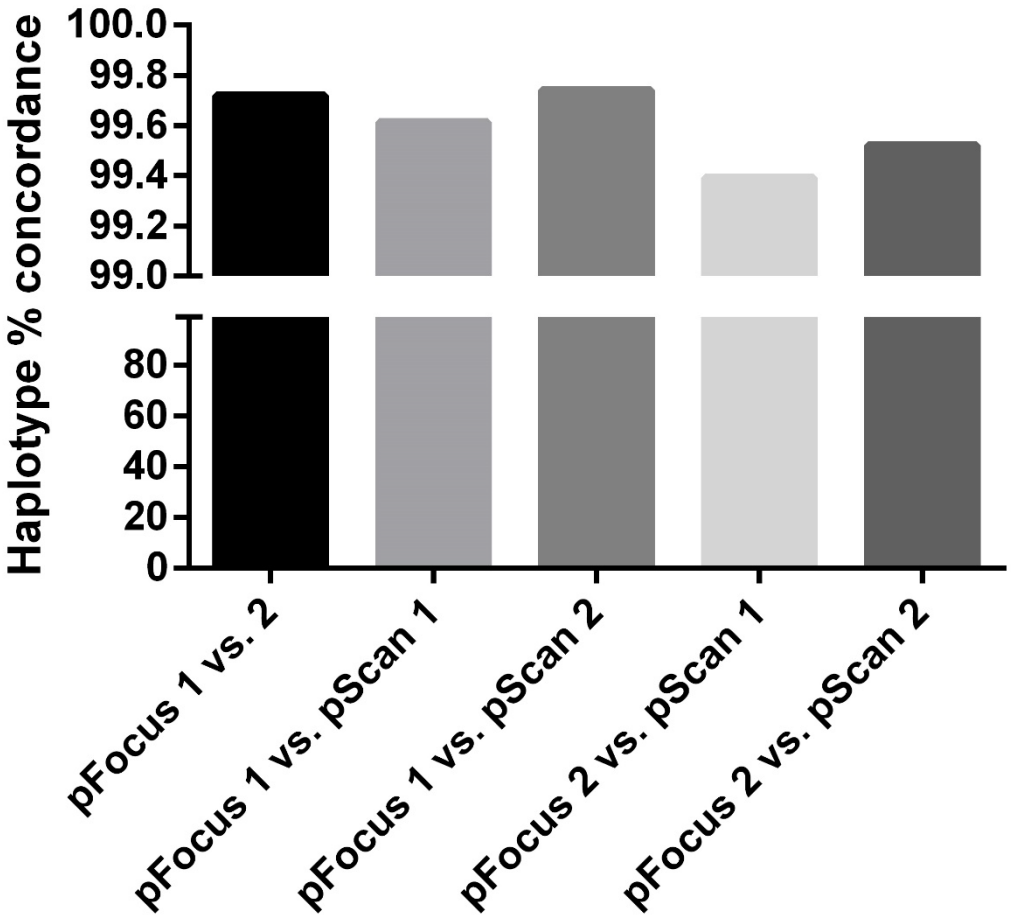

Figure 2: Haplotype level concordance. Relevant PGx gene haplotype concordance between the different pFocus plates and the pFocus and pScan plates was observed to be greater than 99% across all samples.

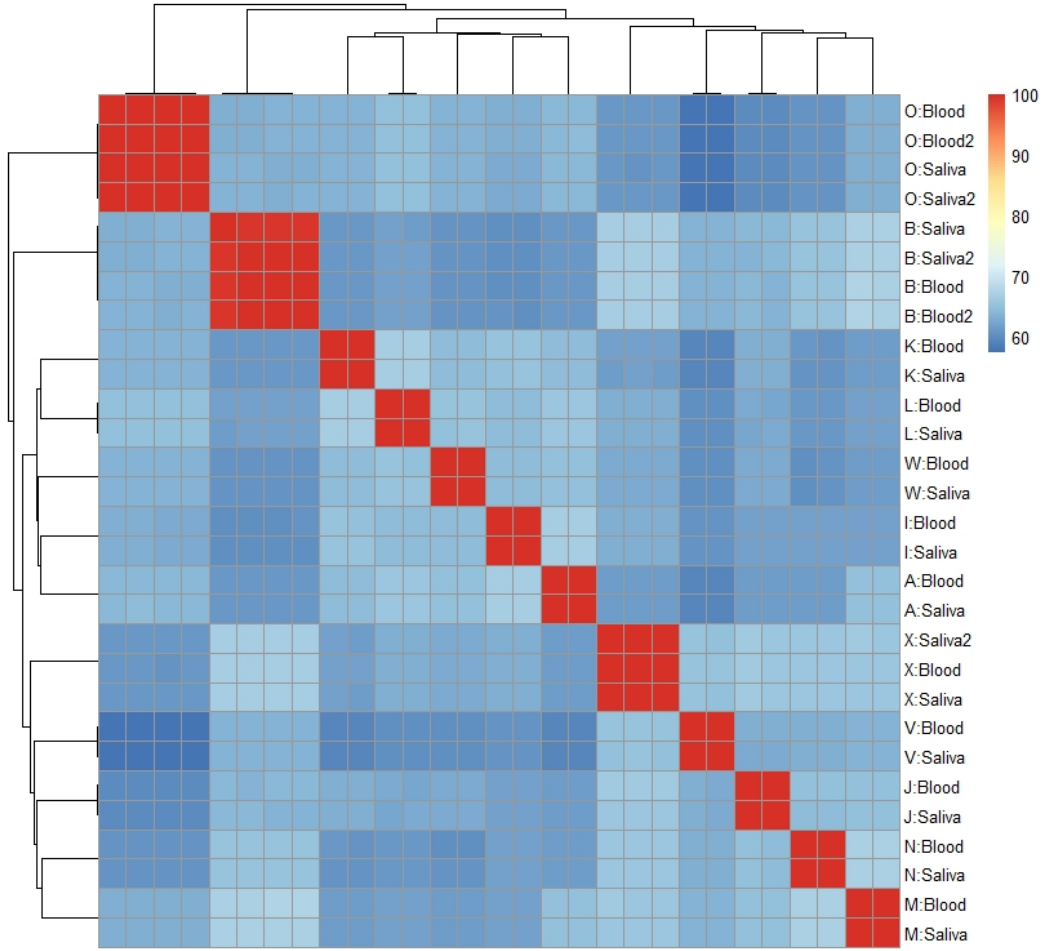

Figure 3: Genotype homology across different biological specimen type. The genotypes for a sample using different specimen types of DNA (saliva and blood) were compared. A high level of genotype homology (median >99.5%) between the different specimen types from the same donor (red boxes) was observed. The blue boxes represent low level of genotype homology between samples from different donors regardless of specimen type. The sample names on the graph are presented as "Sample:Specimen" (e.g. A:Blood)

Conclusions

- We evaluated the Axiom™ PharmacoFocus™ assay (pFocus), a more clinically focused array-based platform derived from PharmacoScan™ (pScan), includes the most clinically relevant and actionable PGx genes and markers.
- The intra- and inter-run results demonstrate that the quality of the genotypes is highly accurate and reproducible.
- We also show that this assay performs well for gDNA samples derived from different source types.
- The targeted yet comprehensive scope of pFocus makes it a high throughput and cost-effective clinical PGx testing platform that may also be used for large scale research and clinical trials.

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