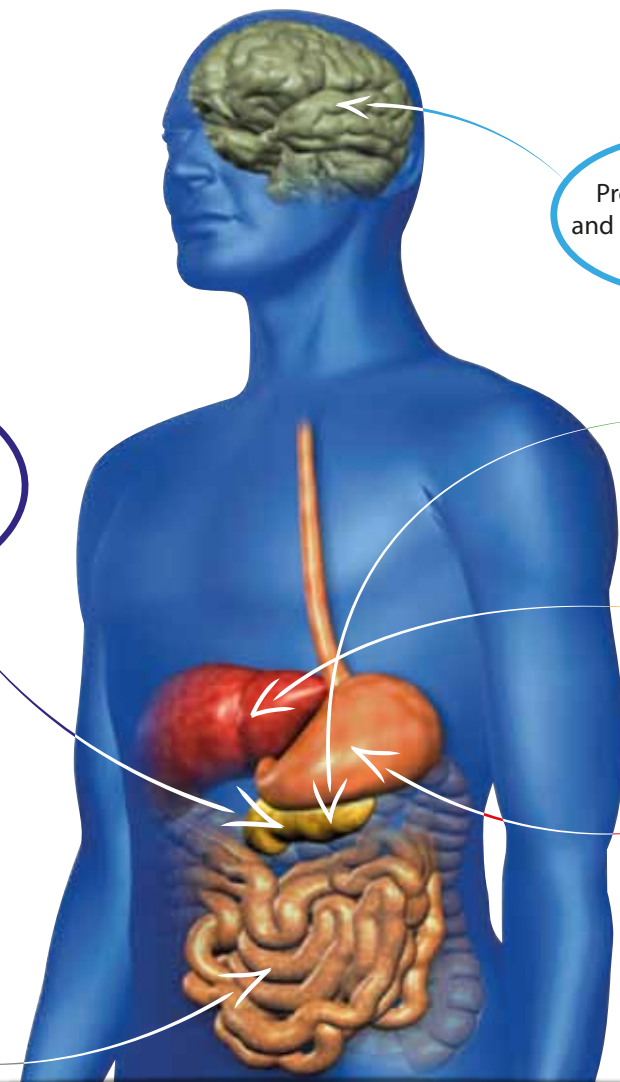




## Understanding the Natural Role of Incretins

GLP.1 (glucagon . like peptide-1)    GIP (glucose - dependent insulinotropic peptide)

incretins are gastrointestinal hormones that cause an increase in amount of insulin released from beta-cells of islets of langerhans after eating.



