



# Diagnostic Biomarker Assay

## Maturity-Onset of Diabetes of the Young (MODY)

RCSI DEVELOPING HEALTHCARE LEADERS WHO MAKE A DIFFERENCE WORLDWIDE

### Introduction

Maturity-Onset of Diabetes of the Young (MODY) is a form of non-insulin dependent diabetes that is currently known to affect 1-2% of people with diabetes. MODY typically presents in late childhood, adolescence, or early adulthood but has been known to develop in adults in their 50s. Many people with MODY are misdiagnosed as having type 1 or type 2 diabetes. MODY patients are able to control their diabetes well with sulfonylurea drugs but are often treated inappropriately with insulin injections. A number of different MODY subtypes exist and these subtypes can be characterised according to the mutated gene that gives rise to the condition.

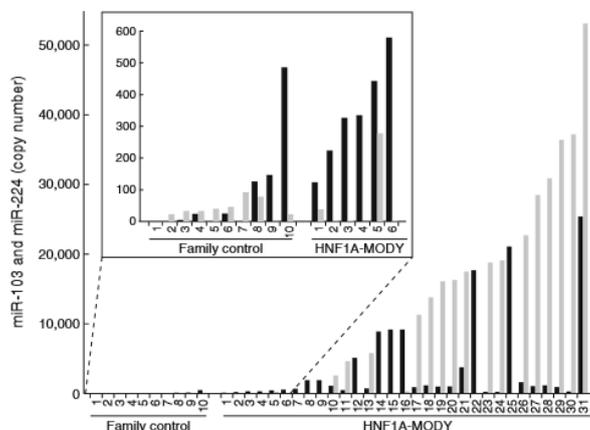
### Technology

Recognising the current practice for MODY diagnosis is sub-optimum as it often fails to separate MODY patients from early-onset Type 2 diabetic patients, a team of clinicians and research scientists at RCSI have developed and patented a highly-sensitive blood test that can identify the majority of MODY patients, namely HNF1 $\alpha$ -MODY patients. HNF1 $\alpha$ -MODY accounts for 69% MODY cases and is caused by mutations in the transcription factor 1 (tcf-1)/hepatocyte nuclear factor1a (HNF1 $\alpha$ ) gene. Analysis of microRNAs extracted from individual serum or urine from HNF1 $\alpha$ -MODY patients and age-, sex- and BMI-matched non-diabetic, MODY-negative family members led to the identification of a small number of miRNAs that were potently upregulated in the sera of HNF1 $\alpha$ -MODY patients compared to the MODY-negative controls.

### Applications

The microRNAs HNF1 $\alpha$ -MODY biomarkers identified may be used for:

- **Diagnostic purposes:** The current approach provides a highly sensitive blood or urine test (based on PCR) for HNF1 $\alpha$ -MODY.
- **Therapeutic development:** The microRNAs HNF1 $\alpha$ -MODY biomarkers identified represent novel targets for therapeutic intervention in the treatment of HNF1 $\alpha$ -MODY.



**Figure 1:** HNF1 $\alpha$ -MODY carriers show elevated serum levels of miR-103 and miR-224. miR-103 (black bars) is significantly higher in HNF1 $\alpha$ -MODY than in MODY negative family controls

### Advantages

- **Easy to implement in a clinical laboratory:** The HNF1 $\alpha$ -MODY diagnostic assay developed at RCSI uses instrumentation and skills routinely found in clinical laboratories resulting wider relevance and lower cost than “deep sequencing” based diagnostic approaches.
- **Enables the appropriate treatment delivery:** MODY patients are able to control their diabetes well with sulfonylurea drugs but are often misdiagnosed and treated inappropriately with insulin injections. The HNF1 $\alpha$ -MODY diagnostic assay provides a new sensitive blood test that enables clinicians to more accurately identify cases of MODY and deliver the most appropriate treatment and prevent chronic diabetic complications.