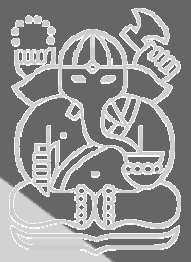
af THE ASAHI GLASS FOUNDATION

Stem cell transplantation into pancreas of diabetes rats



Marselina I Tan

Anggraini Barlian

Ahmad Ridwan

STUDENTS:

Erika

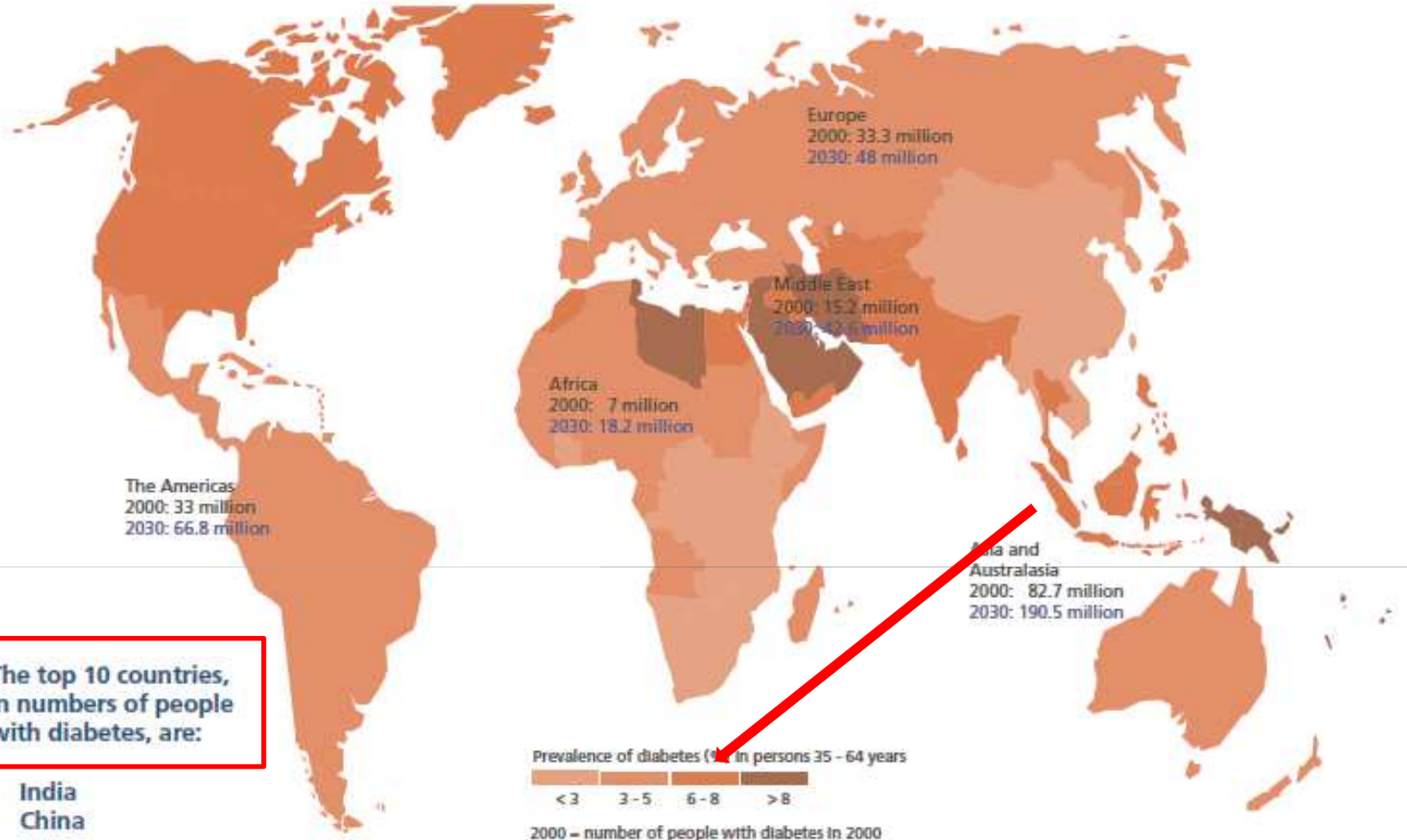
Ariananda Hariadi

Ignatia Yesie Primastuti

Outline

- Background
- Research objectives
- Result and discussion
- Summary
- Acknowledgment

Prevalence of diabetes



The top 10 countries, in numbers of people with diabetes, are:

India
China
USA
Indonesia
Japan
Pakistan
Russia
Brazil
Italy
Bangladesh

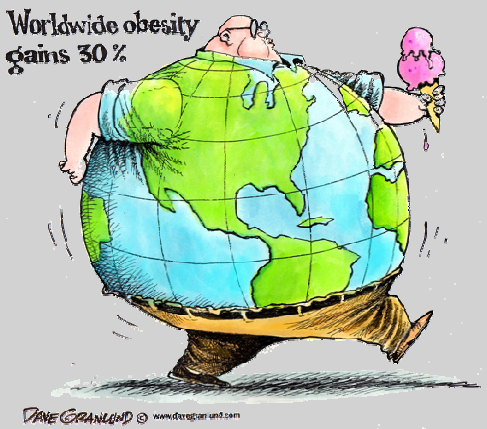
Year		2000	2030
Ranking	*Country*	*People with diabetes (millions)*	
1	India	31.7	79.4
2	China	20.8	42.3
3	United States of America	17.7	30.3
4.	**Indonesia**	**8.4**	**21.3**