Promotes satiety and reduces appetite

Alpha cells: Reduced Postprandial glucagon secretion

Liver: Reduces Hepatic Glucose Output

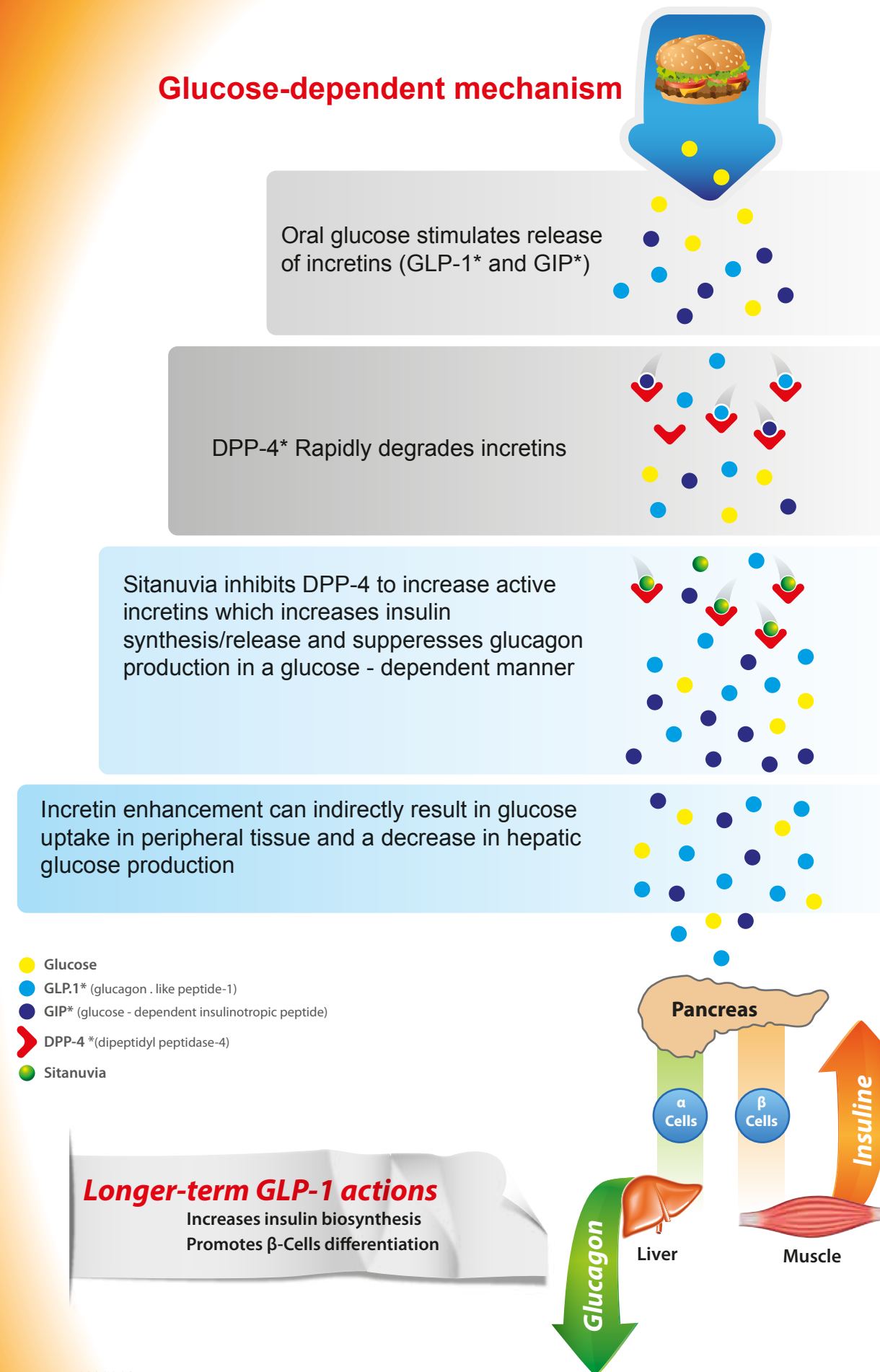
Stomach: Helps regulate gastric emptying

