RANDOX
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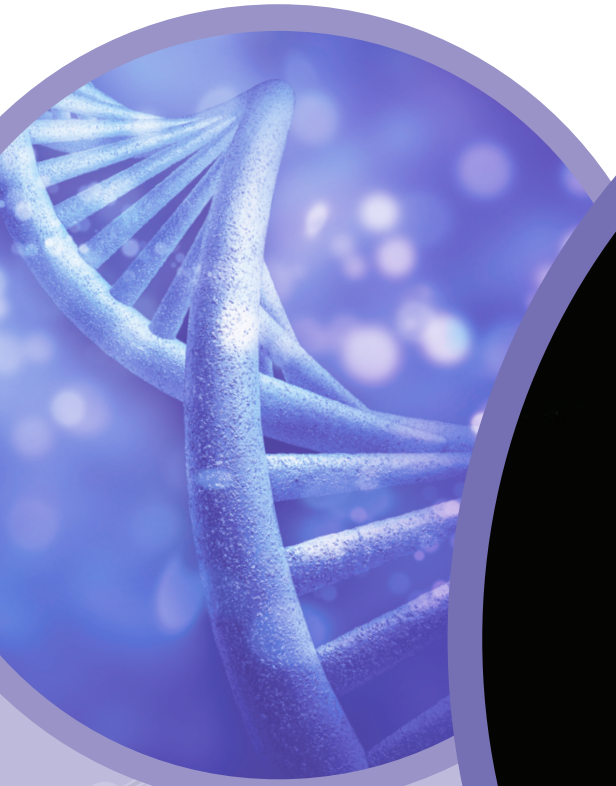
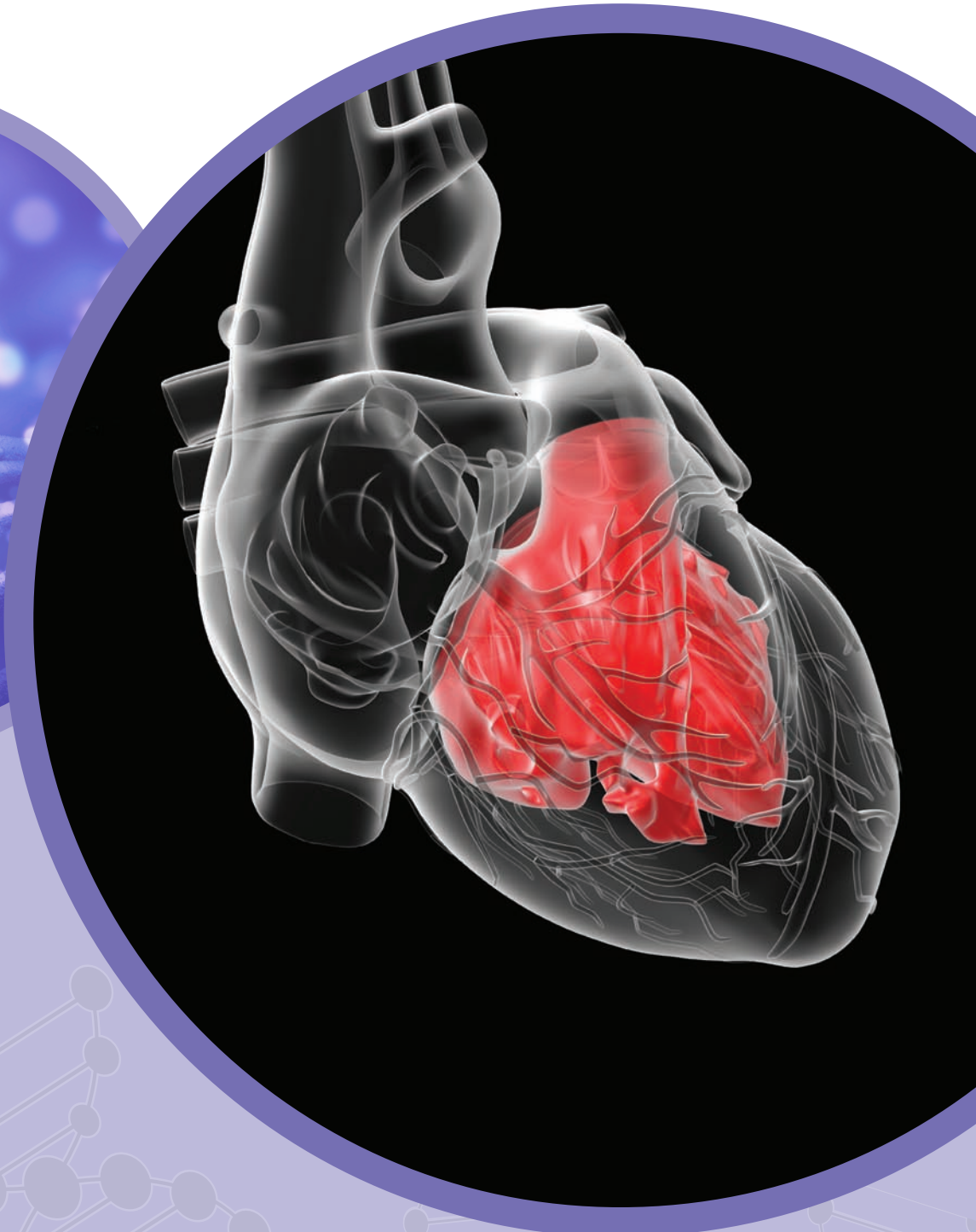
Cardiac Risk Prediction Array

