



Altered Mouse Adipose Tissue IGF-1 Expression Influences Glucose Control

Jan Trost

Prof. Gudrun A. Brockmann

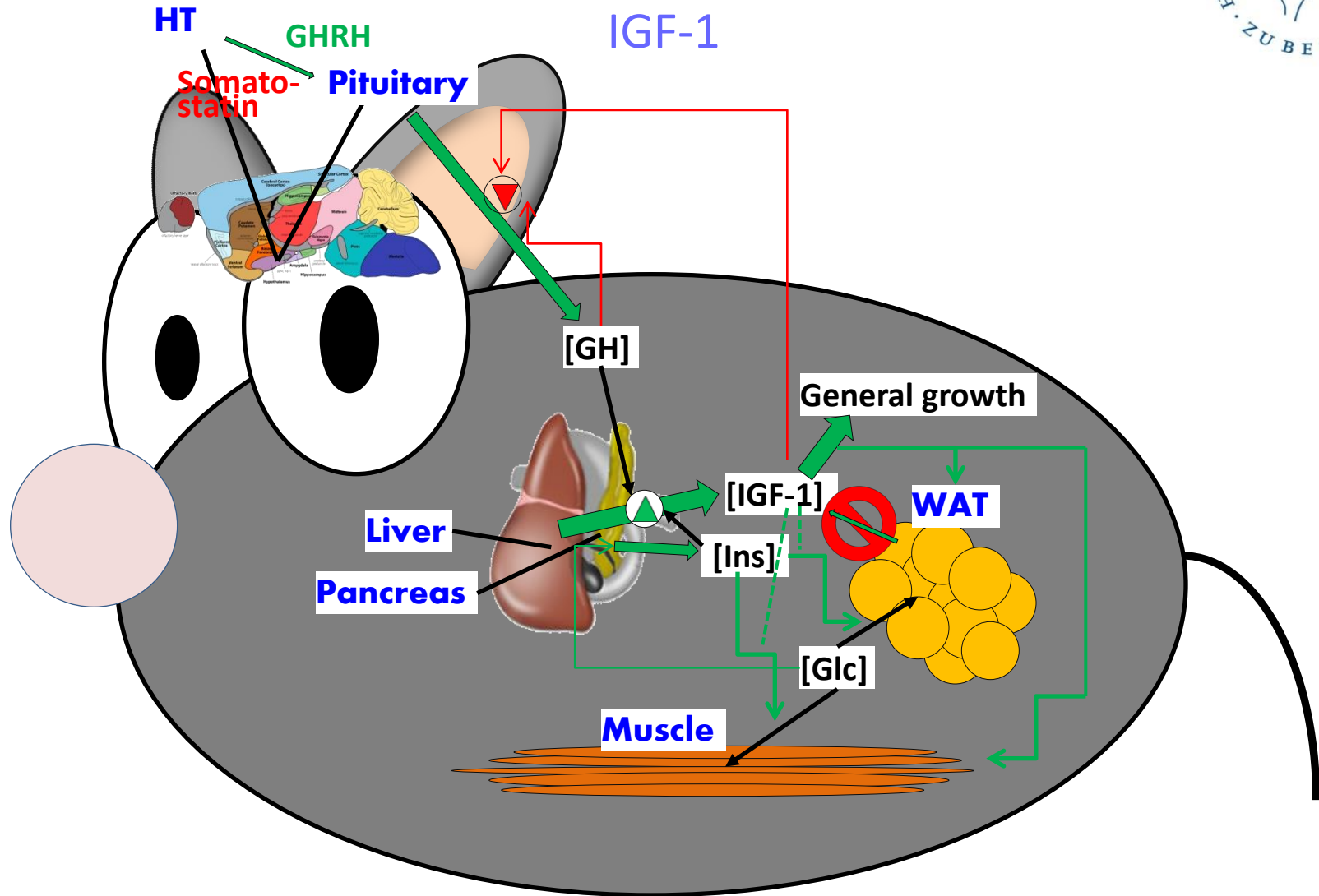
Humboldt Universität zu Berlin

Department of Crop and Animal Sciences

Breeding Biology and Molecular Genetics



Introduction

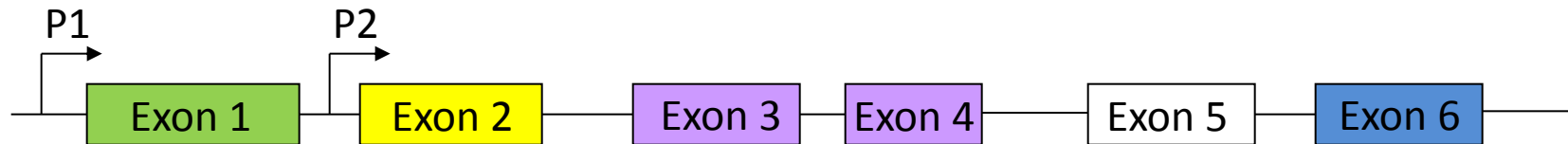




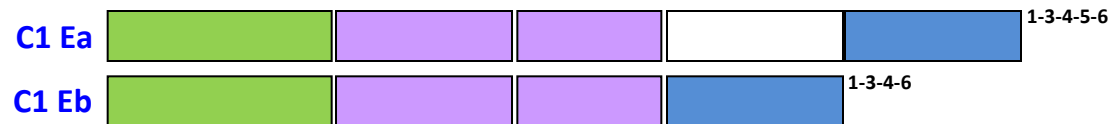
Introduction

IGF-1

- *Igf-1* gene in mice is located on chromosome 10 (~ 87,8 – 87,9 Mb)