The number of people with diabetes is increasing due to:

Population growth ↑

Aging

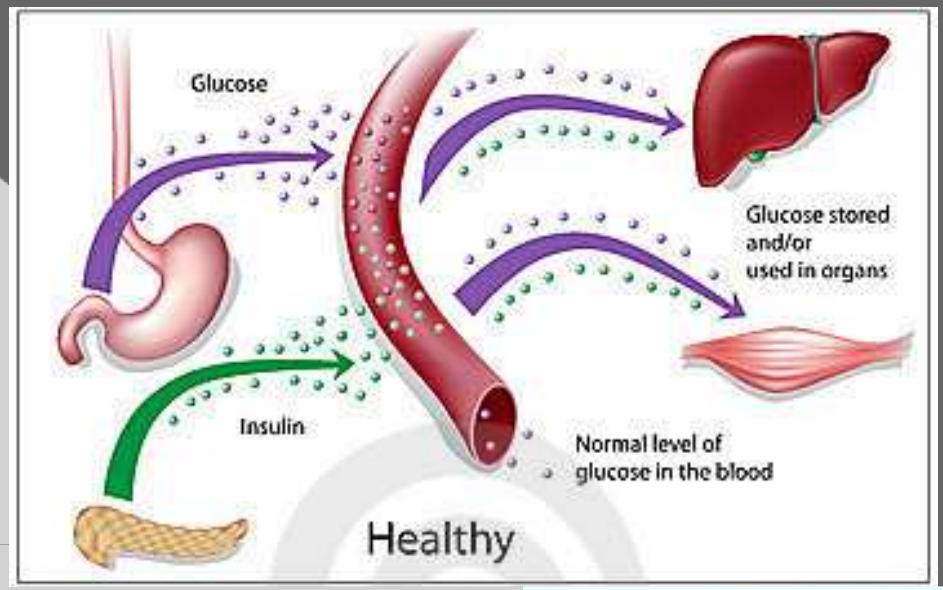
Urbanization

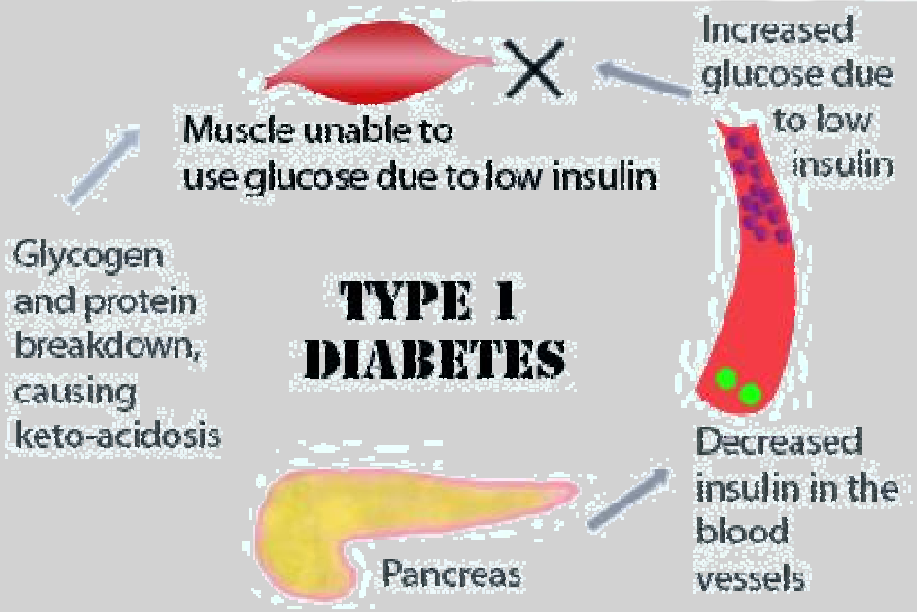


