Accepted Manuscript

Lysine demethylase inhibition protects pancreatic β cells from apoptosis and improves β-cell function

Marie Balslev Backe, Jan Legaard Andersson, Karl Bacos, Dan Ploug Christensen, Jakob Bondo Hansen, Jerzy Jòzef Dorosz, Michael Gajhede, Tina Dahlby, Madhusudhan Bysani, Line Hyltoft Kristensen, Charlotte Ling, Lars Olsen, Thomas Mandrup-Poulsen

PII: S0303-7207(17)30355-6

DOI: 10.1016/j.mce.2017.07.001

Reference: MCE 10000

To appear in: *Molecular and Cellular Endocrinology*

Received Date: 1 February 2017

Revised Date: 27 June 2017

Accepted Date: 2 July 2017

Please cite this article as: Backe, M.B., Andersson, J.L., Bacos, K., Christensen, D.P., Hansen, J.B., Dorosz, Jerzy.Jò., Gajhede, M., Dahlby, T., Bysani, M., Kristensen, L.H., Ling, C., Olsen, L., Mandrup-Poulsen, T., Lysine demethylase inhibition protects pancreatic β cells from apoptosis and improves β-cell function, *Molecular and Cellular Endocrinology* (2017), doi: 10.1016/j.mce.2017.07.001.

Lysine demethylase inhibition protects pancreatic β cells from apoptosis and improves β-cell function

Marie Balslev Backe[a, 1], Jan Legaard Andersson[b, 2], Karl Bacos[c], Dan Ploug Christensen[a, 3], Jakob Bondo Hansen[a, 1], Jerzy Jòzef Dorosz[b], Michael Gajhede[b], Tina Dahlby[a], Madhusudhan Bysani[c], Line Hyltoft Kristensen[b, 4], Charlotte Ling[c], Lars Olsen[b], Thomas Mandrup-Poulsen[a*].

[a] Immuno-endocrinology Laboratory, Department of Biomedical Sciences, University of Copenhagen, Denmark.

[b] Section of Biostructural Reseach, Department of Drug Design and Pharmacology, University of Copenhagen, Denmark

[c] Unit for Epigenetics and diabetes, Department of Clinical Sciences, Lund University, Scania University Hospital, Malmö Sweden

Present address (if changed since address where work was carried out):

[1] Department of Neurosciences and Pharmacology, University of Copenhagen, Denmark

[2] Nuevolution A/S, Copenhagen, Denmark

[3] Department of Cellular and Molecular Medicine, University of Copenhagen, Denmark

[4] Symphogen A/S, Ballerup, Denmark

*Corresponding author: Thomas Mandrup-Poulsen, tmpo@sund.ku.dk

Running title: *Lysine demethylase inhibition protects β cells*

Abbreviations[1]

[1] ATF = Activating transcription factor; ChIP = Chromatin immunoprecipitation; CHOP = C/EBP homologous protein; DP = Death promoting gene; ER = Endoplasmic reticulum; FDH = Formaldehyde dehydrogenase; FDR = False discovery rate; GLUT = Glucose transporter; GSEA = Gene set enrichment analysis; GSIS = Glucose-stimulated insulin secretion; HSP = Heat shock protein; H3K4me = Histone 3 lysine 4 methylation; H3K27me = Histone 3 lysine 27 methylation; INS = Insulin; KAT = Lysine acetyl transferase; KDAC = Lysine deacetylase; KDM = Lysine demethylase; KMT = Lysine methyltransferase; MafA = v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog a; NO = Nitric oxide; OG = Oxo-glutarate; PTM = Posttranslational modification; PPAR = peroxisome proliferator-activated receptor; PUMA = p53 upregulated modulator of apoptosis; P2RY2 = purinergic receptor P2Y, G-protein coupled 2; P2RX7 = purinergic receptor P2X, ligand-gated ion channel, 7; SAHA = Suberoylanilide hydroxamic acid; SERCA = Sarco/endoplasmic reticulum Ca^{2+}-ATPase; siRNA = Small interfering RNA; TSA = Trichostatin A; VPA = Valproic acid.