- Class I transcripts



- Expression of **auto and paracrine** acting IGF-1

- Class II transcripts



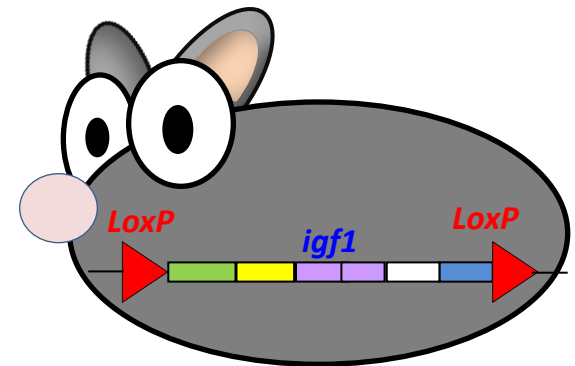
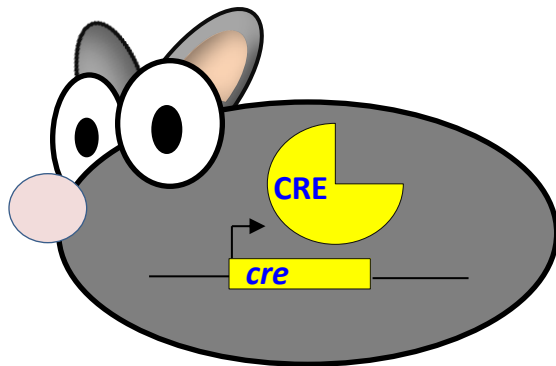
- Expression of **endocrine** acting IGF-1

Introduction

Cre-LoxP and Adipose Tissue specific KO of IGF-1

Requirements for adipose tissue specific IGF-1 KO:

- Cre : recombinase that cuts and merges DNA at specific sequences
- LoxP: sequence driven cutting targets of Cre
- aP2: Promotor specific for gene expression in Adipose Tissue (AT)

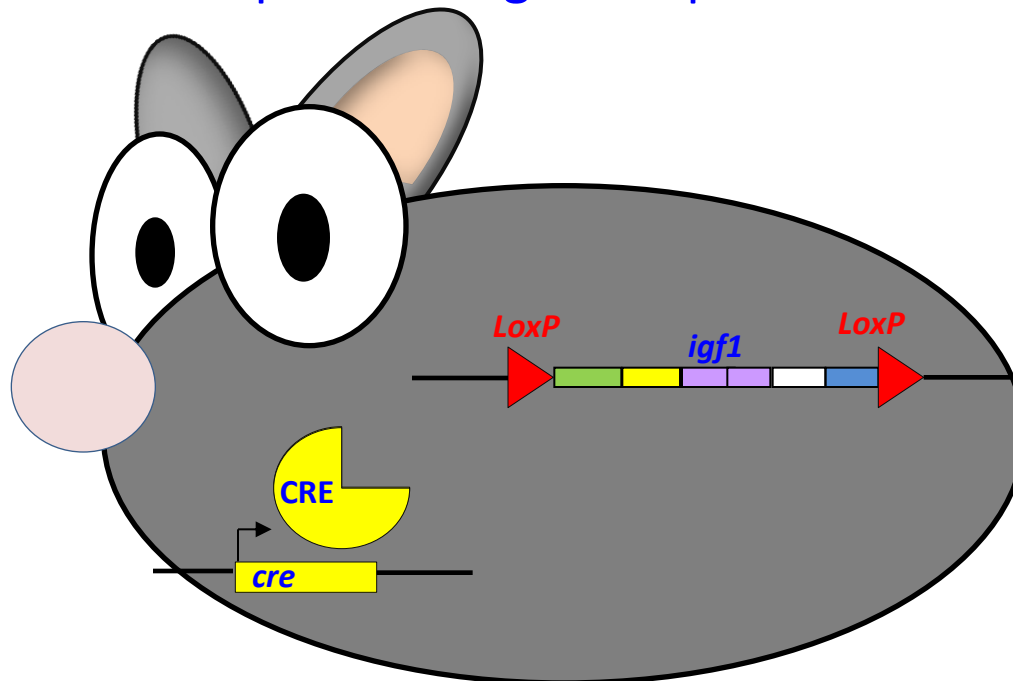


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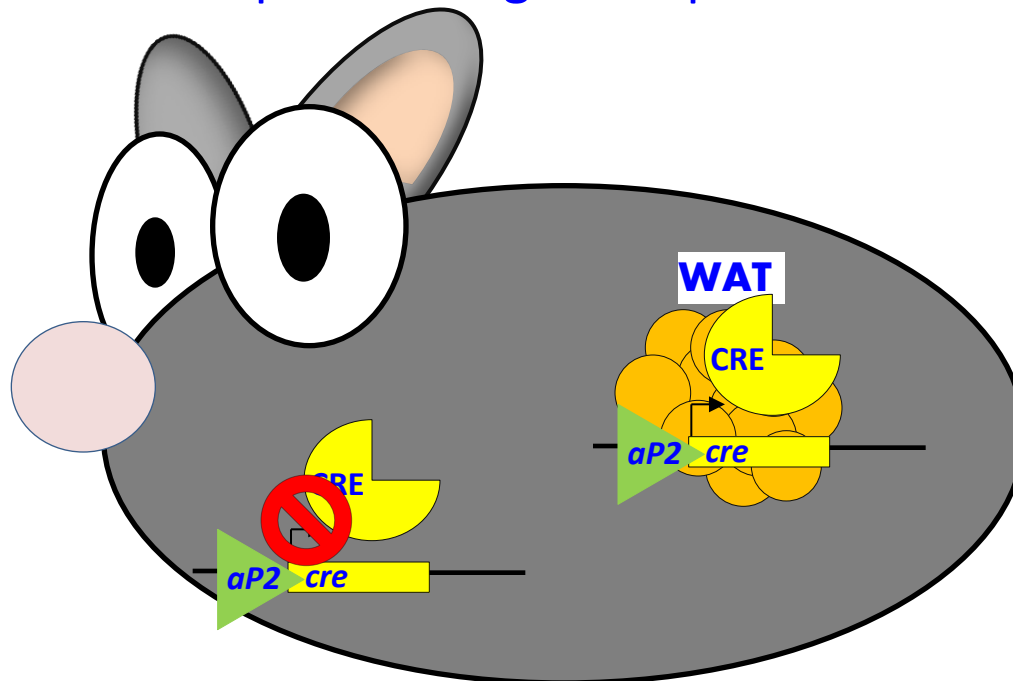