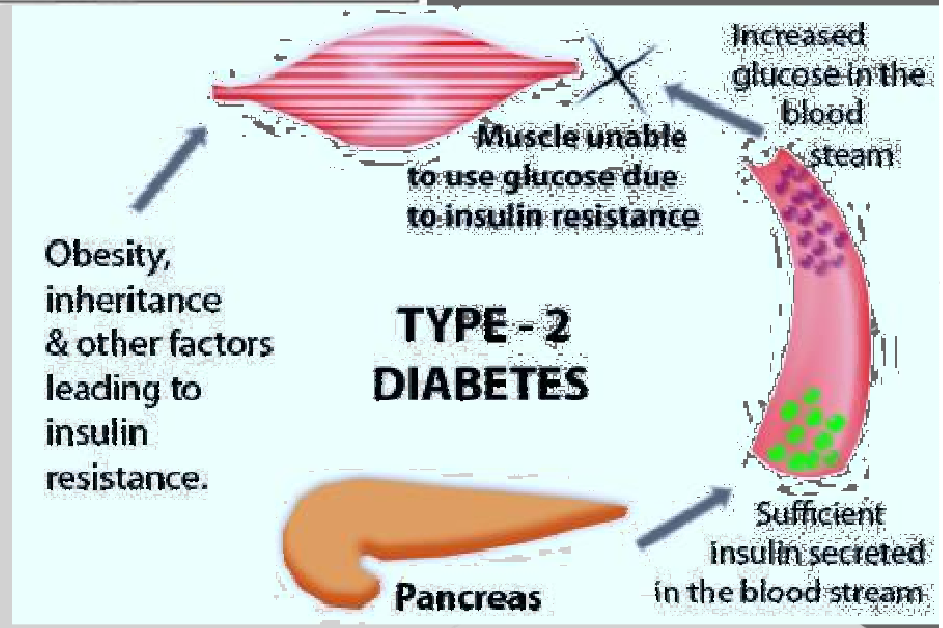
prevalence of obesity ↑

physical inactivity ↑

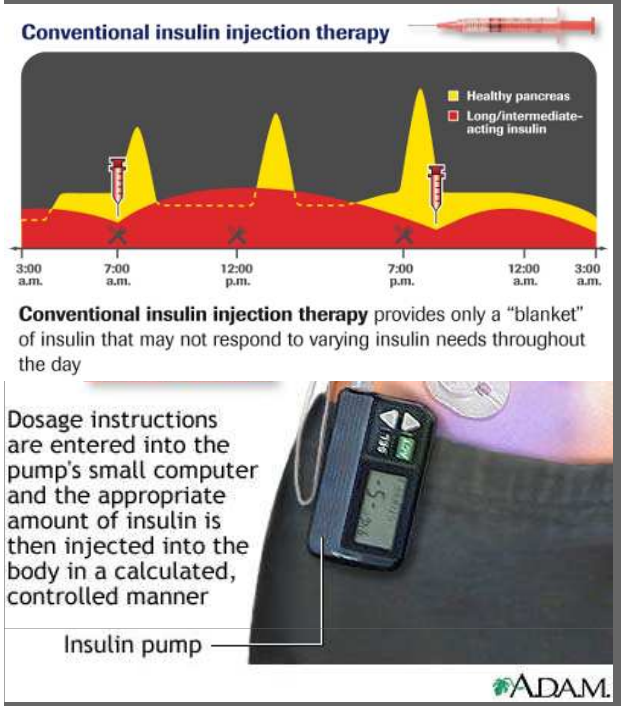
What is diabetes?



