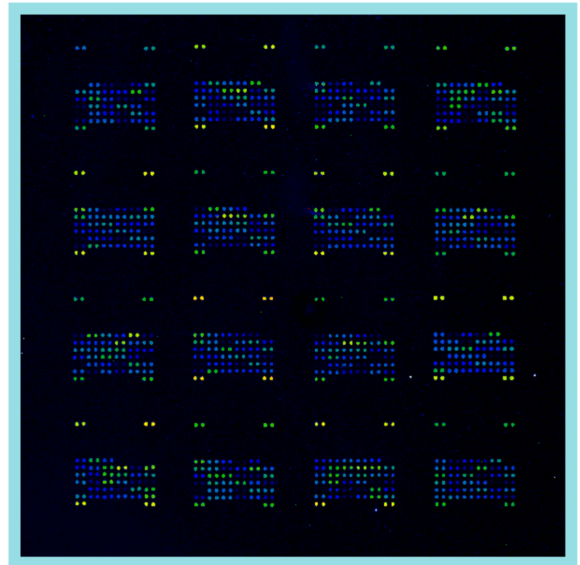
PROGENIKA

DRUGCHIP®
Drug Metabolism DNA Array

July 2006, Drugchip v.1.4

The Objective

Interindividual differences in response to drug are based on factors like age, sex, disease, drug-drug interactions... but also on genetic features.
Adverse drug reactions (ADRs) are significant health problems that contribute to patient morbidity and mortality. There are many different types of ADRs, affecting every organ system in the body. Identification of pharmacogenetic factors influencing drug response is a promising strategy in the search for predictors of response to drugs. For example, several single nucleotide polymorphisms (SNPs) have been associated with increased/decreased activity of enzymes involved in drug metabolism.
Drugchip DNA array is a pharmacogenetic tool for genotyping of SNPs involved in regulation of drug metabolism. This glass-based oligonucleotide-array interrogates variations belonging to phase I enzymes (cytochrome P450s), phase II enzymes (NAT...), drug transporters, neurotransmitter receptors....
Drugchip DNA array allows accurate, rapid and cost-effective screening for 90 SNPs enabling a better assessment of the risk of suffering adverse drug reactions or no response to the pharmacological treatment.
In addition, Drugchip DNA array is a flexible tool which can be updated if new SNPs are described to be significantly associated to ADRs.



METHODS

Oligonucleotide design

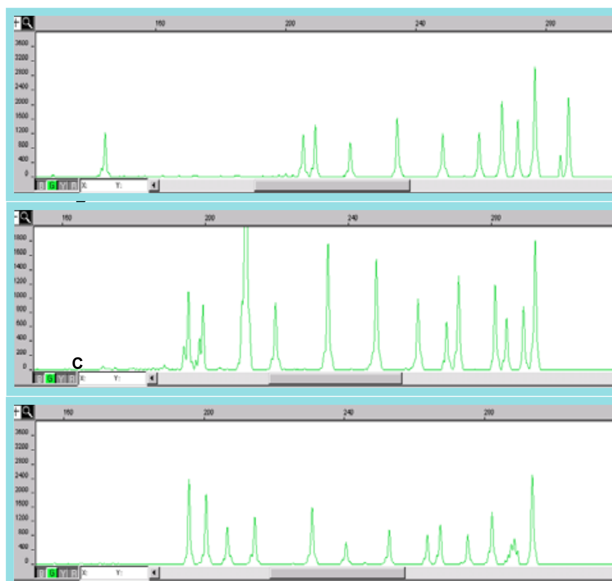
Progenika's genotyping methodology is based on allele-specific oligonucleotide probes printed onto glass supports. The length of the oligonucleotides ranges from 19 to 27 nt with the target polymorphic nucleotide located in the central position of the oligonucleotide in order to maximize hybridization specificity.

DNA array design, fabrication and quality controls

Several replicates of each oligonucleotide probe are spotted onto glass slides using a robotic microarrayer. Positive and negative hybridization controls are also printed. Control DNA is used to evaluate the quality of the process in terms of hybridization signal, background signal, specificity, sensitivity, reproducibility of each probe replicate, as well as the size and shape of the oligonucleotide features.

Target-DNA preparation and hybridization

Target DNA for hybridization is prepared in six independent multiplex PCR reactions (A, B, C, D, E and apoE) allowing amplification of 66 PCR fragments to analyze 90 SNPs. Following amplification, the PCR products are fragmentated and terminal transferase is used to catalyse the addition of biotin-labeled dNTPs to the 3' OH ends of the double stranded DNA fragments. Finally, the biotinylated amplicons are hybridized to the array in an automated hybridization station and stained with Cy3 conjugated streptavidin.



Data analysis and genotyping software

After scanning and quantifying the hybridization signals from the array, the export file from the scanner is processed by Progenika's propietary genotyping software (MG v1.0).

VERIFICATION

Specificity and sensitivity

The specificity and sensitivity of the DNA-array are tested with DNA samples in which the SNPs to be tested have been previously identified by nucleotide sequence analysis. The overall specificity and sensitivity coefficients for all the tested SNPs are 99,7% and 99,9%, respectively. For each SNP, homozygous AA subjects, heterozygous AB patients and homozygous BB patients clustered perfectly in three groups when the signal intensity of the specific probes for the A allele and the specific probes for the B allele were plotted on a xy scatter plot.

ORDERING INFORMATION:

Ordering information, please contact: /www.progenika.com/
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