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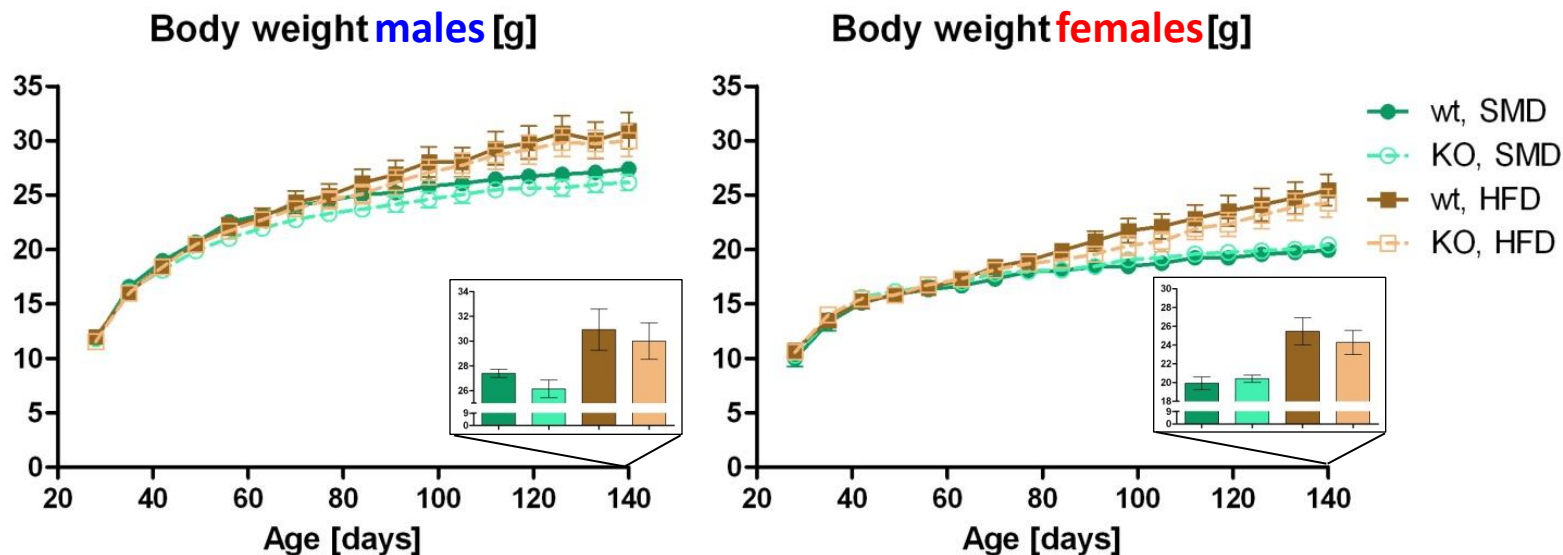
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Results on B6N

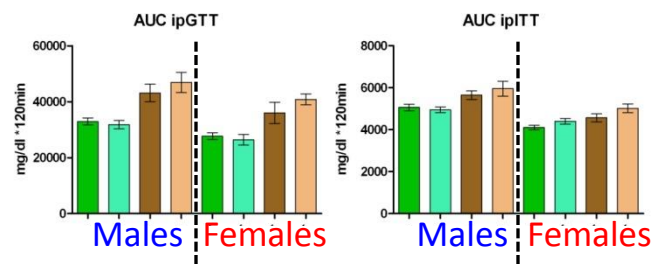
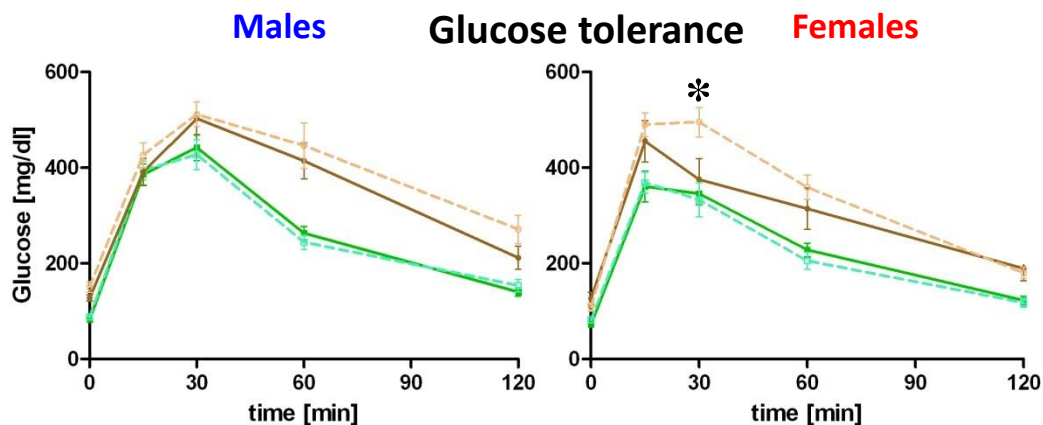
- Body weight
B6N wt vs. aP2 driven adipose tissue specific IGF-1 KO (AT-IGF1-KO)
on SMD and HFD



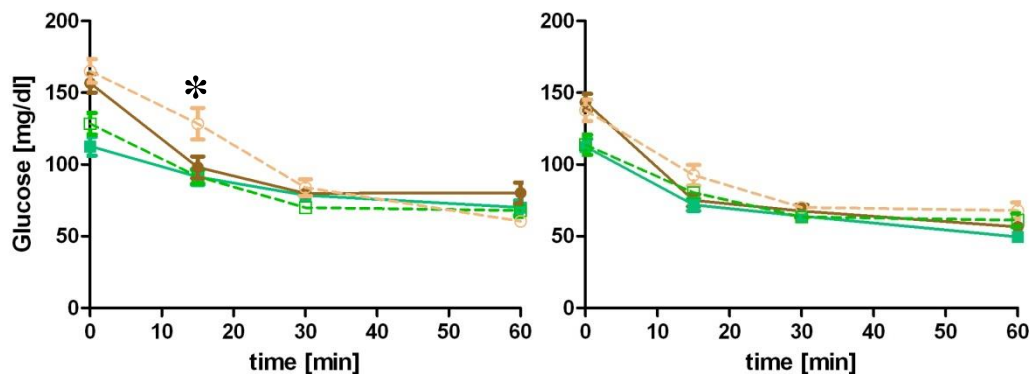
→ In AT-IGF1-KO mice no significant reduction of BW, LM, FM compared to wt.