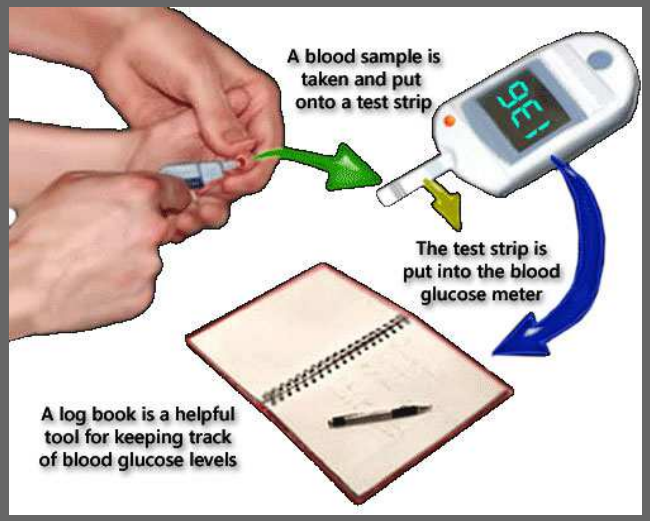




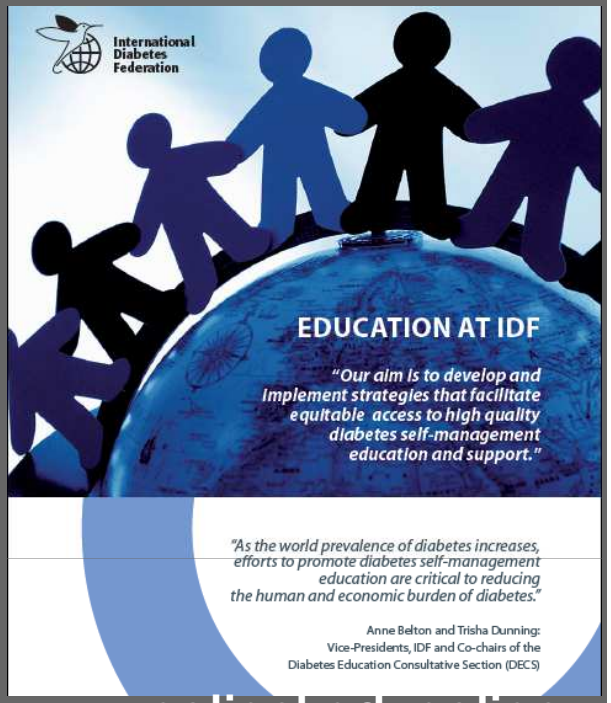
Current effective medication



Tight control of blood glucose by conventional or intensive insulin treatment



Tight control of blood glucose by self blood glucose monitoring,



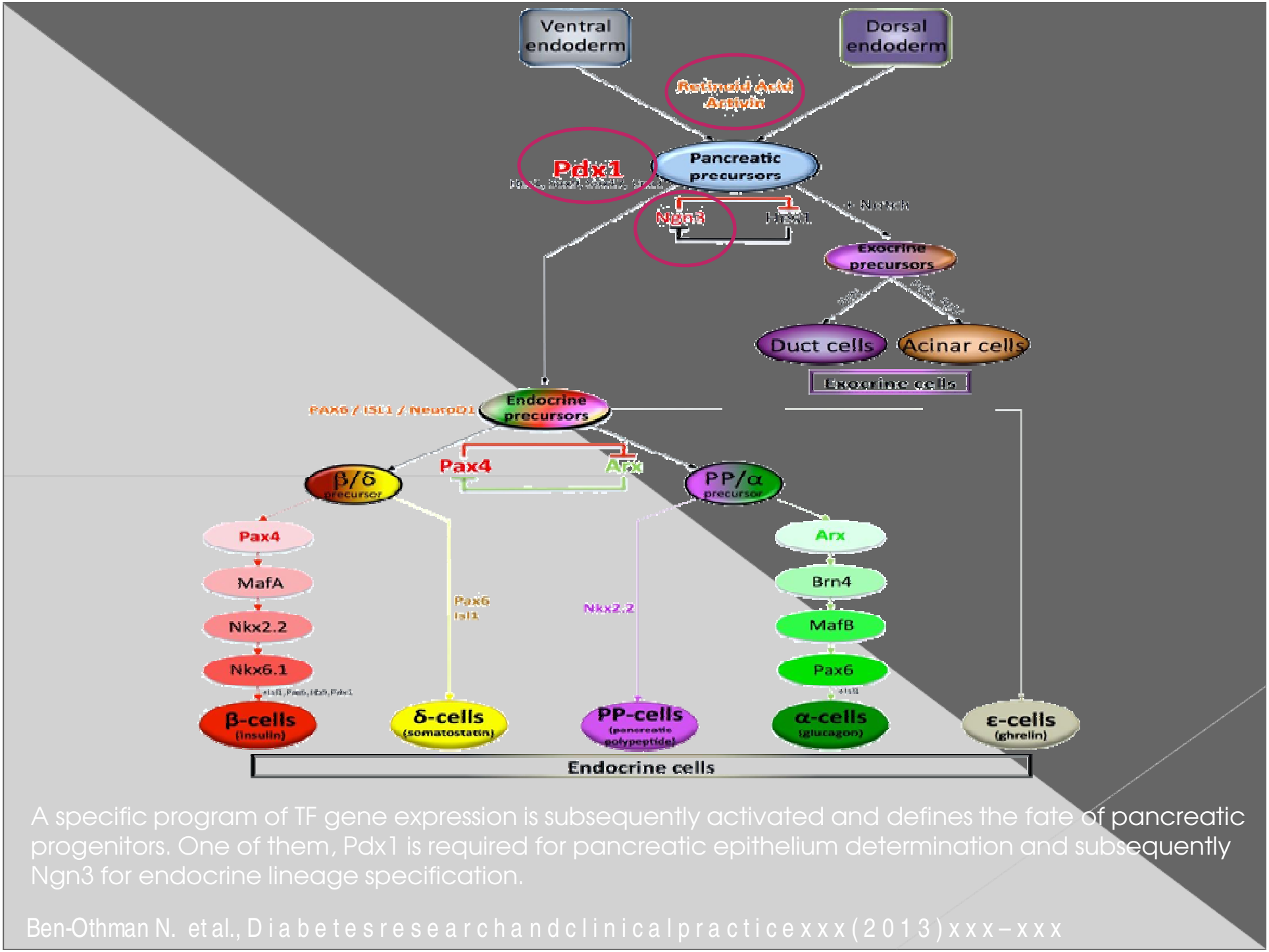
patient education

can efficiently ameliorate glycemic abnormalities, and reduce the risk of distressing [illegible] complications

