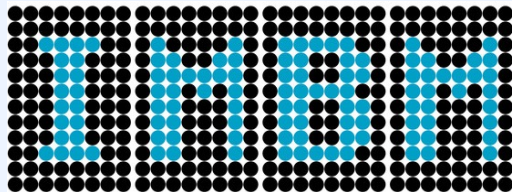


The Dynamics of Extracellular DNA and Neutrophil Extracellular Traps Formation in Mouse Models of Chronic Liver Disease

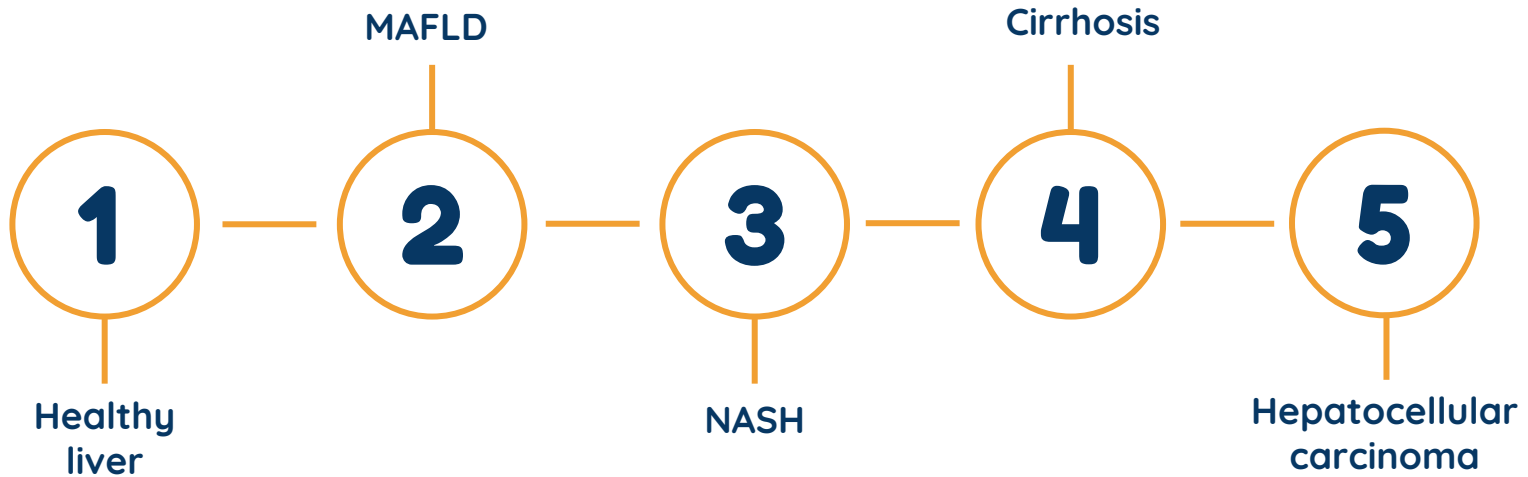
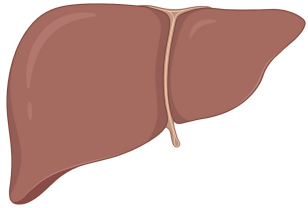
Paulína Belvončíková

Andrej Feješ, Alexandra Hladíková, Anna Farkašová, Jázmin Orsolya Takácsová, Barbora Gromová,
Emil Bečka, Jakub Janko, Roman Gardlík



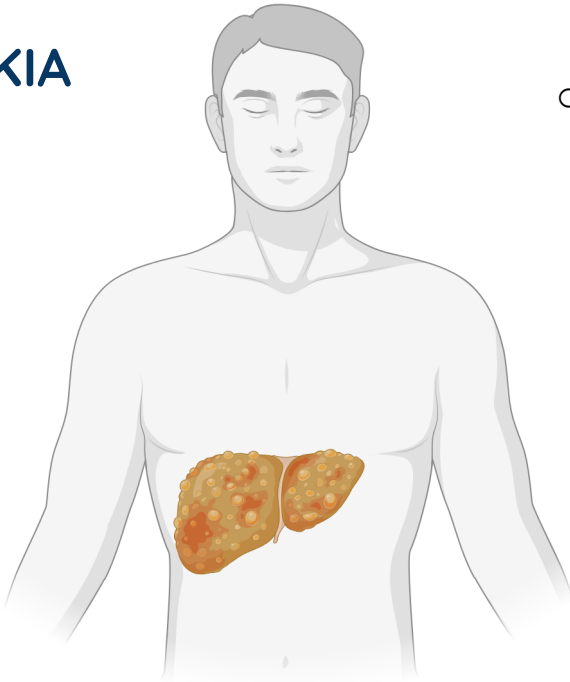
INSTITUTE OF MOLECULAR BIOMEDICINE
Faculty of Medicine, Comenius University in Bratislava
imbm@imbm.sk
paulina.belvoncikova@imbm.sk

