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CYP2D6 CNV Caller Software

A free software application for calling copy number variants in the *CYP2D6* gene using Infinium™ genotyping arrays.

Introduction

The Infinium Global Screening Array-24 v3.0 BeadChip is a commercially available genotyping microarray that enables clinical research applications, including complex disease studies, wellness characterization, pharmacogenomics, and more. The cytochrome P450 2D6 (*CYP2D6*) gene encodes an enzyme that is primarily expressed in the liver and is responsible for metabolizing ~25% of clinically used drugs.[1] Given its function in drug metabolism and the fact that the gene is impacted by copy number variation (CNV), the *CYP2D6* gene is important to pharmacogenomics. The CYP2D6 CNV Caller software application enables CNV calling in *CYP2D6*, previously not supported for the Infinium Global Screening Array-24 v3.0 BeadChip. This software allows for deeper interrogation of the role of *CYP2D6* in drug metabolic pathways and strengthens the utility of the Infinium Global Screening Array-24 v3.0 BeadChip for use in clinical research applications.

Caller capability

The CYP2D6 CNV Caller is a standalone command line software solution that calls gene level and a subgenic copy number for intron 2, intron 6, and exon 9 of *CYP2D6*. It detects copy number (0, 1, 2, 3, 4, and 5+) events. In addition to CNV calling, the software calls genotypes for the whole array and outputs them in a VCF file format for use in downstream analysis (Figure 1). Auxiliary summary files are generated to provide the information necessary to assess the quality of the data. The algorithm has been optimized for the Infinium Global Screening Array-24 v3.0 content, due to its potential use in clinical research applications.

Trainer capability

The CYP2D6 CNV Caller includes a trainer module that allows users to optimize the commercially available model file. This step is recommended for customers who have already optimized their cluster file using their own “gentrain” data set. The trainer can also be used to generate a new model for the Infinium Global Screening Array-24 v3.0 BeadChip with custom add-on content. The CNV model generated by the trainer is then used by the software to call CNVs.

Analytical performance evaluation

To demonstrate the performance of the CYP2D6 CNV Caller. a data set of 115 unique truth samples, consisting of 11 with copy number (CN) gains, 7 with CN losses, and 103 with neutral CN, were evaluated for CNV calling. With CNV detection rates > 90% (Table 1) and CNV calling accuracy > 0.90 for regions across *CYP2D6* (Table 2), the CYP2D6 CNV Caller shows exceptional analytical performance.

To learn more about the CYP2D6 CNV Caller, email informatics@illumina.com

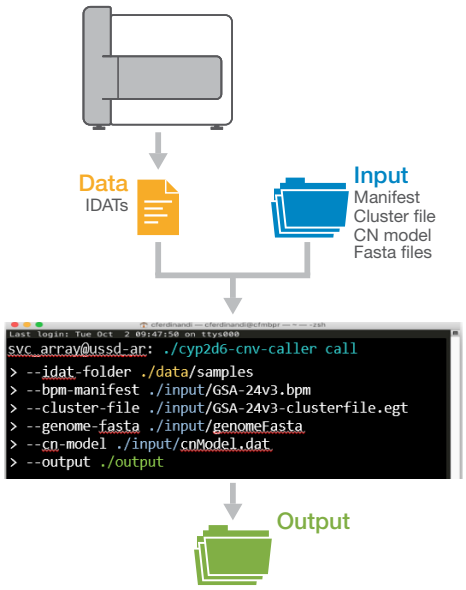

Figure 1: CYP2D6 CNV Caller workflow—Array scanner data and auxiliary files are input to the algorithm, which outputs CNV calling results.

Table 1: Analytical performance evaluation: algorithm sensitivity

CN status	Present in data set	Detected by algorithm
CN loss (CN < 2)	50	48 (96%)
CN neutral (CN = 2)	794	782 (98.5%)
CN gain (CN > 2)	70	65 (92.8%)

Table 2: Analytical performance evaluation: algorithm accuracy

Region	F measure[a] gain	F measure loss
CYP2D6	0.83	0.91
Intron 6	0.95	0.90
Intron 2	0.96	0.92
Exon 9	1	0.93
Overall performance	0.92	0.92

a. F measure is a test of correctly predicted copy number changes (gains or losses) used to evaluate the CNV calling accuracy of the algorithm.

References

1. Ingelman-Sundberg M, Sim SC, Gomez A, Rodriguez-Antona C. Influence of cytochrome P450 polymorphisms on drug therapies: pharmacogenetic, pharmacoepigenetic, and clinical aspects. *Pharmacol Ther*. 2007;116(3):496–526.

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