However, cost of benefit : 3 x increase

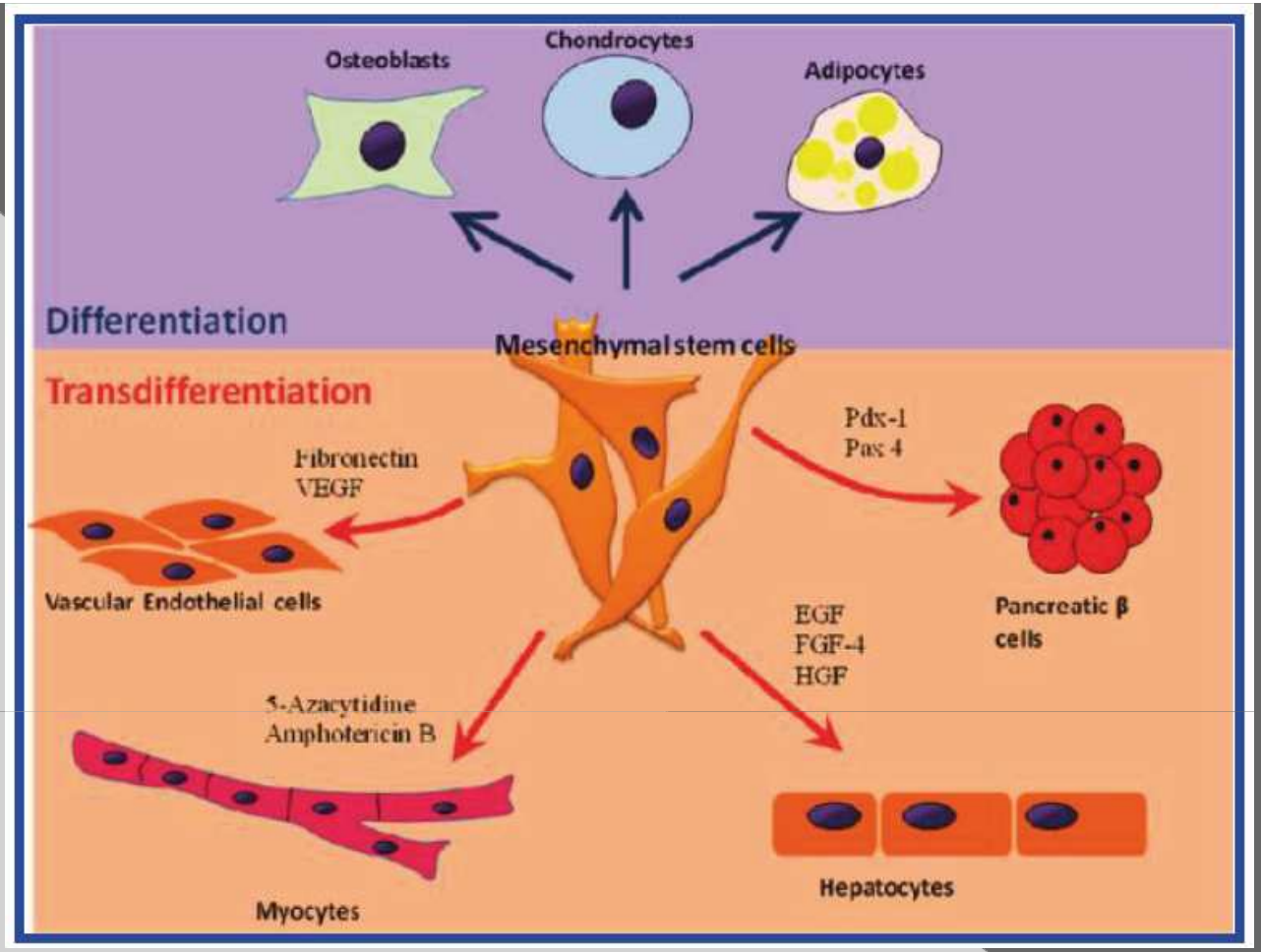
- Best strategies:
  - promote the expansion of existing beta-cells within the body

stem cell derived insulin-producing cells



A specific program of TF gene expression is subsequently activated and defines the fate of pancreatic progenitors. One of them, Pdx1 is required for pancreatic epithelium determination and subsequently Ngn3 for endocrine lineage specification.

Ben-Othman N. et al., Diabetes research and clinical practice xxx (2013) xxx–xxx



Differentiation and transdifferentiation of mesenchymal stem cells (MSCs). MSCs have three established differentiation directions: osteoblasts, chondrocytes and adipocytes. Stimulation with chemical or biological signals can induce transdifferentiation of MSCs into vascular endothelial cell, myocytes, hepatocytes, and pancreatic β cells.

Wu H, Ye Z, Mahato RI. Molecular pharmaceutics. 2011 Oct 3;8(5):1458-70.

Research Objectives

- to study bone marrow and pancreatic stem cells differentiation in the presence of retinoic acid and activin A in pancreas of diabetic rats.
- To analyze bone marrow and pancreatic stem cells differentiation in transplanted pancreas of diabetic rats ➔ levels of PDX1 and NGN3 as transcription factors in beta cells will be studied.

