Role of ARHGAP21 on cell proliferation in C57BL/6 mouse islets

Elis G. Azevedo*, 1, Gabriela M. Soares 1, Matheus D. Terrazam 1, Sara T. O. Saad 2, Antonio C. Boscheró 1, Helena C. Barbosa-Sampaio 1
1 Department of Structural and Functional Biology, Biology Institute, University of Campinas, São Paulo, Brazil
2 Haematology Centre, School of Medicine, University of Campinas- UNICAMP, Campinas, Brazil

Abstract
ARHGAP21 participates in cell proliferation, but the mechanisms involved in the role of that GAP are not elucidated. This project aims to investigate the possible involvement of ARHGAP21 in beta cell proliferation mechanisms in pancreatic islet in response to insulin resistance in ARGAP21 haplodeficient mice, after administration of a high fat diet. This project contributes to understanding the cellular mechanisms that lead beta cell mass and proliferation in insulin resistance.

Key words:
ARHGAP21, cell proliferation, pancreatic islet

Introduction
Beta cell proliferation is an important compensatory mechanism in response to peripheral insulin resistance, increasing the size of the pancreatic islet. ARHGAP21 regulates GTases activity and participates in cytoskeletal dynamics, cell cycle progression, transcriptional regulation, cell survival and vesicle trafficking1,2, however its mechanisms in pancreatic islets are unknown. This study aims to investigate the possible involvement of ARHGAP21 in cell proliferation in pancreatic islet cells in the compensatory mechanisms during the high fat diet (HFD) treatment, using the ARHGAP21 haplodeficient mouse (HET), compared to C57BL/6 mouse control (CTL).

Results and Discussion
HET mouse islets express, approximately, 50% less ARHGAP21 gene

ARHGAP21 haplodeficiency impairs insulin, glucagon and cyclinD1 gene expression in HFD-treated mouse islets

As expected, HET mouse islets presented less ARHGAP21 gene content, compared to control, in NFD and HFD. 12 weeks HFD treatment induced no significant decrease in ARHGAP21 gene expression in mouse islets.

ARHGAP21 haplodeficiency reduces insulin, glucagon and cyclinD1 gene expression in HFD-treated mouse islets

Reduced insulin gene expression in HET-HFD corroborates with previous results, in which glucose stimulated-insulin secretion in isolated islets is also reduced. Indeed, HET mice are not able to expand beta and alpha cells in response to a HFD, as indicated by cyclinD1 reduced expression and cells areas. These results suggest a ARHGAP21 role in mechanisms involved in islets response to a nutritional excess.

Conclusions
Our results indicate that ARHGAP21 is essential for beta and alpha cells modulation in response to a nutrient overload in mouse pancreatic islets.

Acknowledgement
Este projeto foi financiado pela Fundação de Amparo à Pesquisa do Estado de São Paulo (Fapesp).

DOI: 10.19146/pibic-2016-51765

1 Vega F & Redley A. FEBS Letters 2008, 582, 2093.