INVITATION

To a Seminar organised by the initiative of the Group of PhD Students and Young Scientists of the Centre of Experimental Medicine, SAS

on

Drug-gut microbiota interaction of novel aldose reductase inhibitor cemtirestat in ZDF rats.

Lecturer

Ing. Marek Lepáček

From

Institute of Experimental Pharmacology & Toxicology,

CEM SAS

Thursday 23.3.2023, 13:00

6th floor, block **A**, room **7.29**

HYBRID FORMAT

We are looking forward to your participation!

PROGRAM OVERVIEW

13:00 – 13:05	**Introduction**
13:05 – 13:20	**Presentation**
13:20 – 13:30	**Discussion**

For ONLINE Attendance:

Join Zoom Meeting
https://us02web.zoom.us/j/83193751683?pwd=ZEhyRHFiNjVuVkNRMHJuUnZTVU1KQT09

Meeting ID: **831 9375 1683**
Passcode: **742280**

ANNOTATION

Drug-gut microbiota interaction of novel aldose reductase inhibitor cemtirestat in ZDF rats.

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The human gut microbiome is a complex ecosystem, that mediates host interactions with its environment [1]. Individual humans are up to 99.9% genetically identical to each other in terms of their host genome, while compared to the gut microbiota, humans can differ from each other by 80-90%. This suggests the uniqueness and importance of the gut microbiome [2]. In addition, the gut microbiome can metabolize drugs, and drugs can change the composition of the microbiome. Currently, these interactions are still relatively poorly described and unclear [3]. For example, the anti-diabetic drugs metformin and thiazolidinediones can change the composition and function of the microbiome [4].

Our study focuses on the new multitarget drug in the therapy of secondary diabetic complications. Cemtirestat is characterized as a highly selective and effective inhibitor of aldose reductases, the first enzyme of the polyol pathway. In addition, multiple antioxidant abilities were observed [5]. In the present study, we focused on 3-month-old "Zucker diabetic fatty (ZDF) "lean" rats treated by cemtirestat in dosage 7.7 mg/kg/day for 2 months. The biochemical analysis of blood was performed. The composition of the intestinal microbiota was determined using a whole genome sequencing method of rat fecal samples. ZDF "lean" rats showed a favorable effect on the amount of microflora compared to the control group.

Biochemical analyses including 20 parameters was performed. The ratio Firmicutes/Bacteroidetes, (F/B) was without significant change in rats feaces treated with cemtirestat. The Shanon index of alpha diversity didn´t show any significant shift compared to the control group, as well as the main phyla abundance. Furthermore, analysis of *Clostridium butyricum* and *Lactobacillaceae* promotes the stimulating effect of cemtirestat on the abundance of mentioned species. We also observed a decrease of *Clostridium difficile* species in rats treated with cemtirestat.

Our study suggests that cemtirestat has not damaging impact on the rats gut microbiome. In addition, cemtirestat shows a stimulatory effect on some species of probiotic bacteria, the decline of which is closely related to the progression of T2DM.

Acknowledgment

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Literatúra

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[3] S. A. Flowers, S. Bhat, a J. C. Lee, "Potential Implications of Gut Microbiota in Drug Pharmacokinetics and Bioavailability", *Pharmacotherapy: The Journal of Human Pharmacology and Drug Therapy*, roč. 40, č. 7, s. 704–712, júl. 2020, doi: 10.1002/PHAR.2428.

[4] A. Whang, R. Nagpal, a H. Yadav, "Bi-directional drug-microbiome interactions of anti-diabetics", *EBioMedicine*, roč. 39, s. 591–602, jan. 2019, doi: 10.1016/J.EBIOM.2018.11.046.