Results on B6



Insulin tolerance

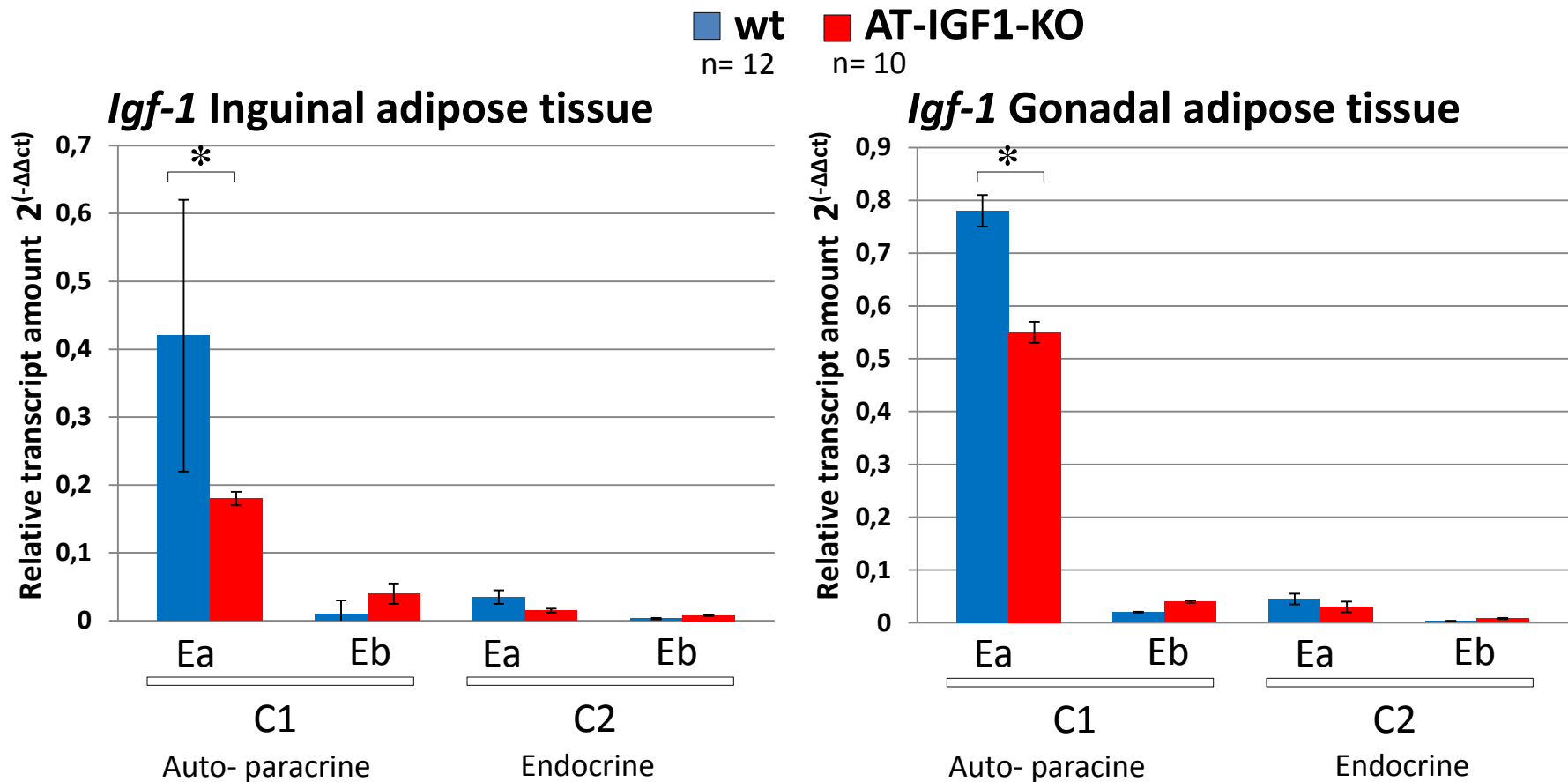


- AT-IGF1-KO **females**:
Glucose clearance is delayed on HFD.
- AT-IGF1-KO **males**:
No significant difference in insulin tolerance on HFD.



Results on B6N

aP2Cre generates only partial KO in adipose tissues



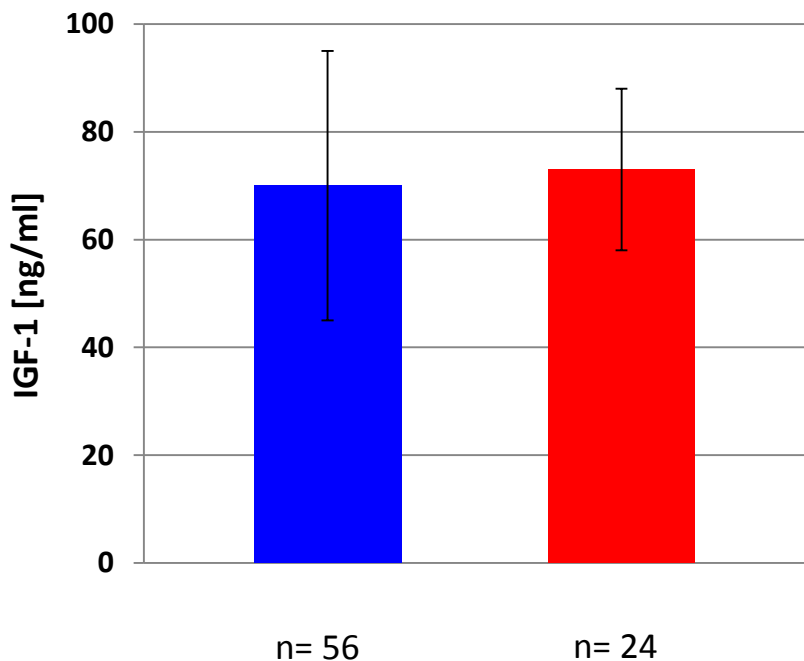
→ Autocrine *Igf-1* in adipose tissue reduced in AT-IGF1-KO