Methodology

Injected with aloxan 150 mg/kg BW ➔ induced diabetes

Ccontrol group: diabetes

(KD)

DMEM into pancreas

Transplant with bone marrow stem cells

(BM):

Bone marrow stem cells into pancreas

Transplant with bone marrow stem cells: treated with Retinoic acid and activin (GF)

Treated Bone marrow stem cells into pancreas

Transplant with cells from pancreas (P300 and P800):

Pancreas cells into pancreas

Normal control

(KN)

Blood sugar measuremment every 3 days n 15 days

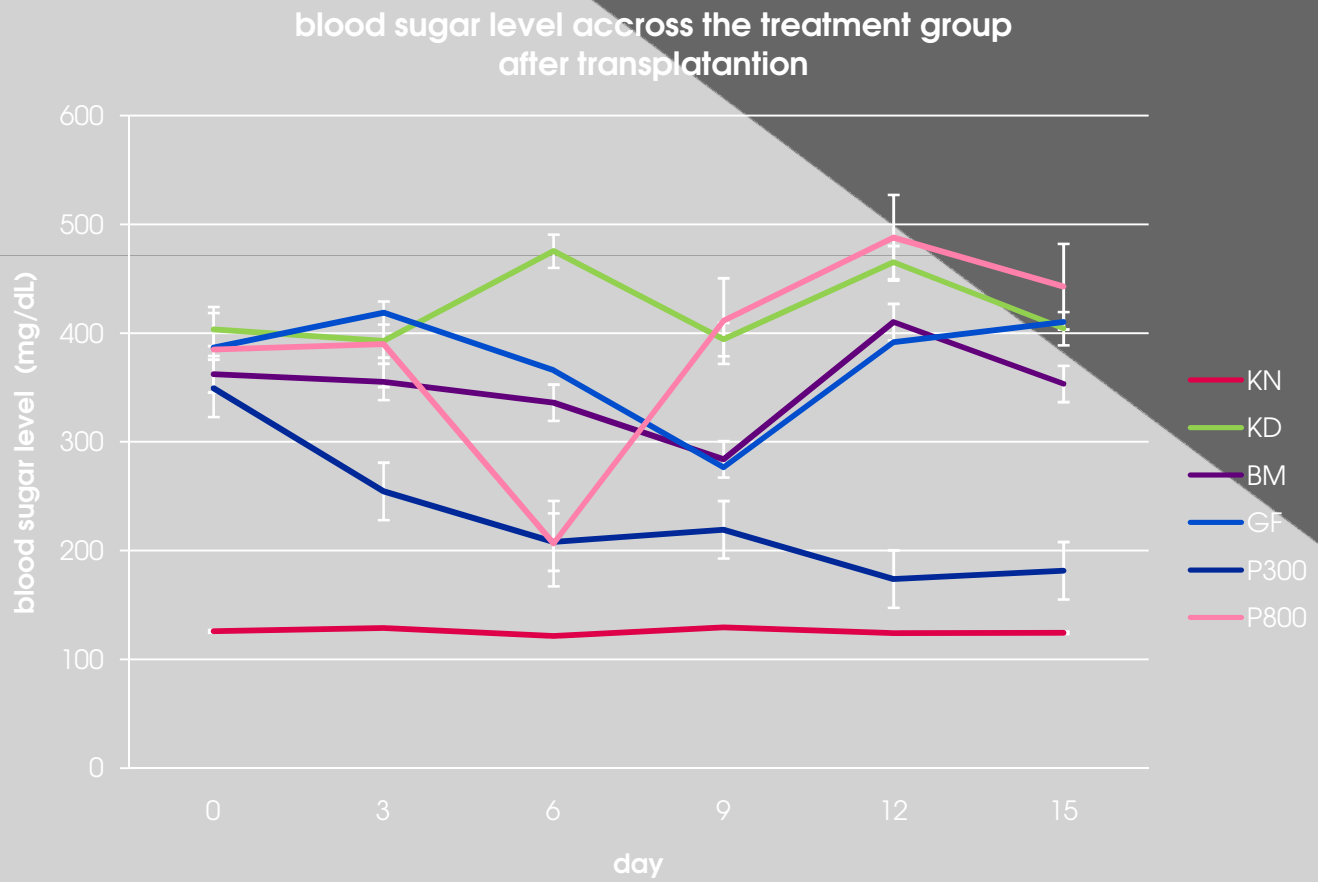
Tolerance test (OGTT) at the 16th day

Pacreas isolation

Protein isolation and westen blotting

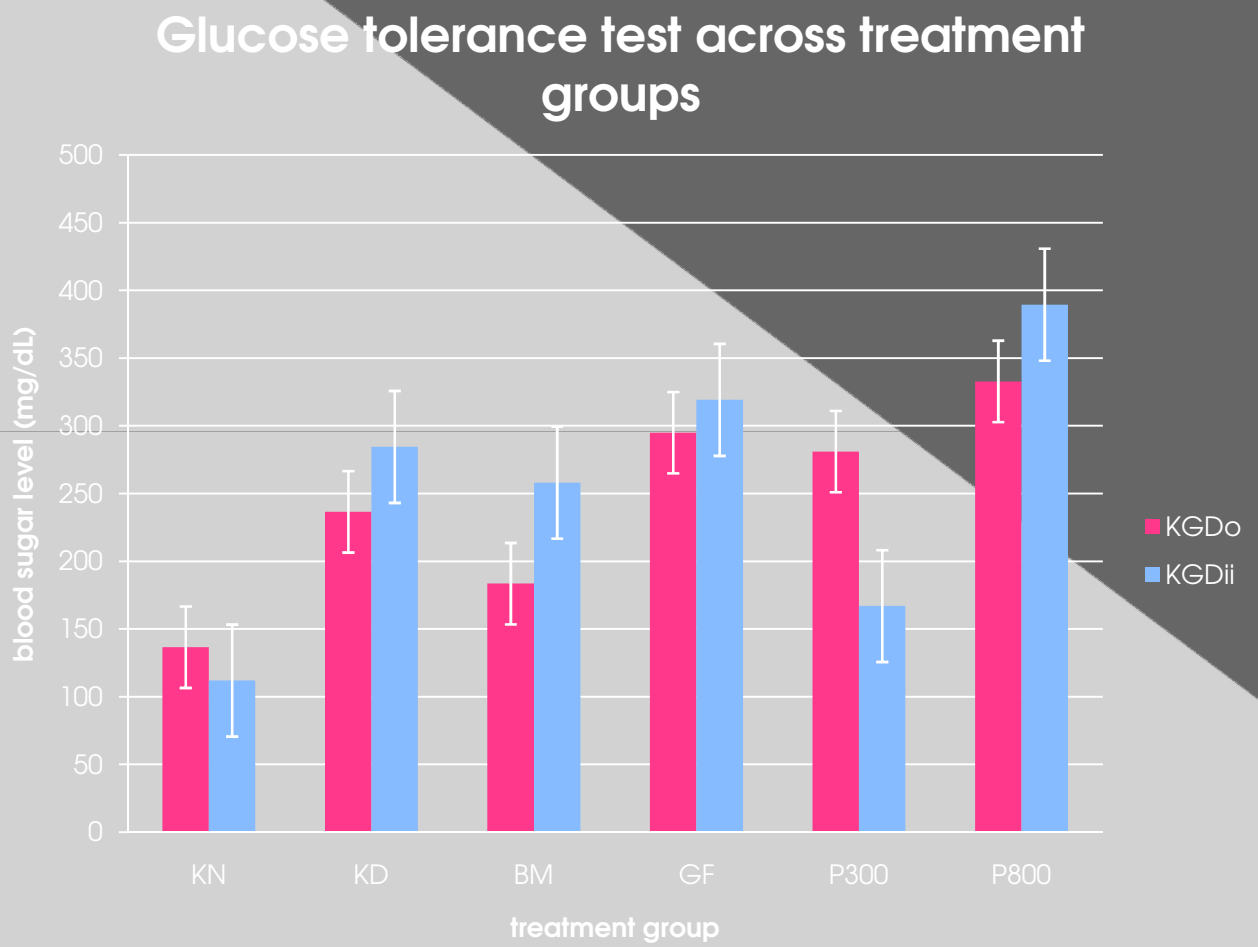
Result and discussion

- Blood sugar level after stem cells transplantion



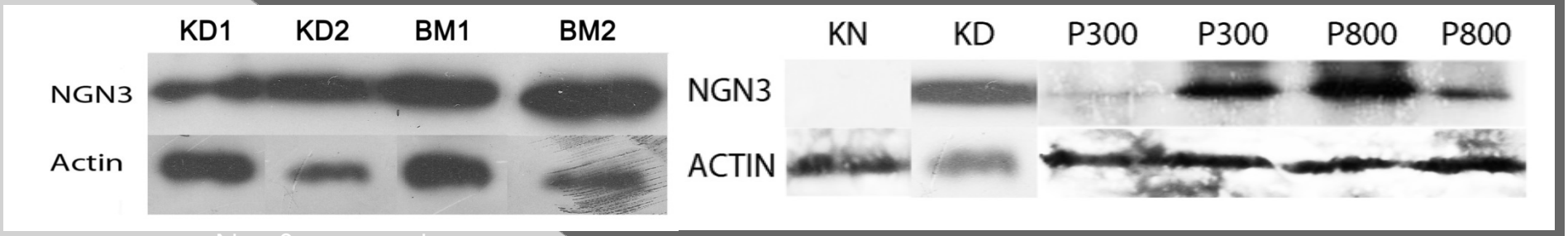
- Blood sugar level in BM group was decreased after bone marrow transplantation
- Growth factor did not increase the ability of bone marrow stem cells differentiation into β cells

