Serbian Biochemical Society

President: Marija Gavrović-Jankulović
Vice-president: Suzana Jovanović-Šanta
General Secretary: Jelica Milošević
Treasurer: Milica Popović

Organization Committee

Vladimir Mihailović
Aleksandar Ostojić
Nevena Đukić
Jelena S. Katanić Stanković
Marko Živanović
Nikola Srećković
Stefan Marković
Slađana Đorđević
Nataša Simin
Milan Nikolić
Milica Popović
Jelica Milošević

Scientific Board

Marija Gavrović-Jankulović
Suzana Jovanović-Šanta
Marina Mitrović
Tatjana Jevtović Stoimenov
Ivan Spasojević
Snežana Marković
Melita Vidaković
Natalija Polović
Aleksandra Zeljković
Romana Masnikosa
Radivoje Prodanović

Proceedings

Editor: Ivan Spasojević
Technical support: Dragana Robajac
Cover design: Zoran Beloševac
Publisher: Faculty of Chemistry, Serbian Biochemical Society
Printed by: Colorgrafx, Belgrade

Serbian Biochemical Society
Tenth Conference

with international participation

24.09.2021. Kragujevac, Serbia

"***Biochemical Insights into Molecular Mechanisms"***

Ferroptosis as a novel determinant of β-cell death in diabetic conditions

Ana Stančić[1*], Tamara Saksida[2], Milica Markelić[3], Milica Vučetić[4], Ilijana Grigorov[1], Vesna Martinović[1], Anđelija Ivanović[1], Ksenija Veličković[3], Vesna Otašević[1]

[1]Department of Molecular Biology, Institute for Biological Research "Siniša Stanković", National Institute of Republic of Serbia, University of Belgrade, Belgrade; Serbia
[2]Department of Immunology, Institute for Biological Research "Siniša Stanković", National Institute of Republic of Serbia
[3]Department of Cell and Tissue Biology, Faculty of Biology, University of Belgrad
[4]Medical Biology Department, Centre Scientifique de Monaco (CSM), Monaco; Monaco

[*]e-mail: ana.stancic@ibiss.bg.ac.rs

Diabetes is a complex metabolic disorder which incidence rises in the epidemic fashion, suggesting the urgent need for new therapies. Its main pathological hallmark is loss of functional β-cells, and to date, several types of β-cell death have been described – necrosis, apoptosis, and autophagy. However, the role of ferroptosis in reducing β-cell population in diabetes remains elusive. In this study we aimed to examine whether and how this type of cell death is implicated in regulation of β-cell destiny in diabetes. For that purpose, Rin-5F insulin-producing pancreatic cells were treated with diabetes-mimicking factors – high glucose (HG) and H_2O_2, as well with commonly used diabetogenic agent streptozotocin (STZ). Results showed that HG, H_2O_2 and STZ induce the death of Rin-5F cells along with the accumulation of reactive oxygen species, lipid peroxides and iron; inactivation of nuclear factor (erythroid-derived 2)-like 2 (Nrf2) and decrease in glutathione peroxidase 4 expression. This is consistent with the effect of the treatment with RSL-3, a well-known inducer of ferroptosis. Ferrostatin-1, a ferroptosis inhibitor, diminished above-stated effects and rescued cells from death. Our data revealed that β-cells underwent ferroptotic cell death under diabetogenic conditions. Results also implicate HG and H_2O_2 as contributing factors to ferroptosis of β-cells and suggest the novel mechanism of STZ diabetogenic action. Furthermore, the results shed a new light on antidiabetic strategy based on Nrf2 activation, putting it into the anti-ferroptotic context. In close, targeting ferroptosis in diabetes might be a new promising therapeutic approach based on preservation of β-cell population.

Acknowledgments

This work was supported by the Ministry of Education, Science and Technological Development of the Republic of Serbia (Contract No. 451-03-68/2020-14/200007), and by the Science Fund of the Republic of Serbia (Serbian Science and Diaspora Collaboration Program: Knowledge Exchange

Vouchers, #Grant No. 6525651, Ferroptosis in the β-cells death: possible strategy for diabetes treatment, acronym: BetFeSis).