Diabetes & Metabolic Syndrome: Clinical Research & Reviews xxx (2016) xxx–xxx

Contents lists available at ScienceDirect

Diabetes & Metabolic Syndrome: Clinical Research & Reviews

journal homepage: www.elsevier.com/locate/dsx

Review

Role of pancreatic duct cell in beta cell neogenesis: A mini review study

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ARTICLE INFO

Article history:
Available online xxx

Keyword:
Beta cell
Diabetes
Hyperglycemia
Pancreatic duct cell

ABSTRACT

Today diabetes mellitus is known as main threatening for health society. Beta cells have pivotal role in energy homeostasis by balance in blood glucose. Proliferation and neogenesis are two factors for preservation of beta cell mass but these have lower rate during adulthood rather than neonatal. Beta cell destruction occurs during diabetes that leads to hyperglycemia. Continues production of beta cell is a therapeutic strategy to keep normal blood glucose and pancreatic duct cell can be one of the sources of new beta cells. Here, we reviewed the role of pancreatic duct cell in production of beta cell based on a chronological order of conducted studies.

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1. Introduction

Beta cells as the main center of blood glucose preservation at normal level have dynamic population result from the balance between production and death of cell [1]. On the other hand, the main characteristic of type 2 diabetes is hyperglycemia, which is associated with selective destruction of pancreatic beta cells [2–5]. In fact, during type 2 diabetes the rate of apoptosis is more than rate of regeneration in beta cells [6]. Therefore, therapeutic approaches that are associated with an increase in the number of beta cells can be very useful for maintaining energy metabolism in diabetic patients [7] (Fig. 1).

Although at birth beta cell proliferation and neogenesis is very active, but during adulthood, these processes perform at lower rate [8]. In the meantime, pancreatic exocrine tissue can play an important role in these processes because it can differentiates into insulin-producing cells under in vitro conditions [9]. In other words, one of the sources of beta cell production is pancreatic duct cells and it has well been known that they have the ability to convert beta cells in the postnatal period and even adulthood [10,11]. It was showed that after glucose administration, the major part of beta cell mass formed by neogenesis rather than proliferation in rats, but the persistence of this condition is associated with increase of apoptosis and eventually the imbalance between neogenesis and apoptosis lead to the reduction of serum insulin level [12]. During the early stages of diabetes (in people

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http://dx.doi.org/10.1016/j.dsx.2016.08.005
1871-4021/

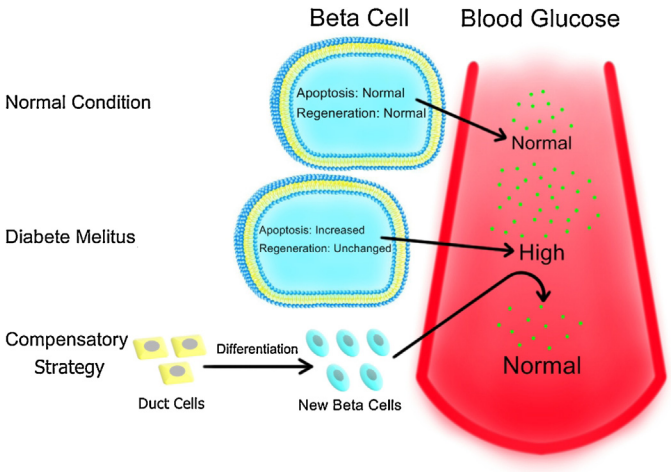

Fig. 1. Schematic plan of blood glucose normalization with compensatory strategy.

with impaired glucose tolerance) increases neogenesis rate while it is limited subsequent of disease progression [13].

Therefore, the beta cell neogenesis is a compensatory process to keep blood glucose and given that it occurs in the early stages of diabetes that peoples are not aware of their situation can be an important clue for both timely diagnosis (through determination of its stimulant in the blood) and effective treatment. Here, we reviewed the role of pancreatic duct cell as a one of the candidates for neogenesis process.

2. Review method

For better access to relevant articles, we searched keywords such as beta cell neogenesis; beta cell replication and regeneration; diabetes mellitus; duct cell and compensatory mechanisms in databases of Wiley; Scopus; Science Direct; Springer and PubMed. Then obtained papers from 1990 to now according to the year publication were classified. Indeed; our goal was evaluation of articles based on chronological order.

Table 1
Conducted studies about role of pancreatic duct cell in beta cell neogenesis.

