

# Metabolic Syndrome Arrays

Simultaneous determination of analytes associated with  
Metabolic Syndrome and related disorders  
for improved patient profiling



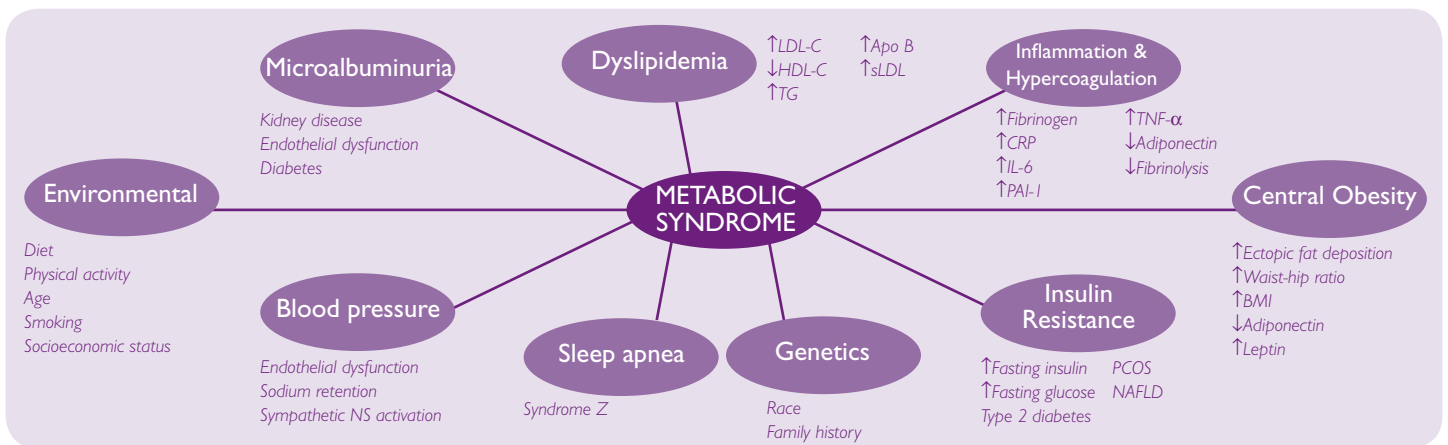


# Metabolic Syndrome Arrays in Clinical Research

## Metabolic Syndrome

Metabolic Syndrome is a clustering of cardiovascular risk factors and with approximately 20-25% of adults affected, it is highly prevalent. It is estimated that having Metabolic Syndrome leads to a person being three times more likely to have a stroke or heart attack and five times more likely to develop diabetes. However, the pathophysiological processes leading to Metabolic Syndrome remain unclear, with no universally accepted definition.

Metabolic Syndrome has been defined by various different expert groups and associations, each using different sets of criteria, that reflect the contrasting views on the pathological mechanisms and clinical application.



## IDF Metabolic Syndrome worldwide definition

The IDF (International Diabetes Federation) has proposed a metabolic syndrome definition for worldwide application.

<b>Must have</b>	
<b>Central obesity</b>	Increased waist circumference* (ethnicity specific)
<b>Plus must have two of the following four factors</b>	
<b>Raised triglycerides</b>	≥150 mg/dL (1.7 nmol/L) or specific treatment for this abnormality
<b>Reduced HDL cholesterol</b>	<40 mg/dL (1.03 nmol/L) for men <50 mg/dL (1.29 nmol/L) for women or specific treatment for this abnormality
<b>Raised blood pressure</b>	Systolic BP ≥130 or diastolic BP ≥85 mm Hg or treatment of previously diagnosed hypertension
<b>Raised fasting plasma glucose</b>	Fasting plasma glucose ≥100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 diabetes If above 5.6 mmol/L or 100 mg/dL, Oral Glucose Tolerance Test (OGTT) is strongly recommended but not necessary to define presence of the syndrome.

\* If BMI is >30 kg/m<sup>2</sup>, central obesity can be assumed and waist circumference does not have to be measured.

## IDF additional metabolic measurements for research

The IDF consensus group highlighted additional parameters that should be included in research studies. Some of these additional parameters can be assessed using Biochip Array Technology.

Additional Parameter	Related Analytes
Abnormal body fat distribution	Leptin and adiponectin
Insulin resistance	Insulin
Proinflammatory state	C-reactive protein (CRP) Inflammatory cytokines (e.g. TNF $\alpha$ , IL-6) Adiponectin
Prothrombotic state	PAI-I
Hormonal factors	e.g. Cortisol, DHEAS, TSH

### Metabolic Syndrome Array I

C-peptide  
Ferritin  
Interleukin-1 $\alpha$  (IL-1 $\alpha$ )  
Interleukin-6 (IL-6)  
Insulin  
Leptin  
Plasminogen Activator Inhibitor-I (PAI-I)  
Resistin  
Tumour Necrosis Factor  $\alpha$  (TNF $\alpha$ )

### Metabolic Syndrome Array II

Adiponectin  
C-reactive Protein (CRP)  
Cystatin C

## Application of Biochip Array Technology to key clinical research areas

### Metabolic Syndrome Research

- Assessment of the additional parameters suggested by the IDF consensus group.
- Identify biomarkers or a combination of biomarkers associated with the different pathological processes.
- Identify biomarkers linking metabolic syndrome with co-morbidities.
- Monitoring and comparing the effects of different treatment strategies.