Comprehensive genetic risk assessment for CHD





Cardiac Risk Prediction Array

Simultaneous genotyping of 19 SNPs for a reliable CHD risk assessment

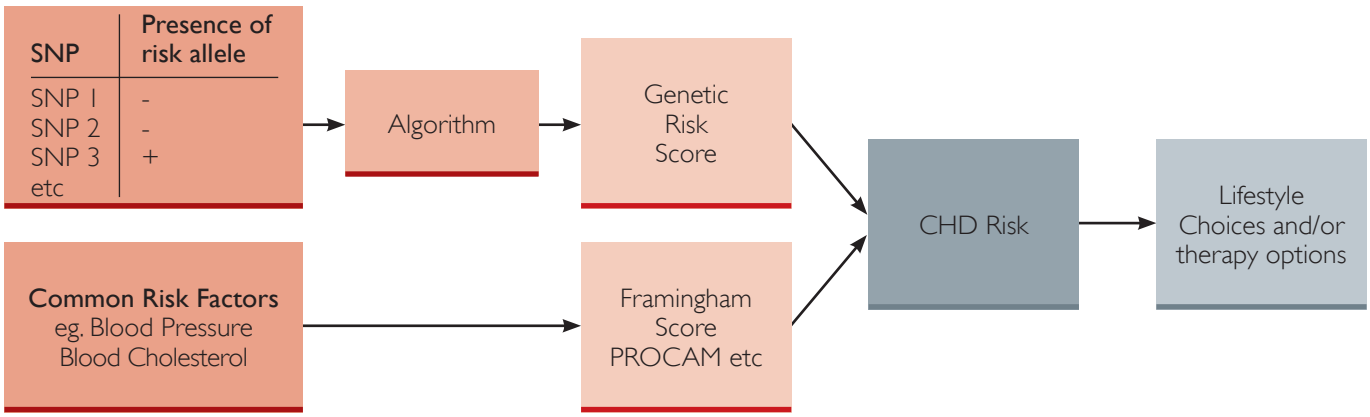
Introduction

Coronary Heart Disease (CHD) is the leading cause of death in the developed world and its prevention is a core activity in general practice worldwide. For example, clinical guidelines from the Joint Cardiac Societies and NICE in the UK recommend that patients at greater than 20% risk of CHD in the next ten years should be classified as high risk and considered for intensive lifestyle intervention and lipid lowering therapy,1 primarily the prescription of statins.