**Beta Cells:**  
- Enhances glucose-dependent insulin secretion.  
- Decreased apoptosis.  
- Beta Cell Regeneration.

- Incretins secreted upon ingestion of food

**Incretins levels are decreased in DM 2**

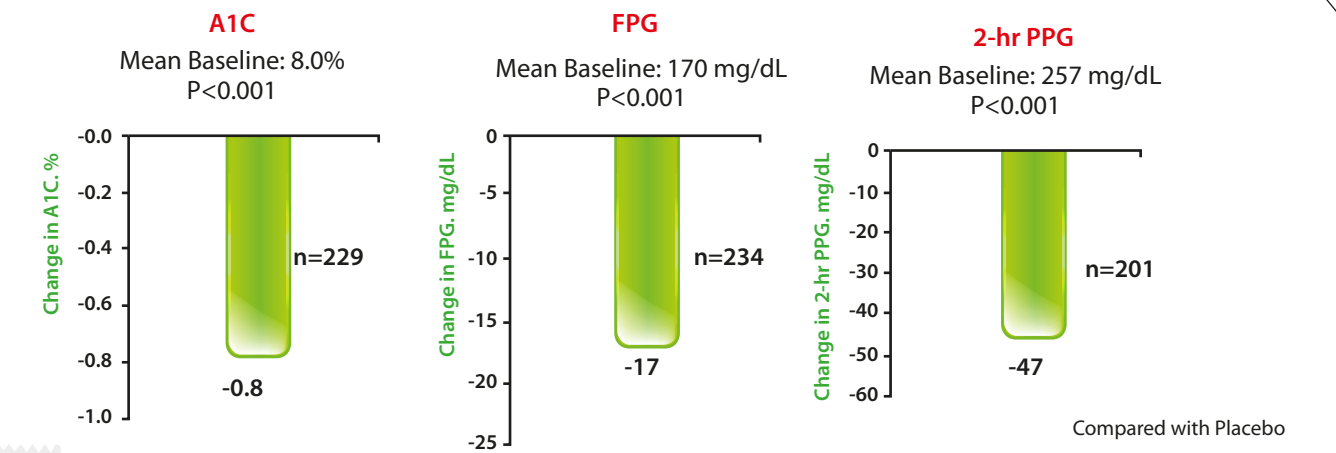
## Glucose-dependent mechanism



The duration of Sitanuvia inhibition is > 16 hours because of initial rapid binding to DPP-4, followed by a slow phase of tight binding allowing for once-daily dosing . (1)

## Sitagliptin Monotherapy Improves Glycemic Control Efficiently.

A1C, FPG, and 2-Hour PPG Placebo-Adjusted Results in a 24-Week Study of SITAGLIPTIN (2)

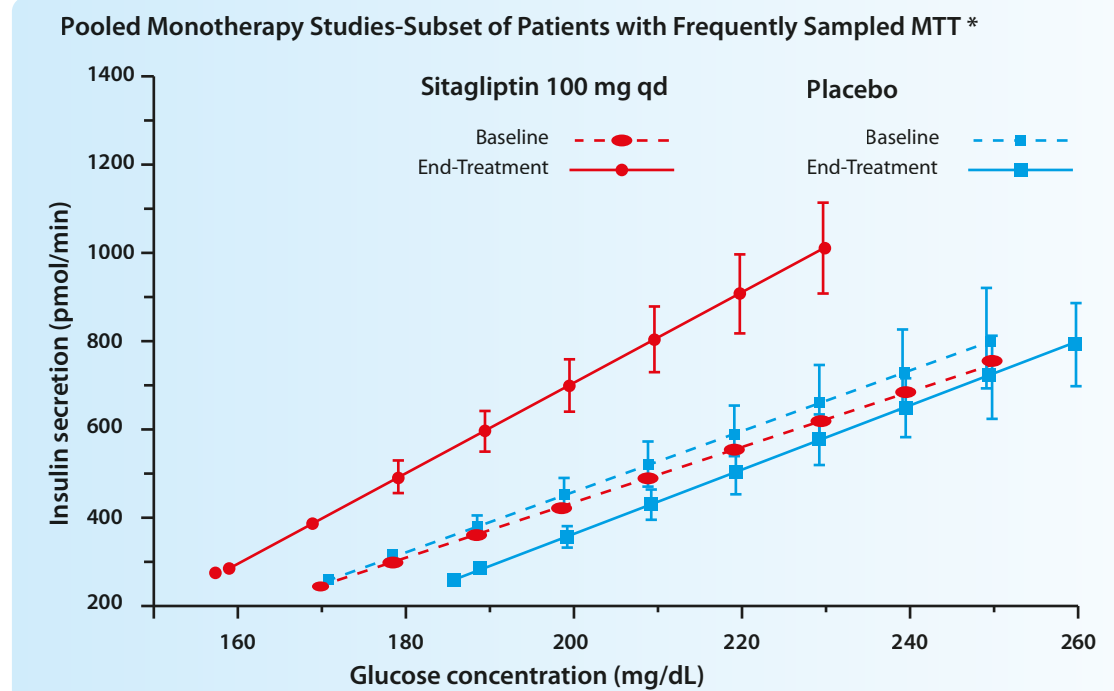


SITAGLIPTIN provided significant improvements in A1C, FPG and 2-hour PPG Compared with Placebo. A1C lowering appears to be related to the degree of A1C baseline level.



## Sitanuvia Enhances $\beta$ -cell function

Sitagliptin Improves  $\beta$ -cell Response to Glucose: Monotherapy Studies (3)



\* MTT=meal tolerance test  
Model-based assessment of  $\beta$ -cell function.