### Benefits

- Multiple assays from one sample using Biochip Array Technology
- Analytes have been carefully selected for application to a wide range of clinical research studies
- Suitable for both serum and plasma samples
- Small sample volume – 100  $\mu$ l to measure all analytes on each array
- Very efficient use of highly valuable patient sample banks
- Biochips are ready to use, saving time and resources
- Semi-automated analyser requiring minimal maintenance
- Quick time to results
- Multi-analyte controls and calibrators
- Excellent assay performance
- Range of associated arrays available for comprehensive studies
- No non-specific aggregation, which is associated with multi-analyte bead assays

### Other Research Areas

- Eating disorders – anorexia nervosa, bulimia nervosa
- Refeeding syndrome

### Co-morbidities of Metabolic Syndrome:

- Cardiomyopathy
- Coronary heart disease
- Atherogenic dyslipidemia
- Peripheral and cerebrovascular disease
- Calcific aortic valvular disease
- Type 2 diabetes
- Polycystic Ovary Syndrome (PCOS)
- Non-alcoholic fatty liver disease (NAFLD)
- Cognitive impairment
- Cancer
- Chronic Kidney Disease
- Mental health conditions

## Sample Volume Comparison - Biochip Array Technology vs Standard ELISA Tests

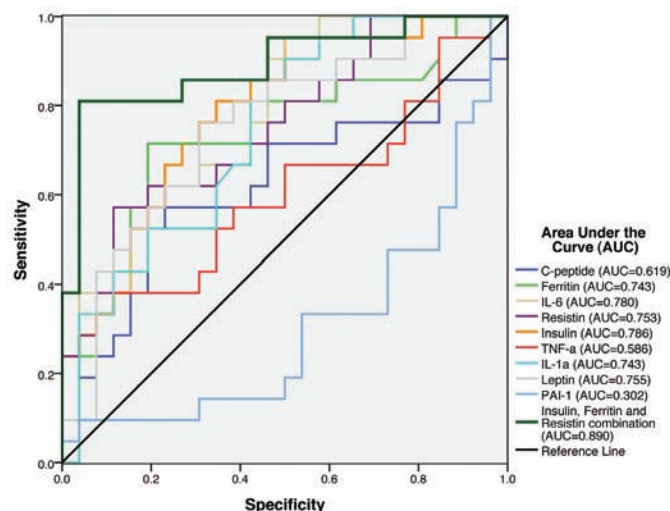
Test Format	Test Details	Total Number of Test Kits	Total Number of Different Analytes	Total Volume of Sample
Multi-analytical profiling using Biochip Array Technology	Metabolic Syndrome Arrays I and II + complementary arrays	15	75	1.22 ml
Single analyte	Individual ELISAs	75	75	7.5 ml*

\* Approximate average sample volume for ELISA analysis was estimated at 100  $\mu$ l

## Research Study on Type 2 Diabetes using Metabolic Syndrome Array I

- In a recent internal exploratory study, serum samples from Type 2 diabetics and non-diabetic controls were analysed using the Metabolic Syndrome Array I (MetS I).
- The study aimed to determine if the serum concentration distributions for the nine analytes in the array were statistically different between the diabetes group and the control group.
- Serum samples from 21 type 2 diabetic patients and 26 controls were analysed using the non-parametric Mann Whitney test. A 99% confidence limit was applied. Receiver Operator Characteristics (ROC) curves were also constructed for all 9 analytes.

### ROC Curves



### Mann-Whitney test results

MetS I Analyte	Asymptotic Sig	MetS I Analyte	Asymptotic Sig	MetS I Analyte	Asymptotic Sig
C-peptide	0.164	Resistin	0.003	IL-1 $\alpha$	0.005
Ferritin	0.005	Insulin	0.001	Leptin	0.003
IL-6	0.001	TNF- $\alpha$	0.315	PAI-1	0.021*

■ Significant level is 0.01

\* Significant level is 0.05

### Results

- The Mann-Whitney test shows the difference in the distribution of serum concentrations for the analytes tested between the two groups. These differences were found to be statistically significant for Ferritin, IL-1 $\alpha$ , IL-6, Insulin, Leptin and Resistin. PAI-1 was within 95% confidence limits.
- ROC evaluation of single analytes indicates that Insulin has the highest diagnostic ability to predict Type 2 diabetes (AUC=0.786). However, when evaluated together with Ferritin and Resistin, the predictive diagnostic ability is increased (AUC=0.890).

### Conclusions

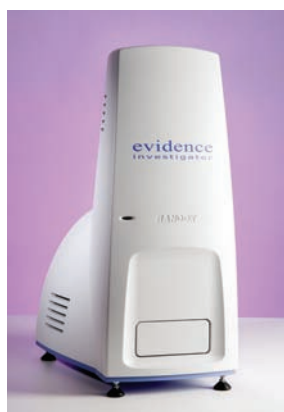
- This exploratory study shows how the serum levels of certain analytes related to Metabolic Syndrome vary between a group of diabetic patients and controls. The multi-analytical approach indicates a strong association for these analytes with Type 2 diabetes.
- This approach may be applied to other Metabolic Syndrome clinical research studies.

## Complementary Arrays available from Randox

Adhesion Molecules Array  
Cardiac Arrays

Cerebral Arrays  
Cytokine Arrays  
Endocrine Array

Fertility Hormone Array  
Thyroid Arrays



### Biochip System Evidence Investigator

- Evidence Investigator is a semi-automated bench-top analyser
- Virtually maintenance and service free
- System comes complete with all components required to run assays
- Same image time required no matter how many assays on the array
- Windows® based software
- LIMS integrated

Metabolic Syndrome Array I Cat. No. EV3755

Metabolic Syndrome Array II Cat. No. EV3759

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