Liver diseases



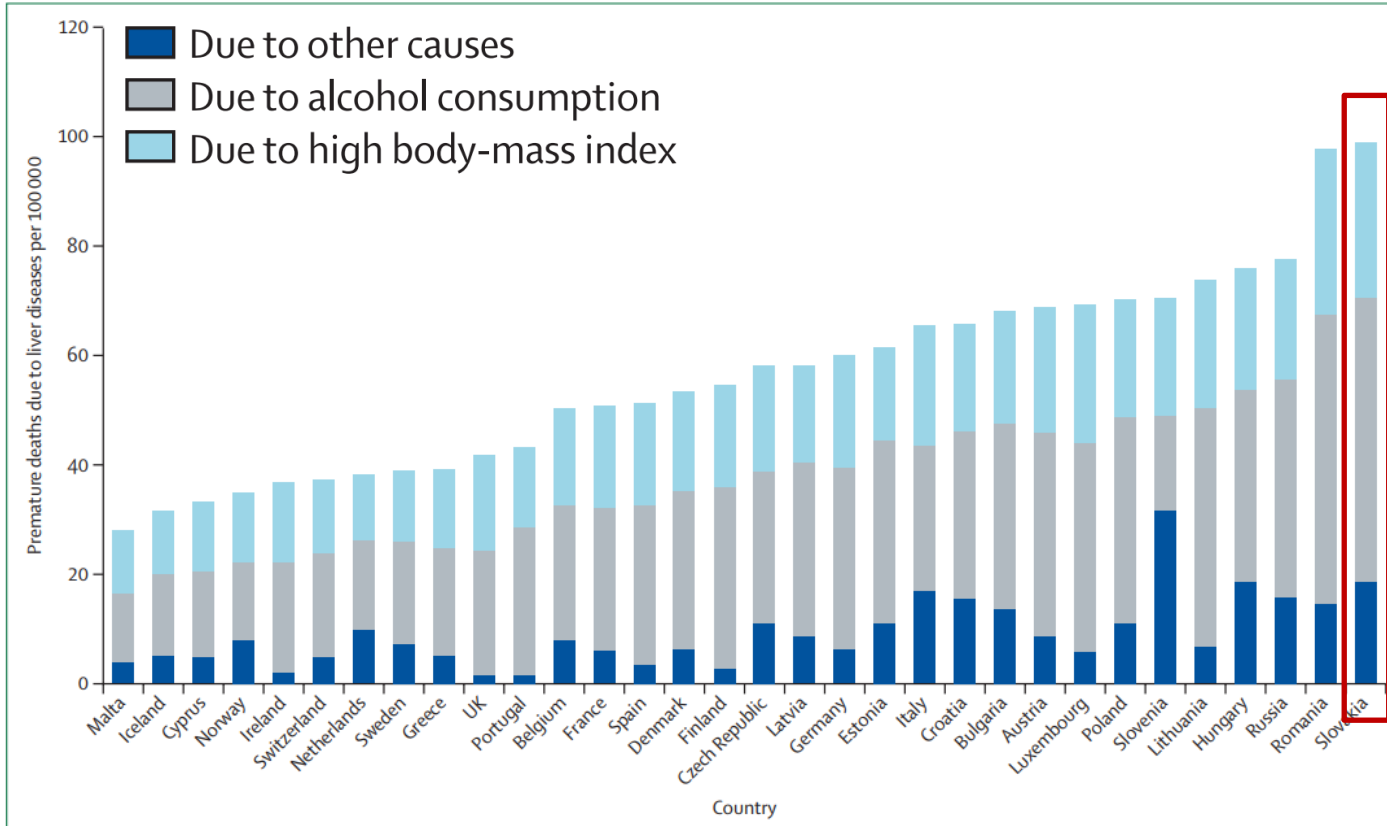
Liver diseases

SLOVAKIA



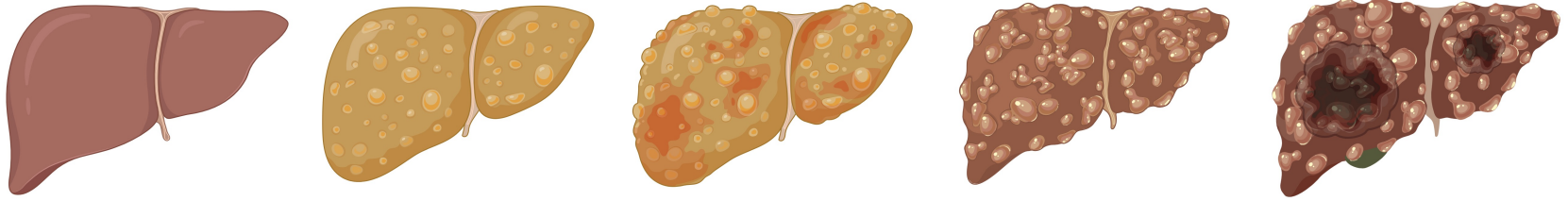
- The highest premature deaths to liver diseases in Europe per 100,000 people (Karlsen et al. 2022)