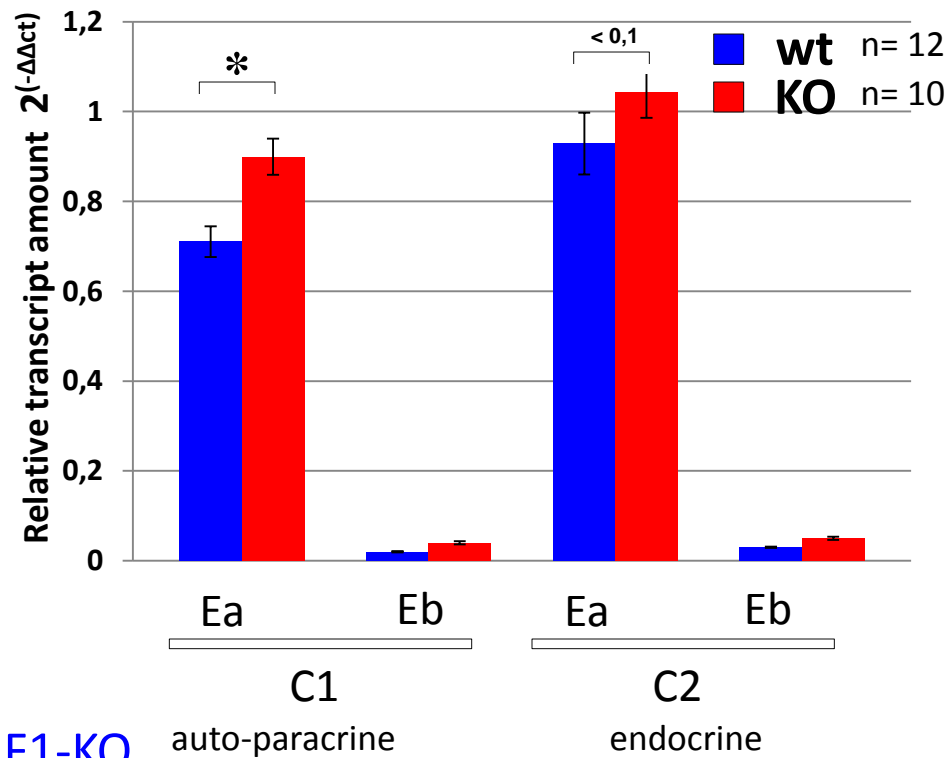
Results on B6N

■ wt ■ AT-IGF1-KO

IGF-1 Serum protein



***Igf-1* expression in liver**



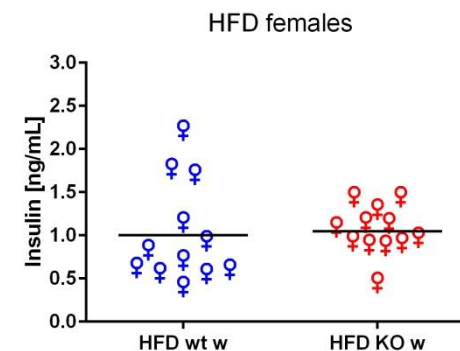
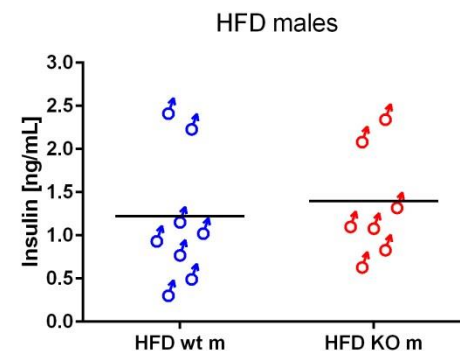
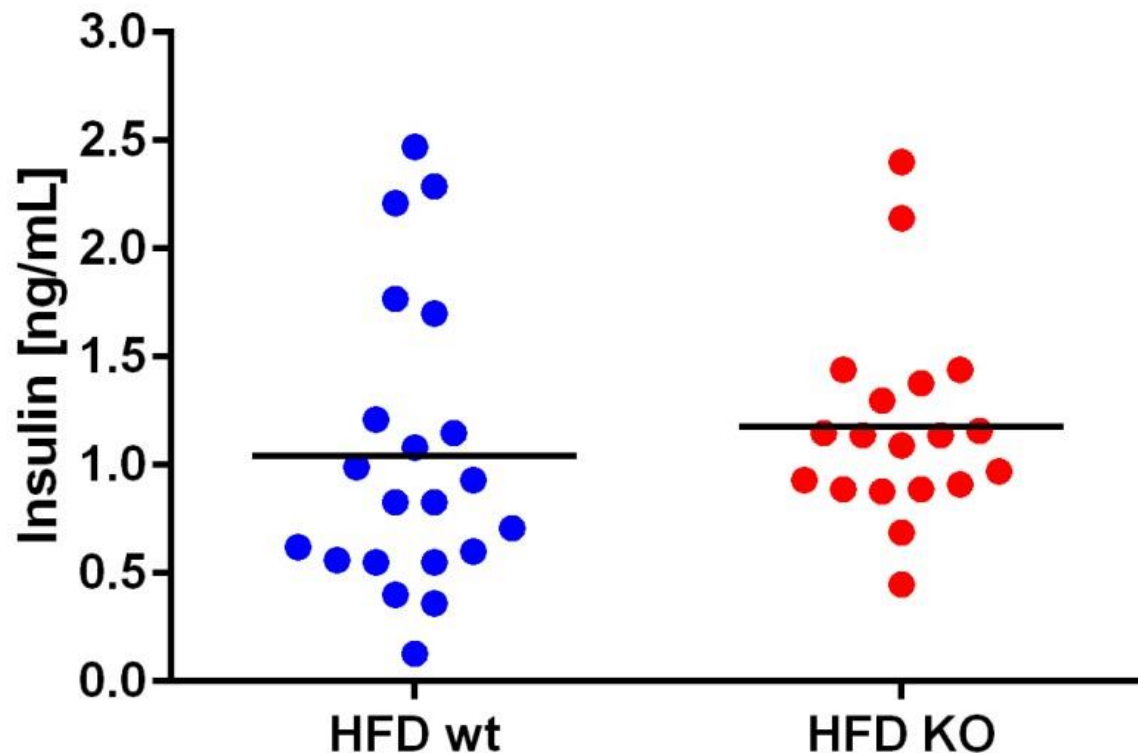
- Autocrine *Igf-1* in AT reduced in AT-IGF1-KO
- Liver *Igf-1* expression elevated in AT-IGF1-KO
- Serum IGF-1 unaltered



