

# microRNAs as a Novel Biomarker for Diagnosis of Diabetes Mellitus

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## Editorial

Diagnosis of diabetes mellitus, according to the World Health Organization, is based on blood glucose levels in the fasted condition and the oral glucose tolerance test. Glucose levels above 7.0 mmol/L (126 mg/dl) in the fast state are known as diabetes and after an oral glucose tolerance test is above 11.1 mmol/L (200 mg/dl). Other serum parameters such as residual C-peptide or serum parameters such as glycated haemoglobin (HbA1c) may also help to diagnose diabetes mellitus [1].

MicroRNAs (miRNAs) are tiny 21 to 23 nucleotide non-coding RNA molecules that serve as translational repressors by partially paired with the 3'untranslated (UTR) target messenger region RNAs. These gene expression regulators were first observed in *Caenorhabditis elegans* and later invertebrates and plants. Accommodating up to 2237 mature miRNAs each with a controllability capacity of hundreds of targets, the human genome encodes more than 1600 miRNA precursors according to recent estimates. As major regulators of gene expression and key controllers of many biological and pathological processes, miRNAs are now widely recognized [2].

A collection of miRNAs is well established for pancreatic  $\beta$ -cells and insulin target tissues. Most of them are not cell-specific, but they are common throughout human tissue. An exception is miR-372, a pancreas-rich miRNA that controls the expression of genes involved in hormone secretion and mass expansion by  $\beta$  cell in reaction to insulin resistance. An important exception is miR-375. Type 1 and Type 2 diabetes mellitus (T1DM and T2DM respectively) would potentially lead to impaired tissue function in disease conditions in the miRNA expression profile of  $\beta$ -cells and insulin target tissues [3]. Indeed, the T1DM islets of pre-diabetic NOD mice contain increased miRNAs, including miR-21, -34a, -29, and -146a, which have adverse effects on  $\beta$ -cell functions. In the islets of the ob/ob, and db/db and two obesity models and T2DM, the majority are affected by the miRNAs and several others. Interestingly, these animals also have an increased expression of miR-29 and -34a in insulin target tissues, which may lead to resistance to insulin [4].

In conjunction with proteins, microvesicles, and/or lipoproteins, a variety of miRNAs are found inside the cells producing them in the blood and other body fluids.

The function of miRNAs remains to be determined but in vitro studies show that miRNAs transported by exosomes or high-density lipoprotein (HDL) can be transmitted to recipient cells in an active form.

This increases the interesting opportunity for miRNAs to engage in a new cell-to-cell mode of communication. Circulating miRNAs are very durable and immune to RNase therapy, freezing/thawing cycles, and other extreme conditions of experimentation. Therefore, the serum or plasma sample can be stored at -20°C or -80°C without major miRNA degradation for several months, indicating the robustness of these small RNA molecules is adequate to be used in the form of biomarkers.

Circulating miRNAs as potential biomarkers have a range of other advantages: they can be identified by highly sensitive and advanced PCR procedures not only in blood, but also in readily accessible organic fluids, such as urine, saliva, amniotic fluid and mother's milk, and most of which are evolutionary preserved, thereby making it possible to move the findings obtained from PCR. Besides, miRNA serum profiles of healthy donors are relatively homogeneous and stable during the day and miRNAs in serum and plasma can be measured [5].

It was first put forward for various types of cancer, autoimmune disease, and sepsis that the idea of using miRNAs as biomarkers was relatively new. The miRNA profile of serum, plasma, or blood cells has also been studied by recent studies to establish new methods for predicting diabetes development and progression. In several physiological and pathological processes, miRNAs are emerging as major regulators of gene expression and key players. Their involvement in the extremely stable extracellular fluid has resulted in their role for application in the diagnosis of several diseases using them as biomarkers.

The diabetologists who started the search for miRNAs that allow for early diagnosis of T1DM and T2DM and their related complications also drew attention to these products. Certainly, before the circulation of miRNAs will achieve diabetes biomarker status, there do need to be addressed a range of scientific and methodological issues, but the information provided indicates that they will shortly become useful new blood parameters that enable physicians to refine their treatments.

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