Premature deaths due to liver diseases



Karlsen et al. Lancet.
2022

Liver diseases



MAFLD

Cirrhosis

1

2

3

4

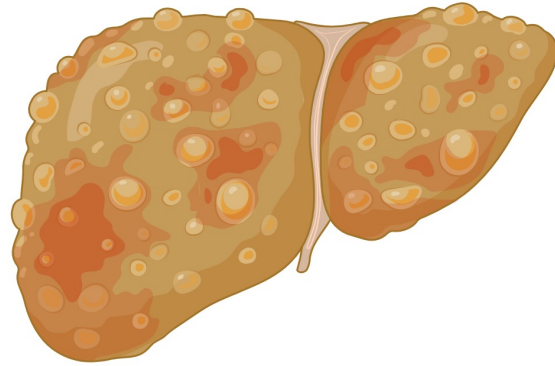
5

Healthy
liver

NASH

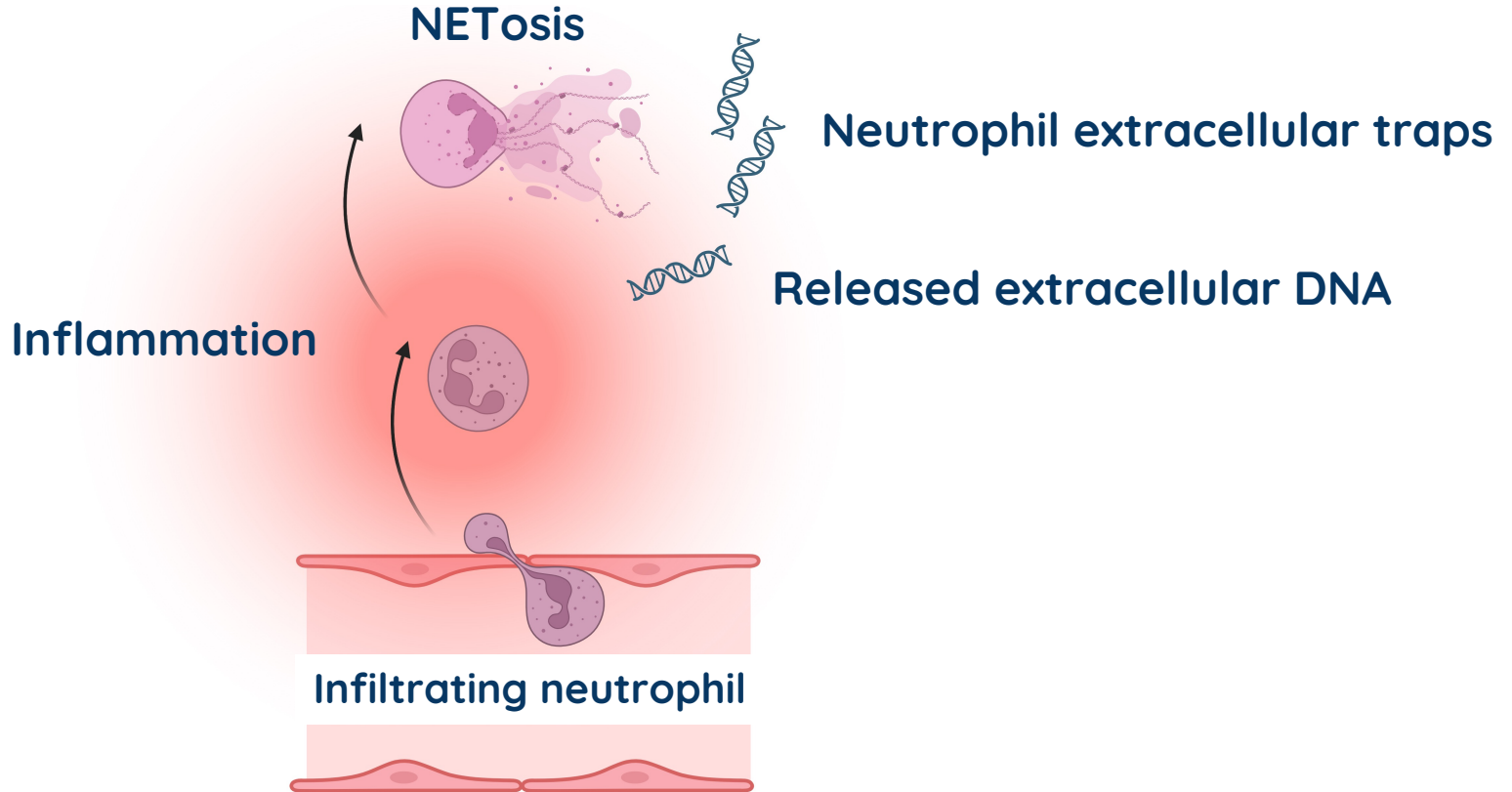
Hepatocellular
carcinoma

Liver diseases



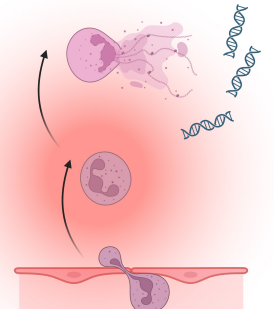
NASH

The role of NETs and ecDNA



The role of NETs and ecDNA

The dynamics of extracellular DNA and neutrophil extracellular traps formation in mouse models of chronic liver disease



Animal models

DIETARY



CTRL CDAA
n=7

Control diet



CDAA
n=10

CDAA diet

Cholin-deficient low-methionine
diet (CDAA diet)

CYTOTOXIC



CTRL TAA
n=7

Control diet
+
saline IP

Intraperitoneal injection of
thioacetamide (TAA)



TAA
n=11

Control diet
+
thioacetamide IP

Animal models

DIETARY



CTRL CDAA
n=7

Control diet



CDAA
n=10

CDAA diet

Cholin-deficient low-methionine
diet (CDAA diet)

NASH without body weight loss

Choline

- Modulation of epigenetic gene regulation
- Cell membrane formation via phospholipid synthesis
- Production of acetylcholine
- Fat metabolism in the liver

Methionine

- Oxidative stress inhibition
- Storing fat in the liver

Animal models

DIETARY



CTRL CDAA
n=7

Control diet



CDAA
n=10

CDAA diet

Cholin-deficient low-methionine
diet (CDAA diet)

CYTOTOXIC



CTRL TAA
n=7

Control diet
+
saline IP

Intraperitoneal injection of
thioacetamide (TAA)



TAA
n=11

Control diet
+
thioacetamide IP

Animal models

Fibrosis with body weight loss

Thioacetamide

- Oxidative stress
- Antioxidant depletion

CYTOTOXIC



CTRL TAA
n=7

Control diet
+
saline IP

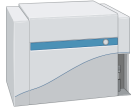


TAA
n=11

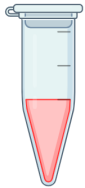
Control diet
+
thioacetamide IP

Intraperitoneal injection of
thioacetamide (TAA)

Timeline



Neutrophil extracellular traps



Extracellular DNA, Dnase activity

Liver enzymes activity: AST, ALT

NETosis markers: MPO, NE



Baseline

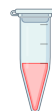
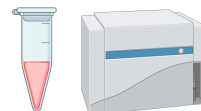
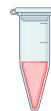
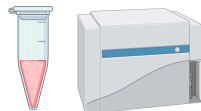
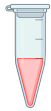
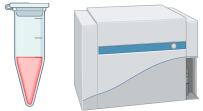
Week 2