Current CHD risk assessment tools based on common risk factors such as blood pressure and blood cholesterol levels (eg. PROCAM and Framingham) have low predictive value2,3,4,5 and take no account of genetic predisposition to CHD. Cooper et al reported only 14% of CHD events during a ten year period were predicted by these algorithmic tools.[6]

In recent years Genome Wide Association Studies (GWAS) have been carried out to identify genetic variants associated with CHD. This involves comparing millions of loci in the genomes of a population suffering from CHD and a control population. Meta-analysis of such studies has identified 19 variants (referred to as single nucleotide polymorphisms (SNPs)) as being associated with CHD. Individually, the presence of an "at risk" variant does not greatly increase the risk of developing CHD. However, the presence of multiple "at risk" alleles can increase the risk of developing CHD two-fold or greater,7 an effect similar to being a current smoker. Combining such genotype information with common risk factors could allow individuals to be more accurately classified7 and preventative therapies and lifestyle advice targeted to those who require it most.

CHD Risk Prediction



The Cardiac Risk Prediction Array

In order to utilise the GWAS findings in a clinical setting, individuals require to be genotyped for each of the 19 CHD "at risk" SNPs. At present this can be a time consuming and expensive process. Together with key opinion leaders in cardiovascular genetics, Randox has developed a rapid array which will allow all 19 SNPs to be genotyped simultaneously. Firstly, a multiplex PCR reaction is performed, where the products amplified correspond to the genotype of the patient sample. The PCR products are then hybridised onto the Cardiac Risk Prediction biochip array and imaged using the Evidence Investigator analyser to identify which PCR products are present. Thus a patient sample can be genotyped within one day. The genotype information is then put into an algorithm which weights each SNP and calculates a CHD genetic risk score. The CHD genetic risk score is combined with common risk factors and an overall CHD risk score is calculated.

Response to statin treatment

A further important SNP which can predict response to particular statin therapies has been included in the array. Individuals who are homozygous (frequency =0.13) for the risk allele are 17 times more likely to suffer from statin-induced myopathy when treated with high doses of simvastatin.8 Identifying patients with a higher risk of suffering statin-induced myopathy would allow clinicians to make more informed decisions when prescribing lipid lowering therapies.

Cardiac Risk Prediction Array Protocol

Benefits of the Cardiac Risk Prediction Array

To the patient

- Randox Cardiac Risk Prediction Array is a rapid simple method for reliable genetic risk assessment of CHD
- Combined with common risk factors, the array allows more accurate classification and preventative actions to be taken
- Identifies patients genetically predisposed to statin-induced myopathy

To the laboratory

- All 19 SNPs can be genotyped simultaneously
- Simple and rapid protocol allows a patient sample to be genotyped in one day
- Streamlined workflow – protocol and reagents optimised for the molecular laboratory
- 36 patient samples can be processed per kit
- Easy to interpret results using Randox Evidence Investigator dedicated software

Evidence Investigator

Multiplexing...proven, perfected, evolved

The Evidence Investigator is a semi-automated, benchtop biochip analyser which offers complete patient profiling.

Save time and costs
Multiplexing reduces time, labour and reagents associated with multiple individual tests

Increase throughput
For greater laboratory efficiency

Consolidation
Of immunoassays and molecular diagnostics, improving laboratory efficiency

Result traceability
Chain of custody features and bar coded reagents

No hidden costs
Package includes imaging module, PC and imaging software, thermoshaker, biochip carrier handling tray and barcode scanner

Ease of operation
Straightforward testing procedure, ready-to-use biochips and minimal sample handling

Extensive QC
Internal quality controls ensure all key assay steps have been performed correctly i.e. amplification

Retrospective reporting
Enabling additional analysis of previously captured sample data

Ordering Details

Description	Size	Cat. No.
Cardiac Risk Prediction Array	72 Biochips	EV3836A & EV3836B
Evidence Investigator Analyser		EV3602

*Note: Extraction reagents are not included

References
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2. Assmann, G., Cullen, P. & Schulte, H. Simple scoring scheme for calculating the risk of acute coronary events based on the 10-year follow-up of the prospective cardiovascular Munster (PROCAM) Study. Circulation 2002;105, 310–315.
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4. Haq IU, Ramsay LE, Wallis EJ, Isles CG, Jackson PR. Population implication of lipid lowering for prevention of coronary heart disease: data from the 1995 Scottish health survey. Heart 2001;86: 289-95.
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