Results on B6N

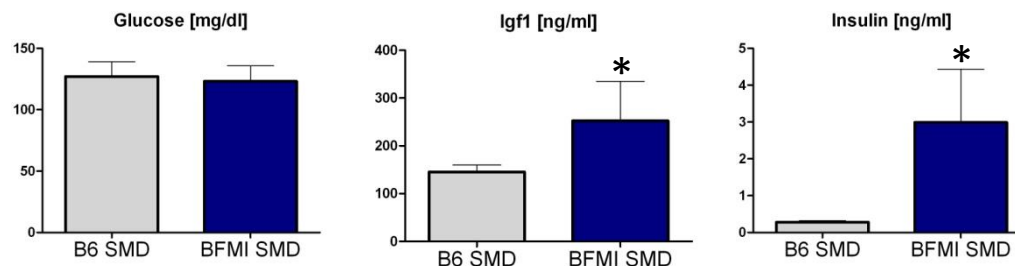
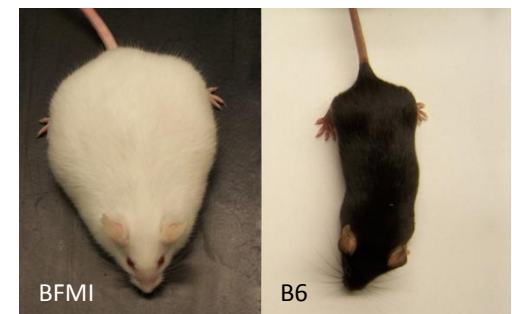
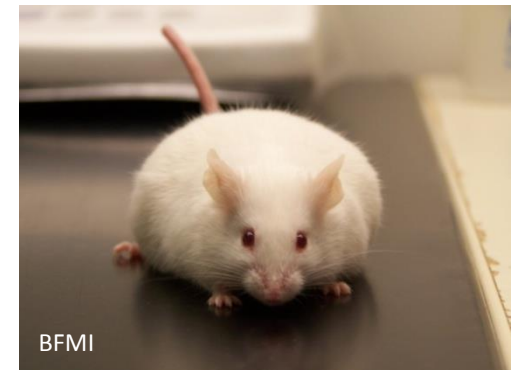
■ wt ■ AT-IGF1-KO

Serum Insulin HFD



AT-IGF1-KO in Berlin Fatmouse Inbred line

- Berlin Fat Mouse Inbred Line 860 (BFMI860)
- Higher body weight, body fat+ and lean mass compared to B6
 - general higher fat mass
 - lean mass marginally increased¹
 - in spite of high fatness
not deficient in blood glucose control^{2;3}
 - but high blood levels of insulin
 - and high blood levels of IGF-1



1: Wagener, Asja et al.; *Physiol Genomics* 27: 264–270, 2006
 2: Hantschel, Claudia et al.; *Obesity Facts* 4:270+277 2011
 3: Schäfer, Nadine et al.; *Growth Factors* 29(6):298+309, 2011

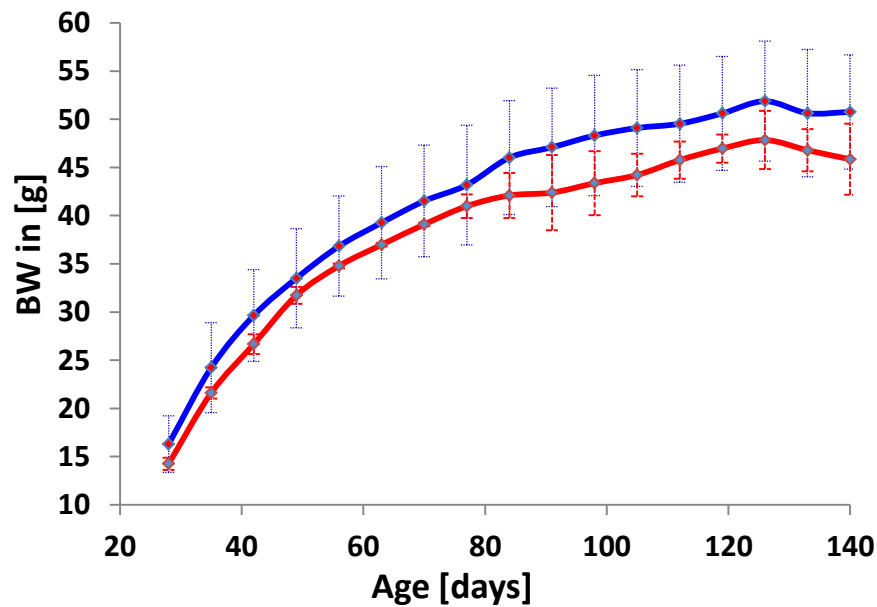
→ Hypothesis: Higher effect of AT-IGF1-KO on BFMI due to higher fat mass