Week 4

Week 6

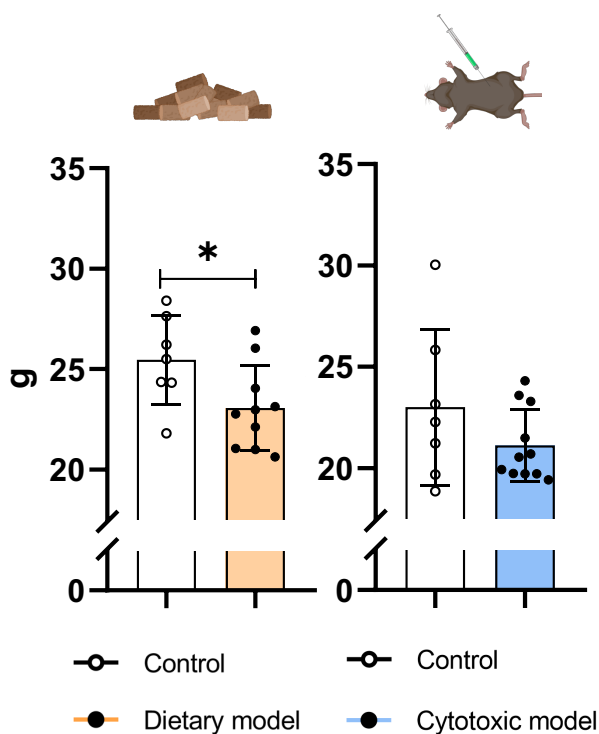
Week 8

Week 10

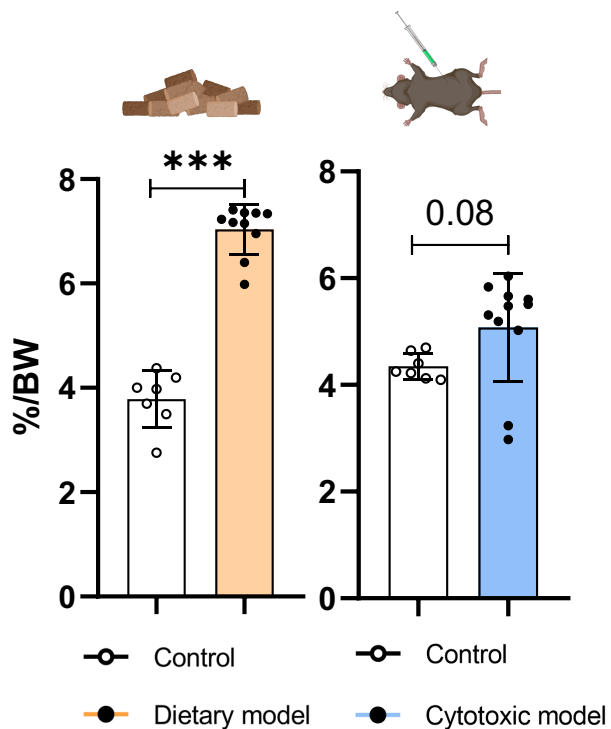


Results

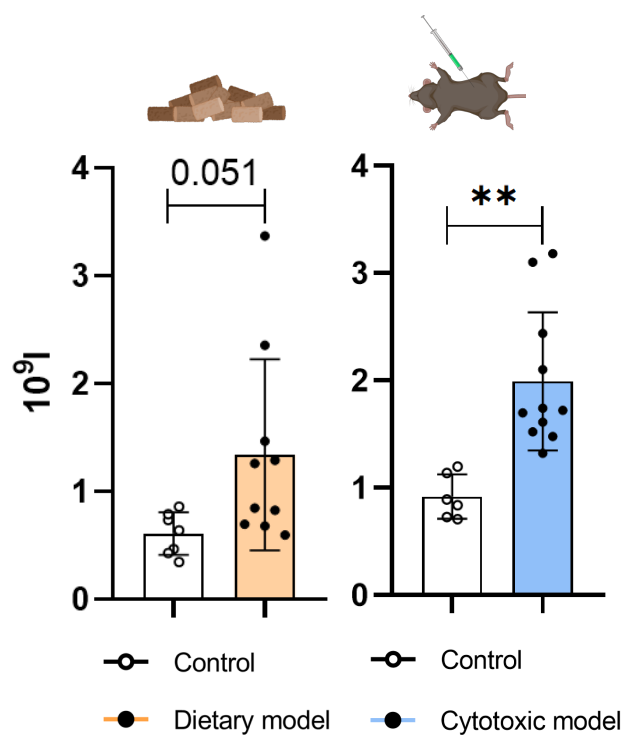
Body weight



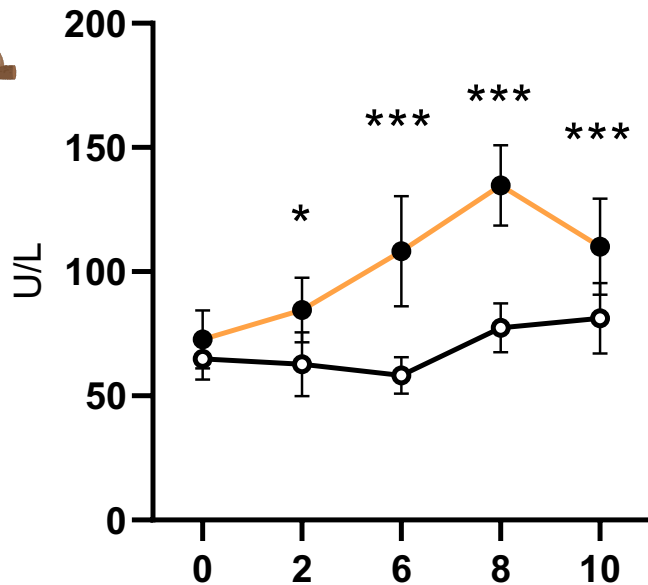
Liver weight/ Body weight



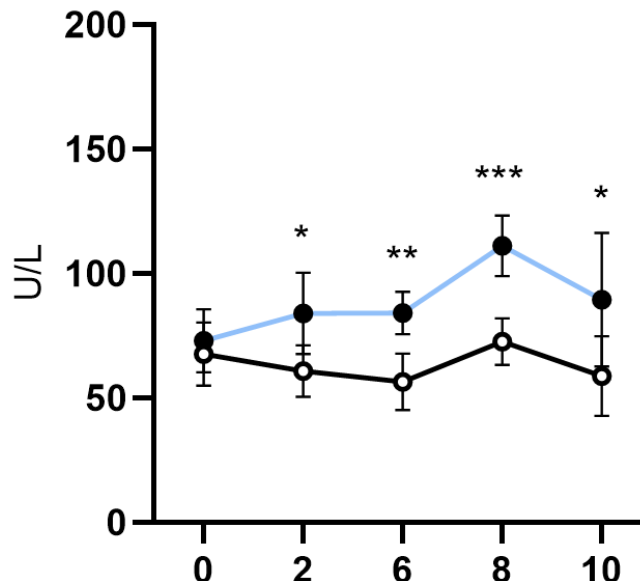
Neutrophil counts



Aspartate aminotransferase activity