Glucose tolerance test



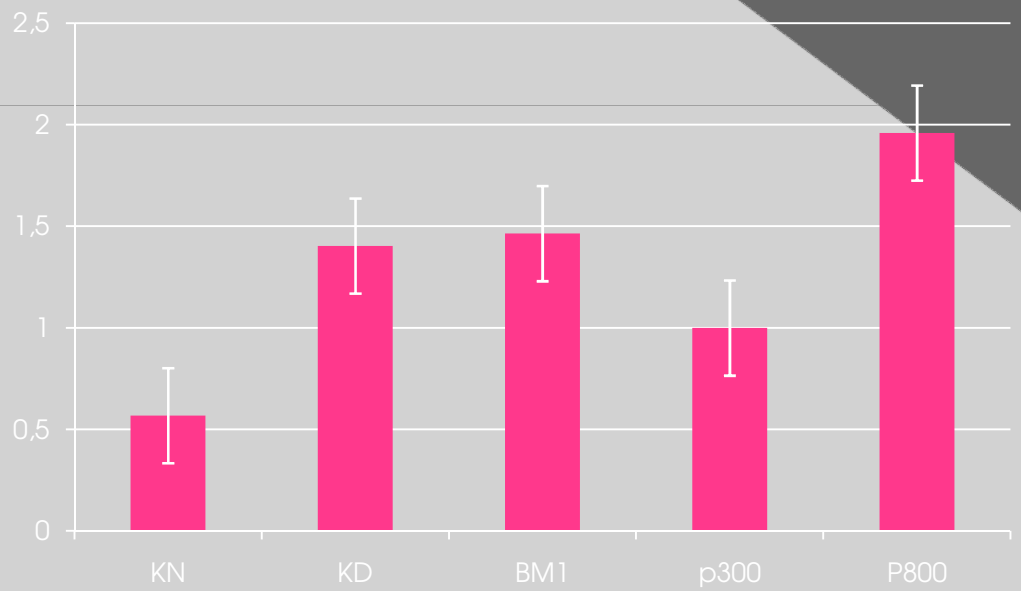
- Glucose tolerance was recovered after bone marrow transplantation
- Growth factor did not increase the ability of bone marrow stem cells differentiation into β cells

NGN3 expression



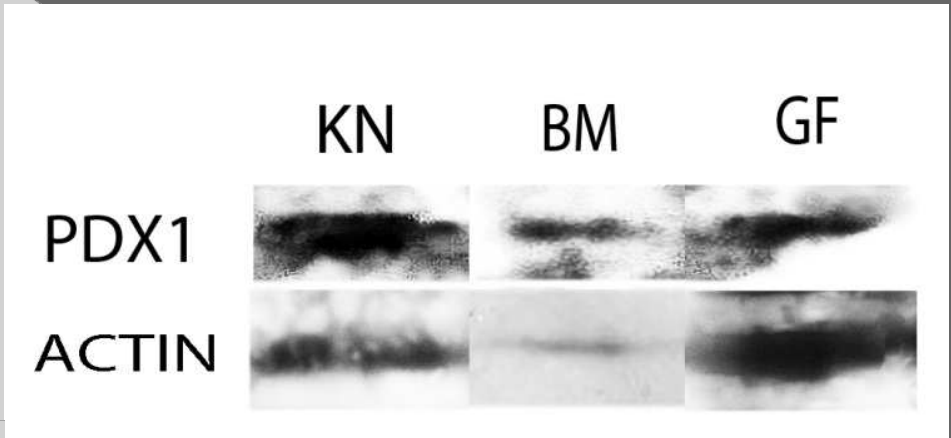
NGN3 KN KD P300 P800

Ngn3 expression

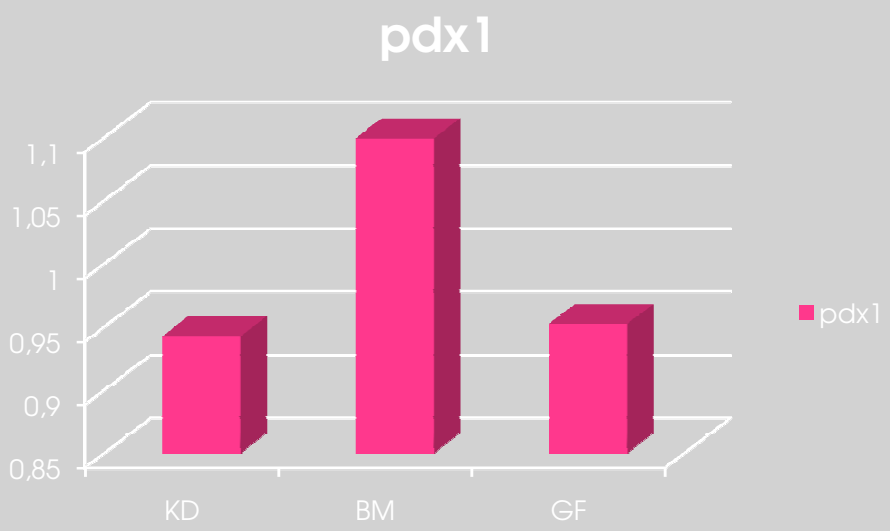


Ngn3 expression is upregulated in all stem cells treatment ➔ probably this gene is upregulated in recovery process in inflammatory condition

PDX1 expression



PDX1 KN BM GF



- Pdx1 is upregulated in the treatment group which are transplanted with bone marrow stem cells
- Growth factor did not facilitate transplanted stem cells to regulate pdx1 expression

Blood sugar level in BM group tend to reduce after transplantation

Summary

- Bone marrow transplantation tends to reduce blood sugar level and glucose tolerance in rats
- This tendency is induced by the pdx1 upregulation in transplanted pancreas

Acknowledgement

- Asahi Glass Foundation who support this research
- LPPM ITB who support this research
- SITH-ITB who help us to perform this research
- Especially thanks to my students who worked very hard for this research :