

# Glucose-Regulated mRNA Instability Element for Diabetes Detection

**R**esearchers at the University of South Florida have developed a potential drug screening assay for Diabetes by a novel method that detects glucose and its analogs.

Diabetes mellitus is an endocrine disorder caused by relative or total deficiency of insulin action. Abnormally high blood glucose level, also known as hyperglycemia, is the diagnostic hallmark of this disease. Various complications arise with hyperglycemia involving the cardiovascular tissue, peripheral nerves, and cells involved in wound healing. Currently, there is a great demand for simpler and more sensitive methods to accurately detect intracellular glucose cells. Recent studies indicate that excess glucose alters signal transduction pathways via activation of protein kinase C isozyme in vascular smooth muscles. Continued research by our scientists in this area has led to the discovery of a glucose-regulated mRNA instability element which has been proven to be a more direct sensor of glucose levels than other glucose-based mechanisms.

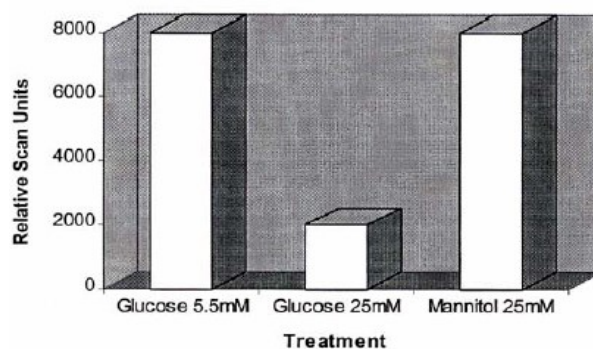
This glucose-regulated mRNA instability element has been mapped to the protein kinase C  $\beta$ II (PKC $\beta$ II) mRNA. When cloned into a reporter vector, the region of PKC $\beta$ II containing the mRNA instability element destabilizes the expression of the reporter gene when glucose levels are elevated. Therefore, the reporter mRNA level can serve as an inverse indicator of how much glucose is present in a cell. Other glucose-based mechanisms for regulating gene expression typically first require metabolism of glucose to other compounds before glucose can function as a regulator of expression. However, using the glucose-regulated mRNA instability element, glucose only has to be phosphorylated to affect mRNA instability. Thus, the element is a more direct sensor of glucose levels than other glucose-based mechanisms.

The vector can be used separately or can be transfected into insulin-sensitive cell line such as L6 skeletal cell line to perform live cell assays. In normal glucose concentrations, the reporter molecule is expressed at high levels. When glucose concentration increases (such as in diabetes mellitus), destabilization of the mRNA results in low levels of the reporter molecule. The levels can be read directly on a plate reader at 510 nm wavelength.

### ADVANTAGES:

- Intracellular glucose Sensor
- Direct glucose-based mechanisms for regulating gene expression
- Can be used to screen potential therapeutic drugs that lower blood glucose

### Direct Glucose Sensor



**FIG 1: 60-75% decrease in PKC $\beta$ (I+II) mRNA was observed under high glucose conditions**

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**Patent #: [6,852,529](#); [8,008,071](#)**