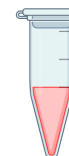


○ Control ● Dietary model

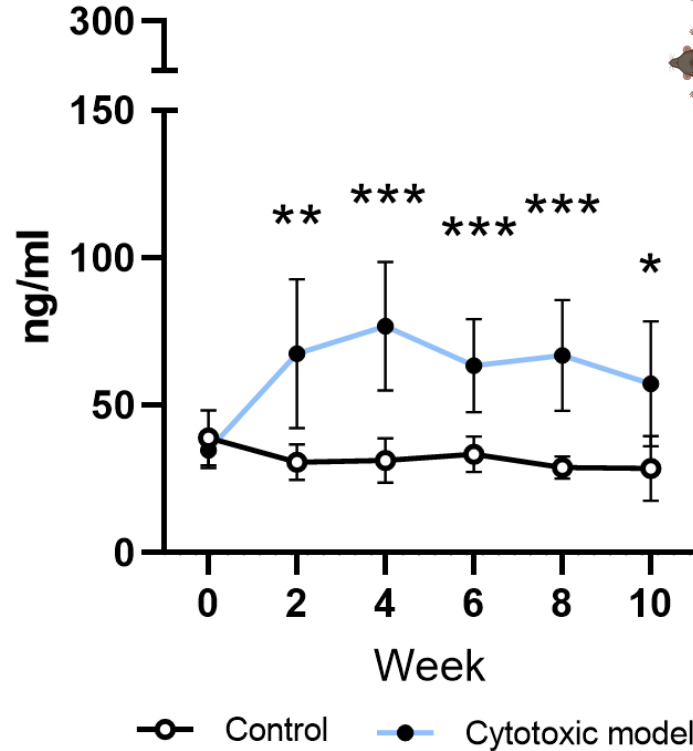
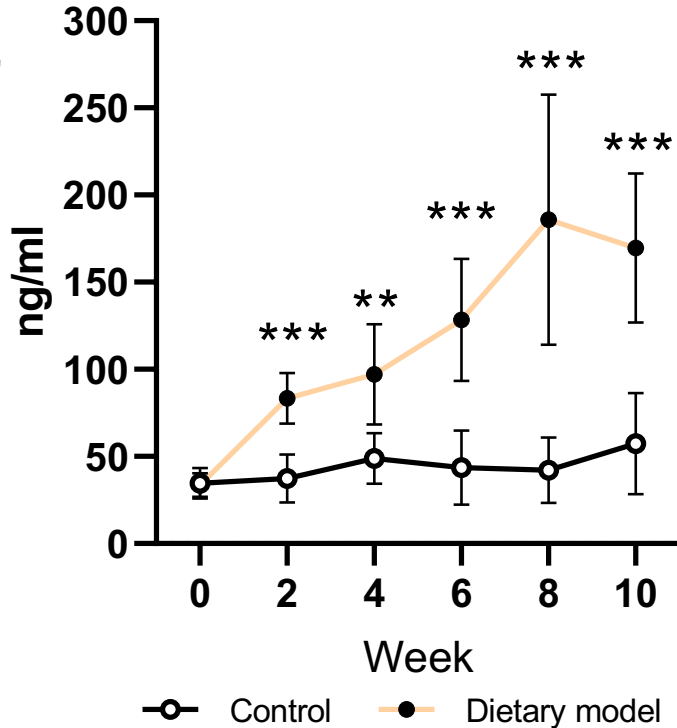


○ Control ● Cytotoxic model

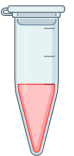
In plasma



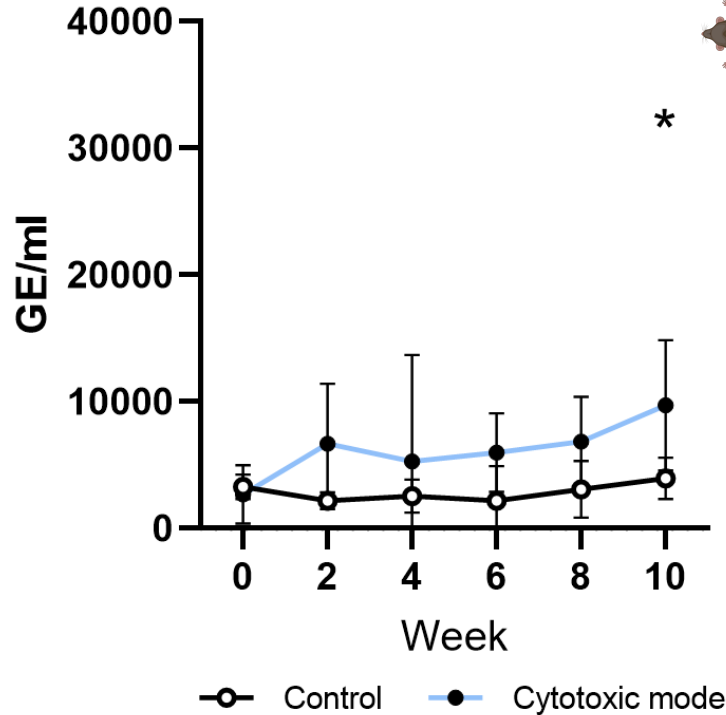
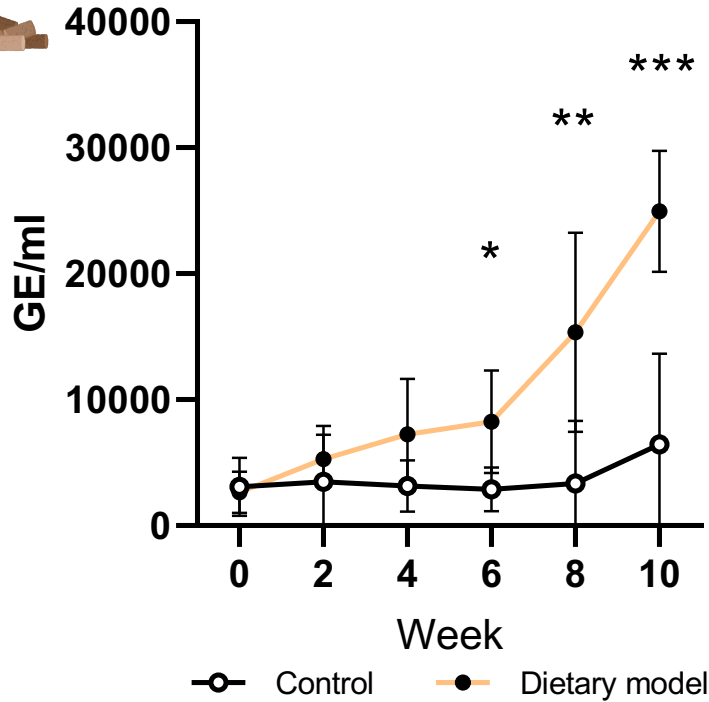
Dynamics of total extracellular DNA concentration