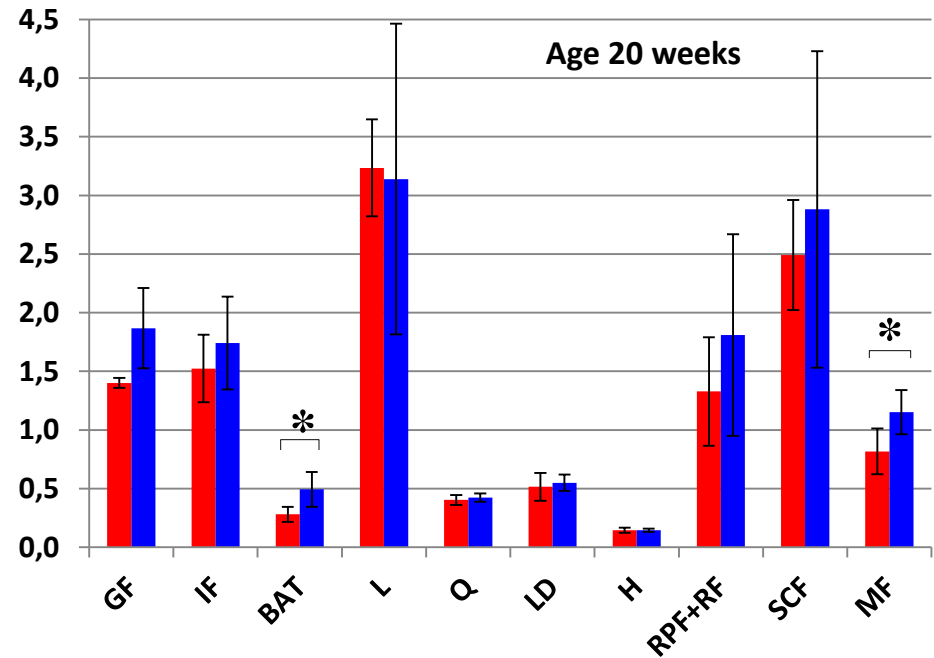
Results on BFMI

■ wt ■ KO
n=7 n=3

Body weight, males



Organ weights, males



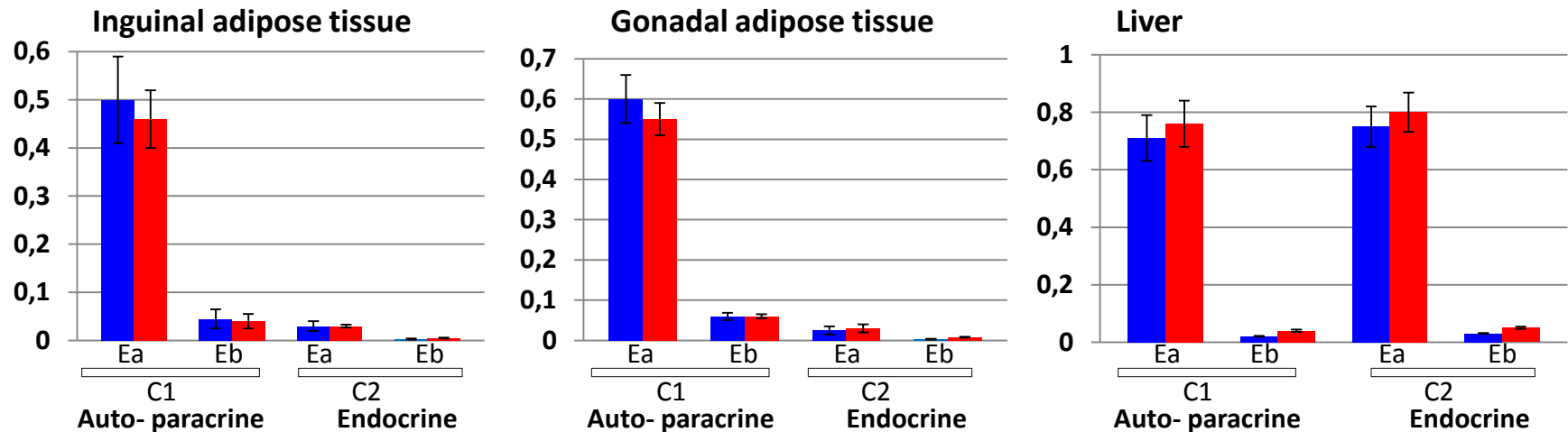
→ Trends similar to B6N, reduced organ weights in BFMI-KO, except for liver



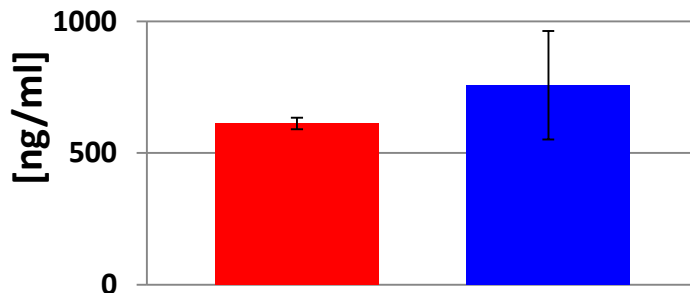
Results on BFMI

■ wt ■ KO
n=7 n=3

Igf-1 relative expression, males, 20 weeks



Serum IGF-1, males, 20 weeks



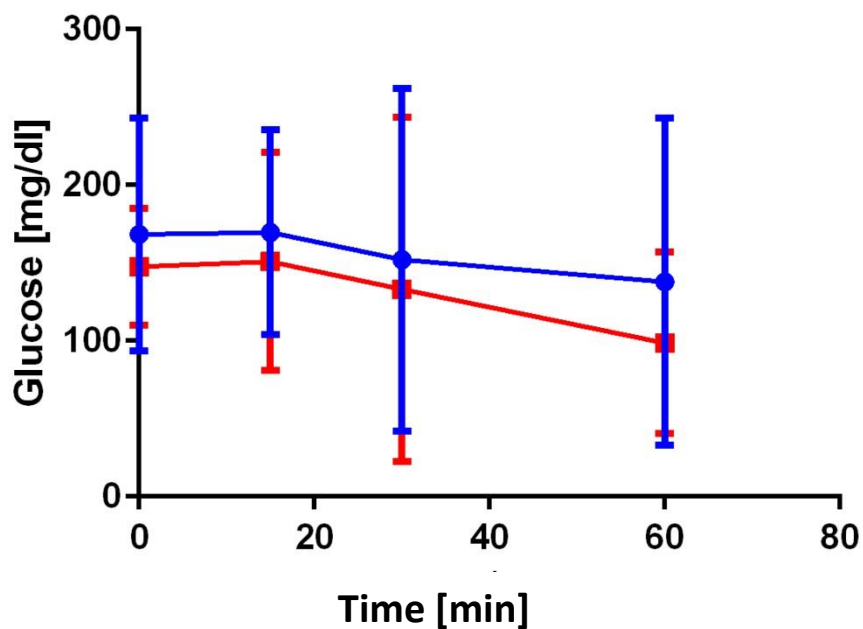
→ No significant differences in *Igf-1* expression or IGF-1 serum levels between KO and wt on BFMI background.