Subject/animal/cell line	Conducted proceedings	Summary of findings	Publication year (reference)
Male wistar rats	Immunocytochemical analysis for determination expression of CKs 7, 19, and 20 in neonatal and adult pancreas	Observation growth of neonatal islets in zone related to growth ducts (peripheral mantle zone)	1994 [14]
Male wistar rats	Comparison of endocrine neogenesis between duct-ligated tail portion and non-ligated head portion by immunocytochemistry and morphometry assays	Confirmation of beta and alpha cell neogenesis after partial pancreatic duct ligation	1995 [15]
Syrian golden hamster	Identification of affect factors on islet cell neogenesis in partial duct obstruction model	Introduction of INGAP as a probably factor related to beta cell neogenesis	1998 [16]
Pancreas prepared from four diabetic men with ACP	Evaluation of morphological immunohistochemical and morphometrical changes and tracing beta cell neogenesis in pancreas during diabetes with ACP	Confirmation of pathological changes in pancreas and also observation of beta cell neogenesis from duct cells	2001 [17]
45 individual of lean or obese either diabetic or non-diabetic	Evaluation of cytokeratin and Ki67 from isolated pancreas by autopsy	Increase of pancreatic ductal replication during obesity and type 2 diabetes	2010 [18]
42 patients from impaired glucose tolerance stage to developed stage	Evaluation of beta cell neogenesis after pancreatectomy	Confirmation of beta cell neogenesis in pancreas ducts during early stage of diabetes	2013 [13]
C57/6 mice	Determination of newly differentiated β cells by coexpression of GFP and mTomato fluorescent proteins and mRNA expression of Ngn3 in pancreatic tissue	Lack of beta cell neogenesis during adulthood under normal and pancreatic ductal ligation	2013 [19]
Male F1 hybrid B6129SF1/J and BALB/cByJ mice	Evaluation of beta cell mass generation, insulin content and progenitors to the β-cell lineage conversion after PDL-induced injury	Lack of change in bête cell mass generation after PDL-induced injury	2013 [20]
Glu-rtTA:TetO-Pax4 mice	Evaluation of α cells role in beta cell neogenesis during adulthood	glucagon^{+} cells as linker cells generation of pancreatic duct-lining precursor cells to beta like cell	2013 [21]
Male 7- to 10-week-old Lewis rats	Evaluation of beta cell neogenesis, beta cell replication and α- to β-cell conversion in STZ-diabetic rats under injury-induced PDL	Lack of beta cell mass expansion after islet cell transplantation	2013 [22]
Four-week-old male ICR mice	Evaluation of beta cell generation (both neogenesis and replication) before and after surgical reversal of duct ligation	Important of beta cell neogenesis before reversal of the duct ligation and massive beta cell ablation	2013 [23]
Reporter cell line mPac-MIP-RFP	Evaluation of in vitro screening of genes involved in reprogramming from pancreatic duct cells into insulin-producing cells by reporter cell line mPac-MIP-RFP (Pdx1, Ngn3, and Mafa)	Using a polycistronic adenoviral vector for infection better than simultaneous infection of three adenoviruses carrying each transcription factor Increase of reprogramming efficiency when expressed Pdx1 prior to Ngn3 or Mafa	2014 [24]
R26-LSL-Ngn3-AA mice	Evaluation of effect of Fbw7 on activation of Ngn3 during beta cell neogenesis	Stabilization of Ngn3 after loss of Fbw7 lead to reprogramming of adult pancreatic duct cells to beta cells	2014 [25]
13 human cadaveric donors	Evaluation of mesenchymal features HDDCs cultured in endothelial growth-promoting media through mesenchymal markers and its Differentiation to beta cell by measurement of insulin content and gene expression	Confirmation of differentiation HDDCs to beta cell	2014 [26]

Abbreviation—CKs, cytokeratins; INGAP, islet neogenesis-associated proteins; ACP, autoimmune chronic pancreatitis; GFP, green fluorescent protein; mTomato, membrane-targeted Tomato; Ngn3, neurogenin 3; PDL, pancreatic duct ligation; STZ, streptozotocin; ICR mice, imprinting control region mice; Pdx1, pancreatic and duodenal homeobox 1; Mafa, Maf transcription factors large/genetics; Fbw7, F-box and WD repeat domain-containing 7; HDDCs, human pancreatic duct-derived cells.

Please cite this article in press as: M. Zare, et al., Role of pancreatic duct cell in beta cell neogenesis: A mini review study, Diab Met Syndr: Clin Res Rev (2016), http://dx.doi.org/10.1016/j.dsx.2016.08.005