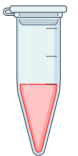
In plasma



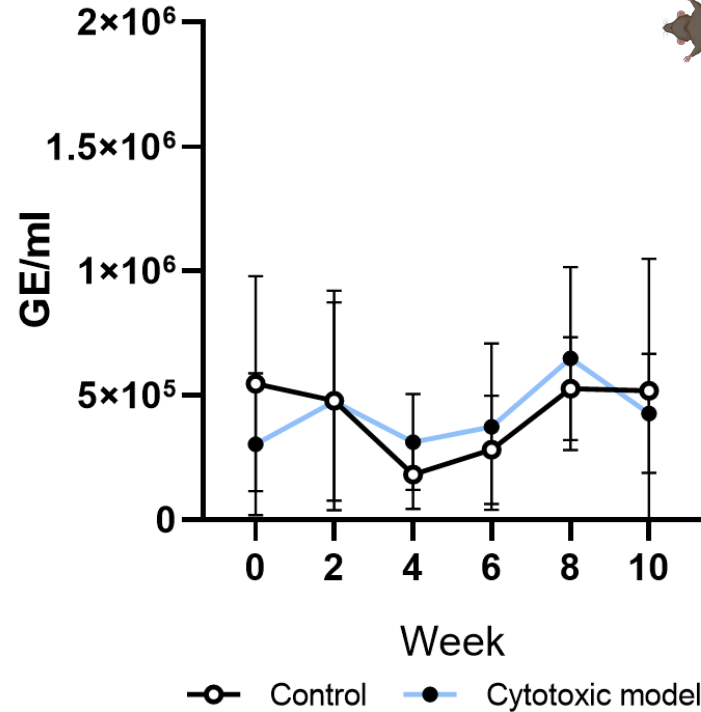
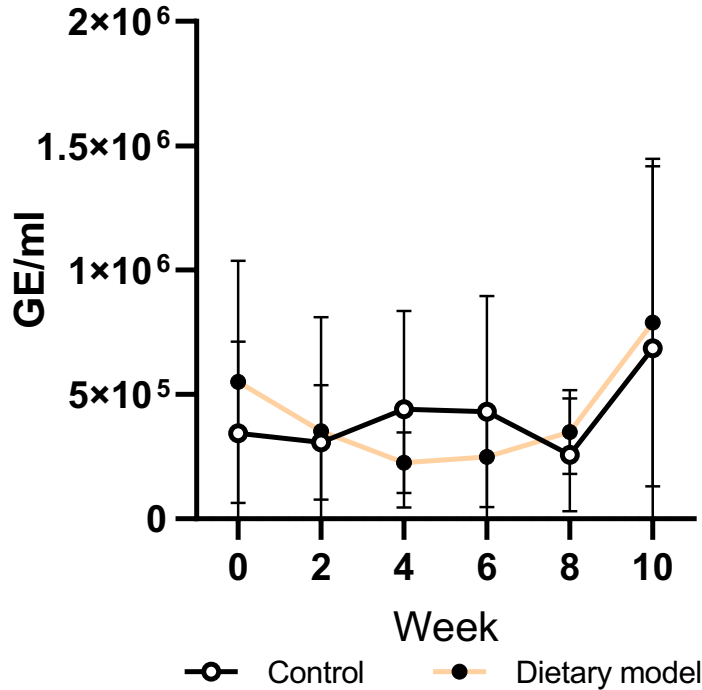
Dynamics of nuclear DNA concentration



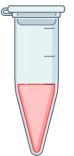
In plasma



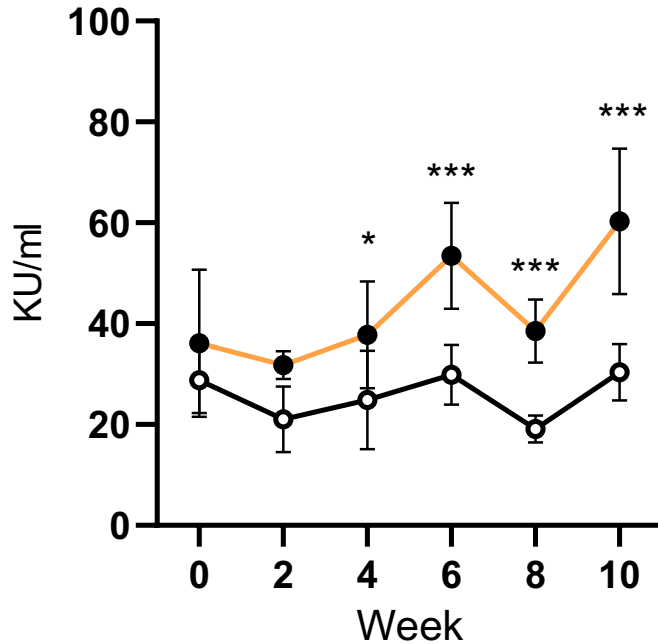
Dynamics of mitochondrial DNA concentration



