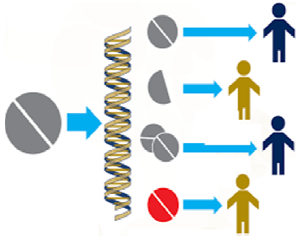
Population pharmacogenomic aspect of glucocorticoids response in Serbian population

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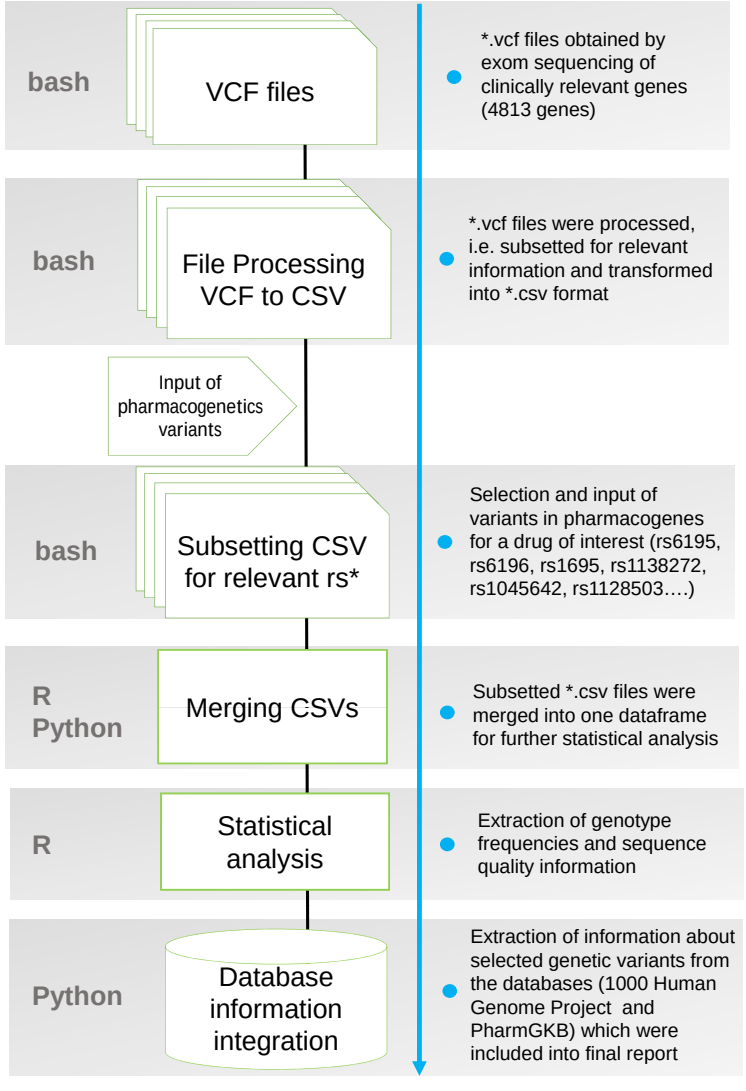
BACKGROUND

Pharmacogenomics represents one of the pillars of personalized medicine. Genetic variants that represent biomarkers of drug efficacy and toxicity vary considerably in frequency between populations. As a consequence, side effects or therapeutic effects of certain drugs might represent serious issue in some populations, and not in others. Also, the cost-effectiveness of pharmacogenomic testing in one country depends on pharmacogenomic disposition of the population. Bearing in mind the importance of population pharmacogenomics, we aimed to optimize procedure for population-genetic data extraction obtained during analyses of clinical exomes (coding region of all clinically relevant genes – 4813 genes) and to apply this procedure to analyze potential pharmacogenomic markers of glucocorticoid response in Serbian population

SUBJECTS AND METHODS

We selected group of 100 individuals of Serbian origin whose clinical exomes were analyzed using TruSight One Sequencing Panel (Illumina) on Miseq system. The variants in pharmacogenes relevant for glucocorticoid response were selected using Pharmacogenomics Knowledgebase (PharmGKB) database and articles available on PubMed (combination of keywords: glucocorticoids, prednisone, prednisolone, dexamethasone, pharmacogenetics, pharmacogenomics, drug response). Seventeen variants that were associated with glucocorticoid response located in *NR3C1*, *ABCB1*, *GSTP1*, *ADRB2* and *TBX21* genes were included. To extract relevant information, Population pharmacogenomic data mining (PoPDaM) pipeline was developed.

PoPDaM WORKFLOW



PoPDaM REPORT

rs number	Gene	Change	Homozygous Wt	Heterozygous	Homozygous Var	Filter passed	Minor allele	Minor allele EUR	Level of evidence
rs6195	NR3C1	c.1068A>G (p.Asn363Ser) - N363S	100	0	0	100.0%	0.0%	1.8%	-
rs6189	NR3C1	c.66G>A (p.Glu22=)	96	4	0	100.0%	2.0%	3.0%	-
rs6190	NR3C1	c.68G>A (p.Arg23Lys)	96	4	0	100.0%	2.0%	3.0%	-
rs72542742	NR3C1	c.685G>A (p.Ala229Thr)	99	1	0	100.0%	0.5%	1.0%	-
rs6194	NR3C1	c.1767C>T (p.His589=)	100	0	0	100.0%	0.0%	0.2%	-
rs6196	NR3C1	c.2301T>C (p.Asn767=)	75	23	2	96.0%	13.5%	14.9%	-
rs1695	GSTP1	c.313A>G (p.Ile105Val)	57	36	7	100.0%	25.0%	33.1%	-
rs1138272	GSTP1	c.341C>T (p.Ala114Val)	92	8	0	75.0%	4.0%	7.1%	-
rs1045642	ABCB1	c.3435T>C/A (p.Ile1145=)	26	49	25	99.0%	49.5%	48.2%	3
rs1128503	ABCB1	c.1236T>C (p.Gly412=)	17	46	37	98.8%	60.0%	58.4%	-
rs2229109	ABCB1	c.1199G>A (p.Ser400Asn)	100	0	0	100.0%	0.0%	3.3%	3
rs104893913	NR3C1	c.1433G>A (p.Arg478His)	100	0	0	100.0%	0.0%	0.0%	-
rs72558023	NR3C1	c.198A>G (p.Pro66=)	100	0	0	100.0%	0.0%	0.0%	-
rs138896520	NR3C1	c.1899G>A (p.Gln633=)	100	0	0	100.0%	0.0%	0.0%	-
rs1042713	ADRB2	c.46G>A (p.Gly16Arg)	40	50	10	97.5%	35.0%	38.6%	3
rs2240017	TBX21	c.99C>G (p.His33Gln)	98	1	1	50.0%	1.5%	2.0%	3

Minor allele frequency of European populations was extracted from 1000 Human Genome Project.
Level of evidence refer to pharmacogenomic relevance of a variant accroding to PharmGKB

CONCLUSIONS

Results of the applied PoPDaM pipeline are relevant for:

- pharmacoeconomic aspect of pharmacogenomic testing for glucocorticoid drugs
- future pharmacogenomic studies of glucocorticoid response in Serbian population.

PoPDaM pipeline could be easily applied to any drug of interest.