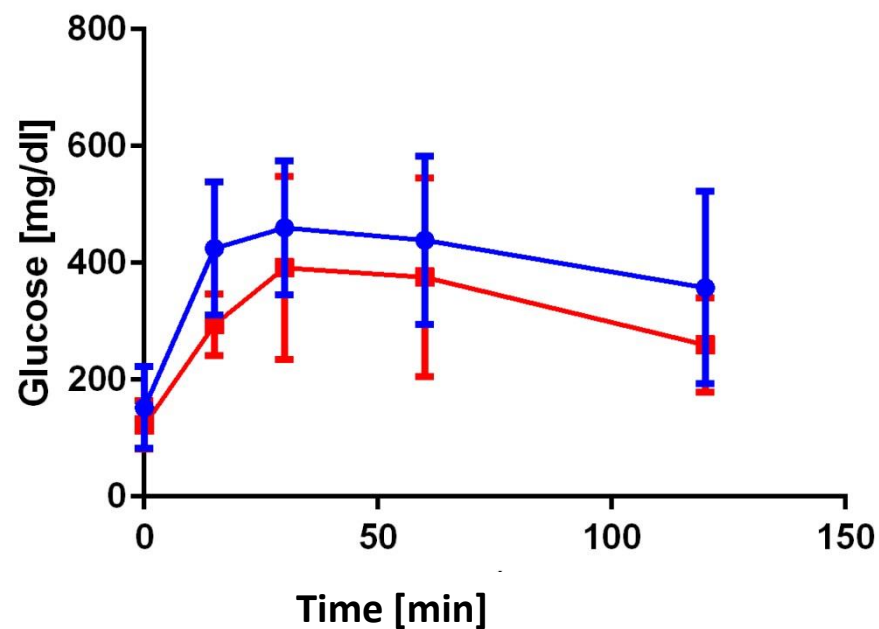
Results on BFMI

■ wt ■ KO
n=20 n=4

ipITT_BFMI_ap2



ipGTT_BFMI_ap2





Discussion/ Outlook

- **Results AT-IGF1-KO**
 - **KO of IGF1 occurs partialy in AT**
 - IGF1 produced in adipose tissue likely contributes to the regulation of glucose homeostasis
 - Effects in the first place on HFD and in fat mice compared to SMD
 - More animals and adipose tissue **wide KO** are needed to confirm the effects
 - A safe KO in the adipose tissue with **another Cre** mouse will be generated



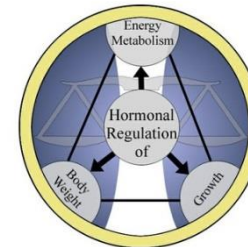
Aknowledgemends

Thanks to

GRK1208 and DFG for funding



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The mice being sacrificed for my researches

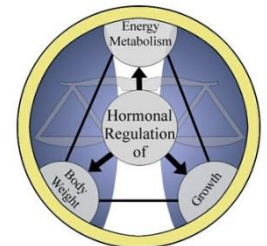


Acknowledgements

Thanks to the whole Group of Professor Brockmann

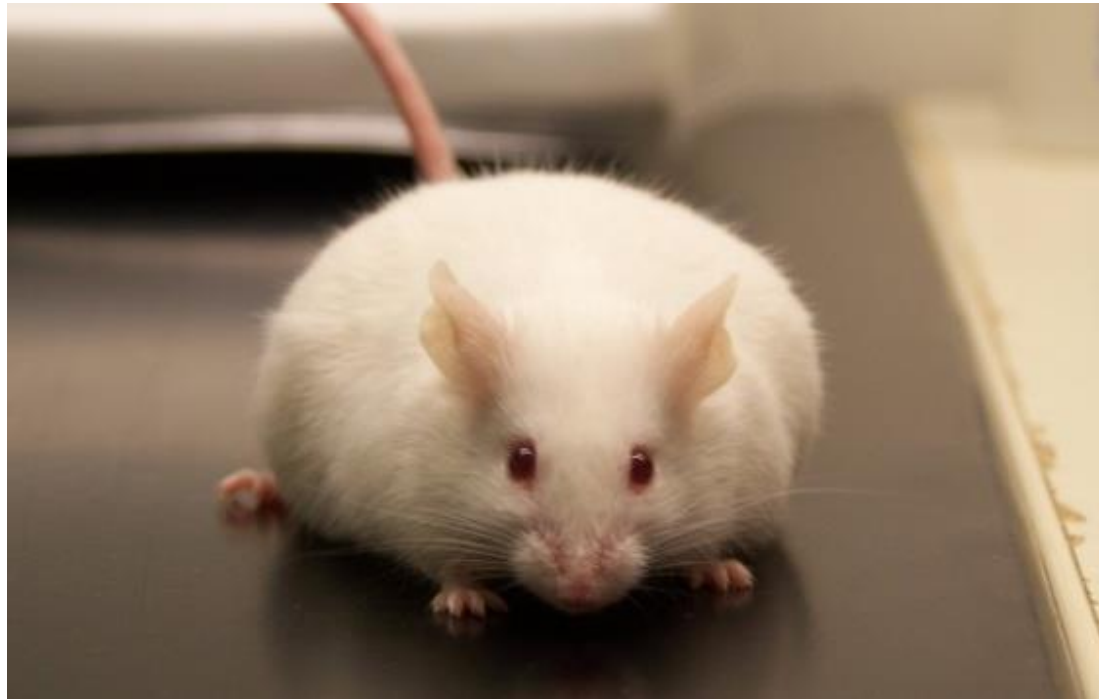


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Thank you for your attention



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