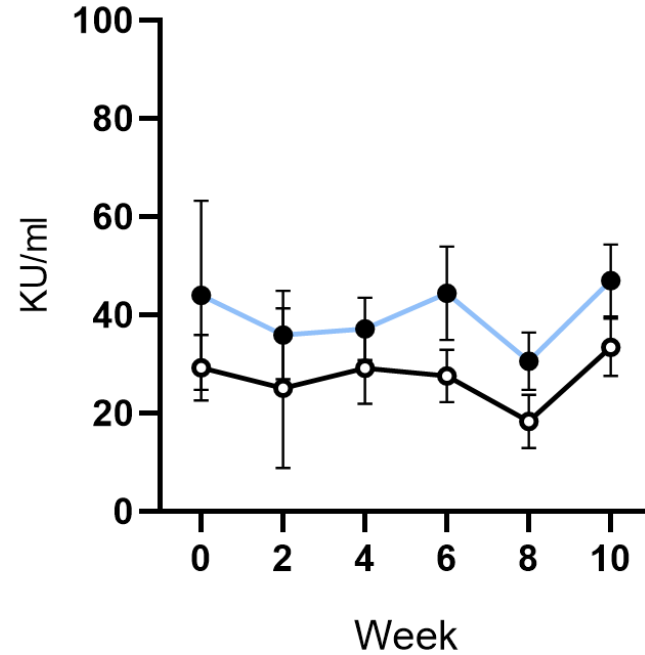
In plasma



DNase activity

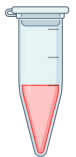


○ Control ● Dietary model

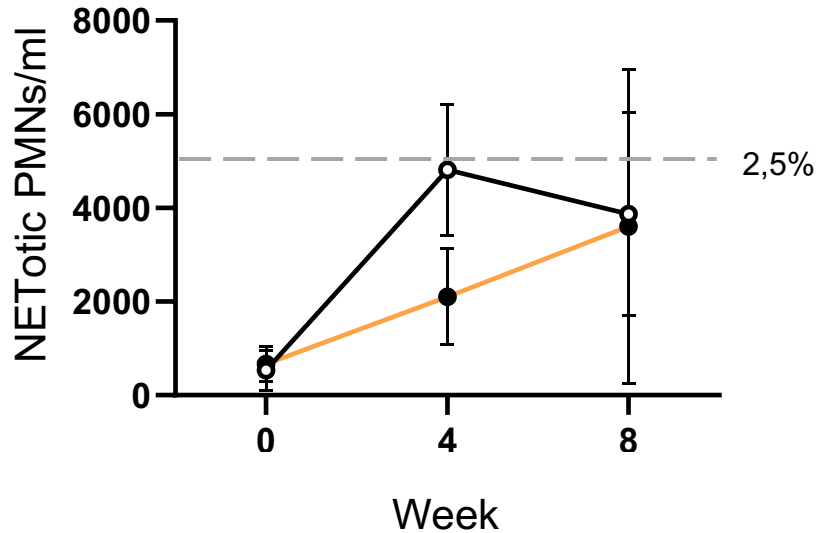


○ Control ● Cytotoxic model

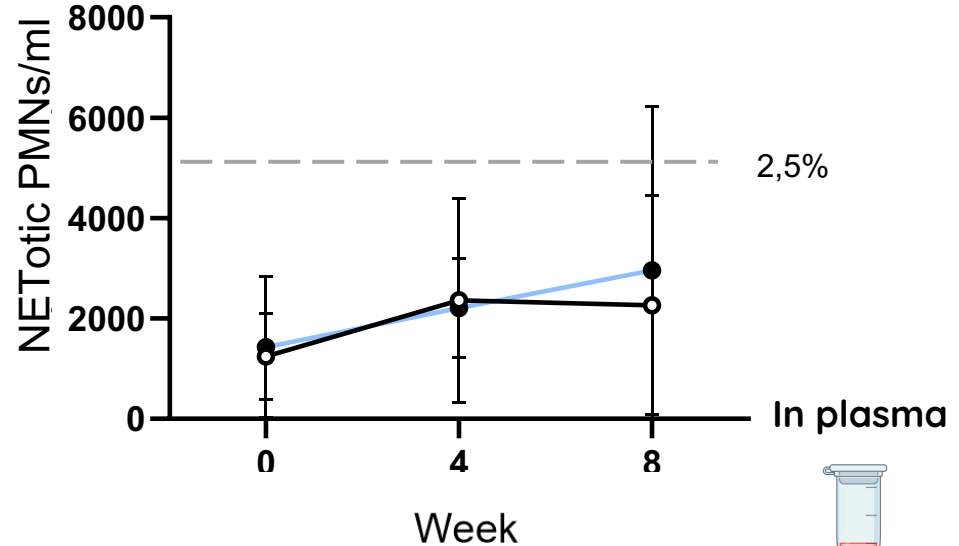
In serum



Dynamics of neutrophil extracellular trap formations

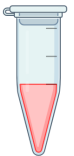


○ Control ● Dietary model

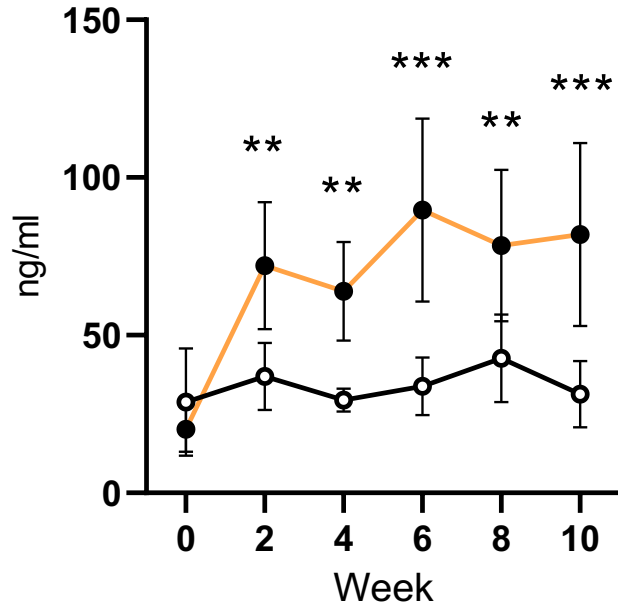


○ Control ● Cytotoxic model

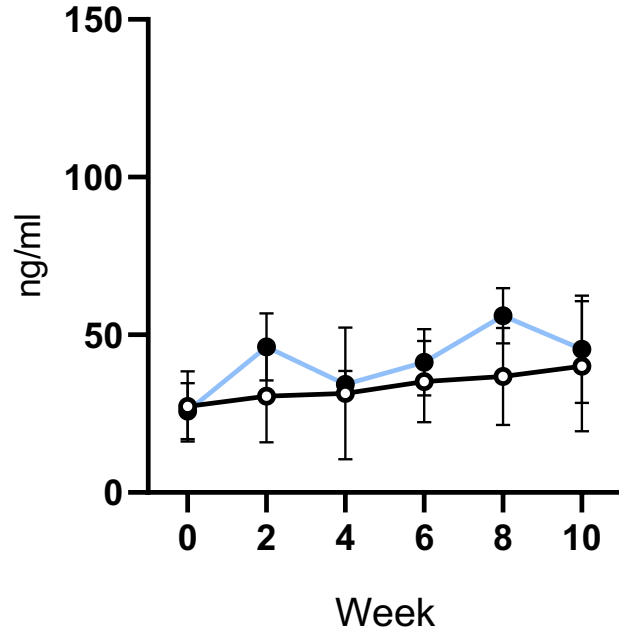
In plasma



Dynamics of myeloperoxidase concentration

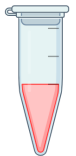


○ Control ● Dietary model

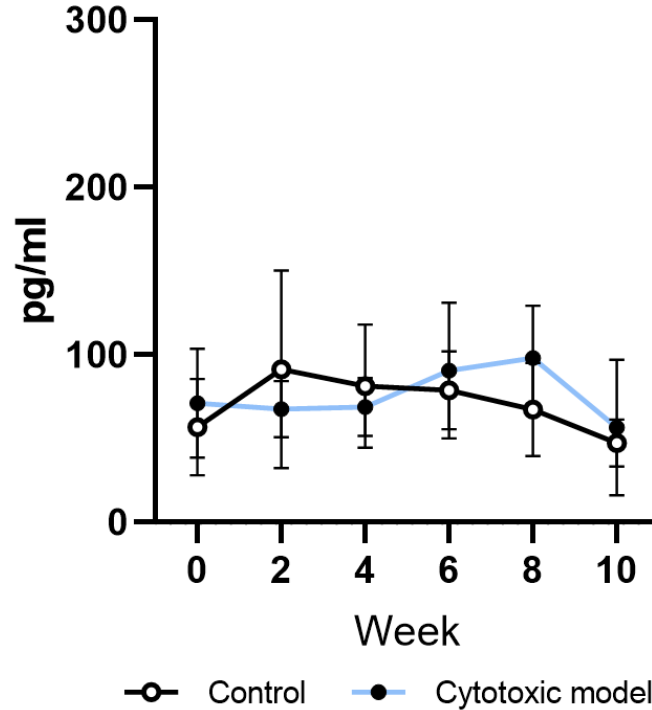
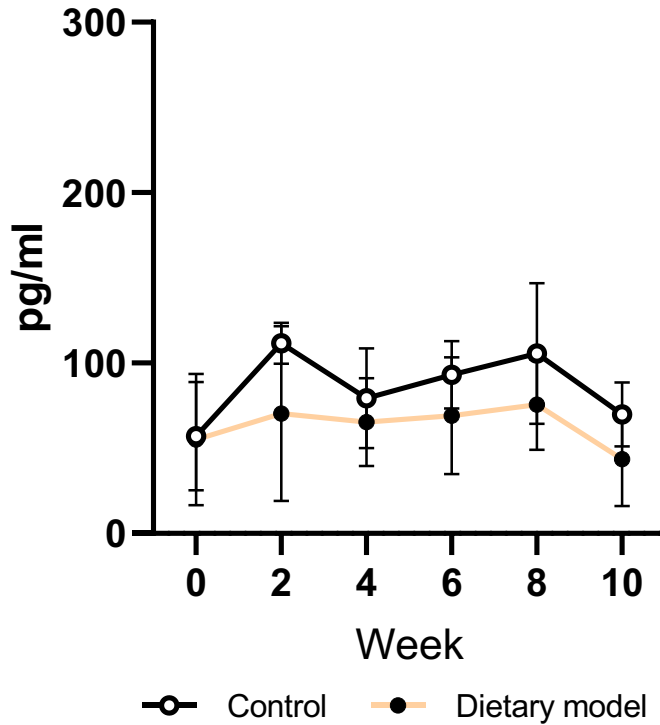


○ Control ● Cytotoxic model

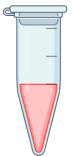
In plasma



Dynamics of neutrophil elastase concentration



In plasma

