THE EFFECT OF 24 WEEKS OF HIGH-FAT AND HIGH-CHOLESTEROL DIET ON RAT LIVER MITOCHONDRIA

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NAFLD

- Nonalcoholic fatty liver disease
  > 30 % of world population
- Atherosclerosis, metabolic syndrome and type II diabetes
- Increased inflammation, reactive oxygen species production, insulin resistance & impaired lipid metabolism

- How does it affect liver mitochondrial respiration?
METHODS

• Male Wistar rats (n=4)
• Commercial Diet (Altromin)
  – **Control**: 10 % energy in fat
  – **HFD**: 70 % energy in fat (lard) + 1.25 % in cholesterol
  – 1, 3, 6, 12 & 24 weeks
• Histology
  – Hematoxylin eosin, Oil red O, Masson’s trichrome
• Mitochondrial respiration
  – Isolated mitochondria
  – OROBOROS Oxygraph-2k
  – Reference protocols 1 & 2
RESPIRATORY PROTOCOLS

Graph showing O2 Flux per mass (A) [pmol/(s*mg)] over time with markers for various compounds such as ADP, Oct, Cyt, FCCP, Gp, Ama, and Azd. The graphs display ranges in h:min: 1:33 and 1:58.
Results
Body weight
Body weight

Rat body weight at the time of termination

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<th>Group</th>
<th>C1</th>
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Liver weight
Liver weight

Rat liver weight at the time of termination

Relative weight

% of body mass

grams
HISTOLOGY

Control - 1 week

Hematoxylin eosin

Oil red O

HFD - 1 week

Hematoxylin eosin

Oil red O
HISTOLOGY

Control - 3 weeks

Hematoxylin eosin

Oil red O

HFD - 3 weeks

Hematoxylin eosin

Oil red O
HISTOLOGY

HFD-3weeks; Masson’s trichrome
**Respiration**

**FAO-OXPHOS capacity; OctM.1<sub>p</sub>**

**Flux control ratio OctM.1<sub>p</sub>**

**Flux control factor Oct<sub>ε</sub>**
Respiration

N-ETS capacity; $\text{PMG}_E$

S-ETS capacity; $S_E$

NS-ETS capacity; $\text{PMGS}_E$
**Respiration**

**Maximal OXPHOS capacity; PMGSGpOct<sub>p</sub>**

**Maximal ETS capacity; PMGSGpOct<sub>E</sub>**
**Summary**

- Mitochondria adapted to HFD by increasing the FCF\textsubscript{Oct} already after one week
- Increase of respiratory capacity after 3 weeks:
  - maximal ETS
  - N-ETS
  - FAO-OXPHOS (3 & 6w)
- Decrease of respiratory capacity after 6 weeks and longer:
  - maximal ETS
  - maximal OXPHOS
  - S-ETS
  - NS-ETS
ACKNOWLEDGEMENTS

• Tutor: prof. Zuzana Červinková, MD. Ph.D
• Team:
  – Pavla Staňková
  – Otto Kučera
  – René Endlícher
  – Katka Nožičková
  – Aml Banni
  – Marie Vaculová
  – Jana Ondráková
  – Monika Pospíšilová
• Funding
  – PRVOUK P37/02
  – SVV-2016-260287
THANK YOU FOR YOUR ATTENTION!