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Infinium® DrugDev Consortium Array

A new array for discovery and translational genomics.

Highlights

- **Wide Applicability**
  Enables drug target discovery and validation, drug repurposing, and drug specificity studies
- **Comprehensive Coverage**
  Provides systematic/dense coverage of ADME genes and the druggable genome
- **Informative Content**
  Includes indel, exome, CNV, and high-value GWAS content

Introduction

Effective drug development depends on proper target validation and an understanding of drug safety and efficacy in a wide population. Current development processes rely on clinical trials to obtain this information. Unfortunately, this process often results in high rates of late-stage failures. In addition, it may not account for the variation in genes encoding proteins involved in drug metabolism that occurs naturally within a diverse population. The Infinium DrugDev Consortium Array combines available genomic data with advanced computational tools to enable researchers to test targets earlier in the development process.

Comprehensive Coverage for Drug Discovery

Most currently available whole-genome arrays have limited coverage of drugged, druggable, and absorption, distribution, metabolism, and excretion (ADME) genes. The Infinium DrugDev Consortium Array extends this coverage, enabling translational genomics at a systematic level (Tables 1–4, 6). Developed in collaboration with leaders in translational genomics and computational biology, the DrugDev array provides researchers with the ability to perform genetic studies using the principle of Mendelian randomization to reproduce the key elements of a randomized trial. This testing ensures that target validation can take place earlier in the development process.

The DrugDev array combines the trusted genome-wide tag single nucleotide polymorphism (SNP) content of the Infinium HumanCore-24 BeadChip (240,000 highly informative genome-wide tag SNPs and over 20,000 high-value markers) with a novel, 180,000 custom marker set designed to support studies of drug target validation and treatment response. The custom marker set, or Human Drug Target Validation and Response module, provides coverage of:

- Genes involved in ADME
- Genes encoding proteins that are known efficacy targets of small-molecule and biotherapeutic drugs, regardless of the clinical phase of drug development (early, late, or approved) as described by the EMBL-EBI ChEMBL database[1]
- Genes encoding proteins closely related to targets of approved small-molecule and biotherapeutic drugs or binding drug-like compounds

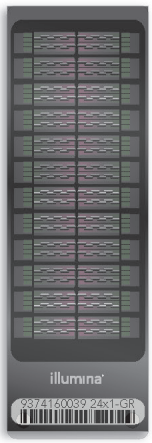

Figure 1: Infinium DrugDev Consortium Array—Providing trusted HumanCore BeadChip content plus > 180,000 markers with known associations to the druggable genome.

- Drugged and druggable mitochondrial genes and nuclear-encoded mitochondrial proteins
- Genes encoding proteins believed to be druggable by small-molecule and biotherapeutic drugs

Wide Range of Applications

The DrugDev array is suitable for patient or population collections in discovery-based genomic studies of disease end-points and/or preclinical disease biomarkers. The systematic, comprehensive coverage of the druggable genome and ADME genes extends the capability of the DrugDev array to various drug discovery and development studies (Table 5).

Summary

Developed through a collaboration between Illumina scientists and leaders in translational genomics and computational chemical biology, the Infinium DrugDev Consortium Array features an average of 48.9 SNPs per druggable gene. This 24-sample BeadChip can be used in patient or population samples for discovery-based genomic studies of disease, and for the analysis of preclinical biomarkers, in academic or industrial research.

Learn More

To learn more about the Infinium DrugDev Consortium Array or place an order, contact consortiamanager@illumina.com, your genotyping specialist, or a local sales representative:
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Other regions: www.illumina.com/company/contact-us.html

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Table 1: Preliminary Product Information for the Infinium DrugDev Consortium Array

Feature	Description	
Total Number of Markers	485,000	
Capacity for Custom Markers	100,000	
Number of Samples per BeadChip	24	
DNA Input Requirement	200 ng	
Assay	Infinium HTS	
Instrument Support	iScan® or HiScan® System	
Sample Throughput[a]	5760 samples/week	
Scan Time per Sample	iScan 2.6 min	HiScan 2.0 min
Variation Captured ($r^2 \geq 0.8$)	**1kGP MAF > 5%**	**1kGP MAF > 1%**
ADME Genes	0.93	0.87
Drug Targets	0.94	0.88
Druggable Targets	0.94	0.88
Likely Druggable Targets	0.81	0.71
All	0.87	0.79

a. Estimate assumes 2 iScan systems, 1 AutoLoader 2.x, 2 Tecan robots, and a 5-day work week.

Table 2: Preliminary Marker Information for Infinium DrugDev Consortium Array

Marker Categories	Number of Markers	
Whole-Genome Tag SNPs	250,421	
Indel/Exome/CNV Detection	> 20,000	
Drug Target Validation and Response Module	199,150	
Exonic Markers	78,125	
Sex Chromosomes	X 8107	Y 1943
X Chromosome Markers	8107	
Mitochondrial Markers	267	
Fingerprint SNPs	93	
Ancestry Informative Markers	800	

Table 3: Preliminary Coverage for Infinium DrugDev Consortium Array

Feature	Markers	Markers per Gene (Average)
ADME Genes	22,332	76
Drug Targets	96,459	80
Druggable Targets	48,700	67
Likely Druggable Targets	64,580	25
All	230,036	49

Table 4: Drug Target Validation and Response Module Content for Infinium DrugDev Consortium Array

Feature	Number of Genes
ADME Genes	289
Drug Targets (targets of approved drugs or those in clinical development)	1137
Druggable Targets (targets of drug-like compounds or closely related to drug targets)	680
Likely Druggable Targets (extracellular proteins or members of drug-target families)	2370
All (all genes from above categories)	4476

Table 5: Applications of Infinium DrugDev Consortium Array

Application	Examples
Drug Target Discovery	Identifying druggable proteins playing a causal role in a disease of interest
Drug Target Validation and Prioritization	Informing if and when to advance an existing drug or drug-like compound through a drug development pipeline
Drug Indication Studies	Identifying new indications for an existing drug by determining the role of a drug target in a different disease from the current drug indication (repurposing)
Drug Specificity Studies	Separating on- vs. off-target effects for both first-in-class and fast-follower drugs
Stratified Medicine Studies	Determining patient subgroups, based on risk and response, for randomized trials or nonrandomized research studies

Table 6: Comparative Features of Whole-Genome Arrays

Infinium Genotyping Array	Number of SNPs Within 5 kb of RefSeq Genes	Number of SNPs Within 5 kb of Druggable Genes	Average Number of SNPs per Druggable Gene	% SNPs (MAF ≥ 1%) in Druggable Genes Covered at $r^2 \geq 0.8$	% SNPs (MAF ≥ 5%) in Druggable Genes Covered at $r^2 \geq 0.8$
DrugDev Consortium Array	335,410	230,036	48.9	0.793	0.870
OmniExpress-24	373,682	115,664	23.1	0.600	0.747
OncoChip	260,740	79,292	16	0.492	0.613
HumanExome-12	237,121	69,203	14.6	0.099	0.115

Reference

1. www.ebi.ac.uk/chembl Accessed 14 June 2015.

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