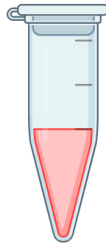


Outcomes

01 | Increased ecDNA concentration
(nuclear origin)

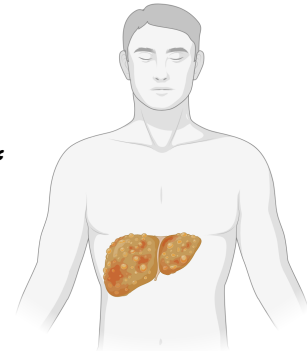
02 | Not increased NETs formations

03 | In progress:
Histology and immunohistochemistry



Plasma

„Is there any NETs formation in tissue?“



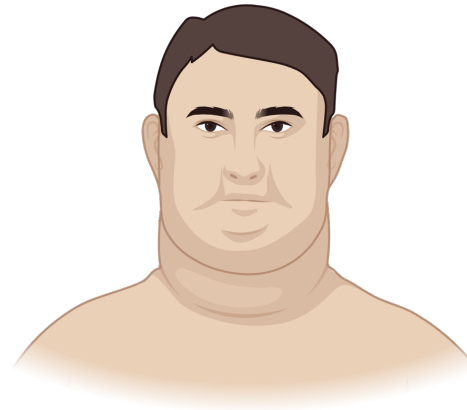
Liver

Future outlooks

- Due to other causes
- Due to alcohol consumption
- Due to high body-mass index



Alcoholic liver disease



Metabolic syndrome



Paulína Belvončíková

paulina.belvoncikova@imbm.sk



Roman Gardlík

Andrej Feješ

Barbora Gromová

Emil Bečka



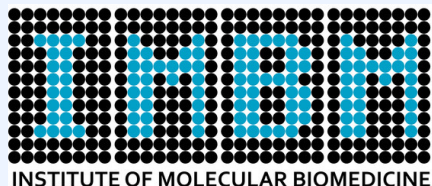
Jakub Janko

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**OUR WEBPAGE
SCAN ME!**



INSTITUTE OF MOLECULAR BIOMEDICINE
Faculty of Medicine, Comenius University in Bratislava
imbm@imbm.sk
paulina.belvoncikova@imbm.sk