

# CIRCADIAN CYCLES IN BROWN ADIPOSE TISSUE

## Implications for postprandial triglyceride metabolism

### Introduction

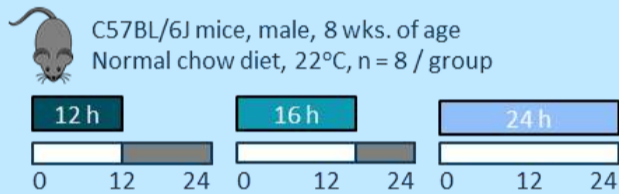
Brown adipose tissue (BAT) combusts triglyceride (TG)-derived fatty acids (FA) in order to produce heat<sup>1</sup>. Recent studies linked the control of the daily rhythm in body temperature and cold-adaptation of mice to circadian BAT activity<sup>2,3</sup>. Here, we hypothesized that circadian BAT activity is also responsible for the daily variations in fasting and postprandial lipid concentrations.

### Aim

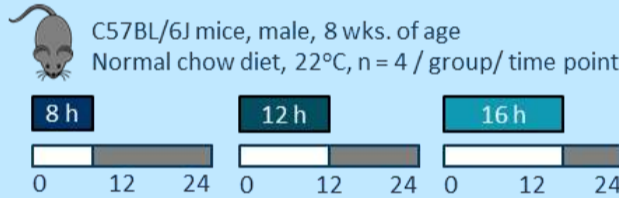
To investigate the involvement of circadian rhythms in BAT activity for (postprandial) lipid metabolism and delineate mechanisms underlying circadian BAT activity.

### Experimental Setup

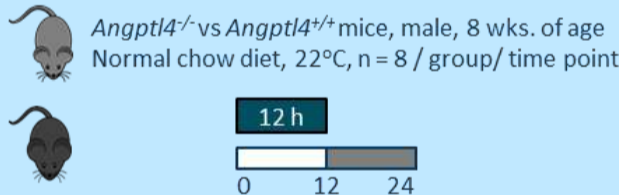
#### A. Metabolic effects of prolonged daily light exposure



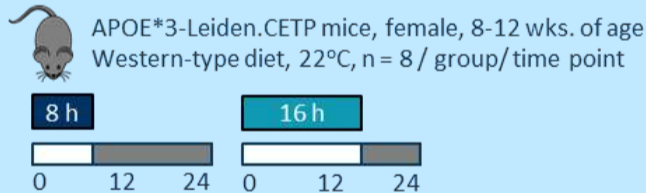
#### B. Circadian distribution of TG-derived FA



#### C. The role of angiotensin-like 4 (ANGPTL4) on BAT rhythmicity



#### D. Circadian fasted and postprandial lipids

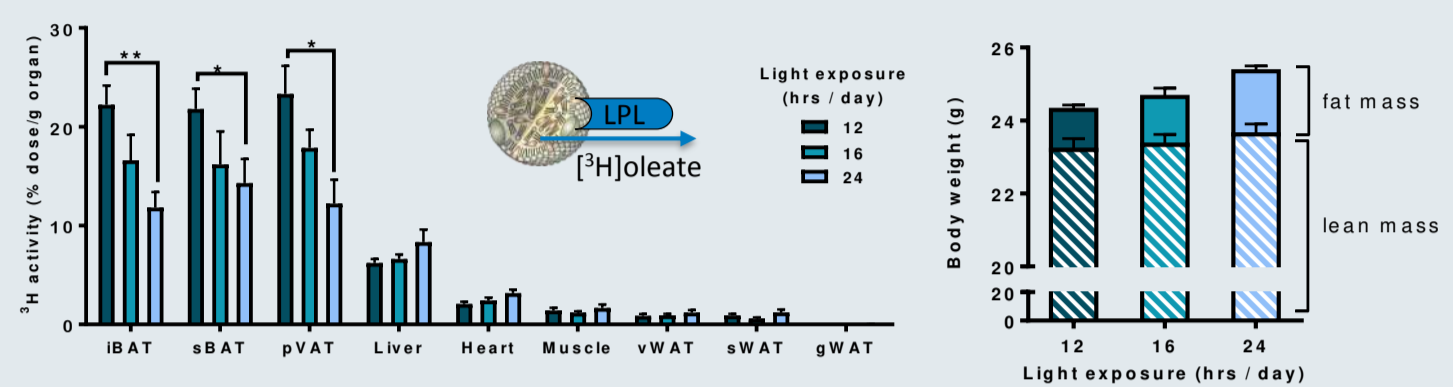


#### E. Circadian postprandial lipids in humans

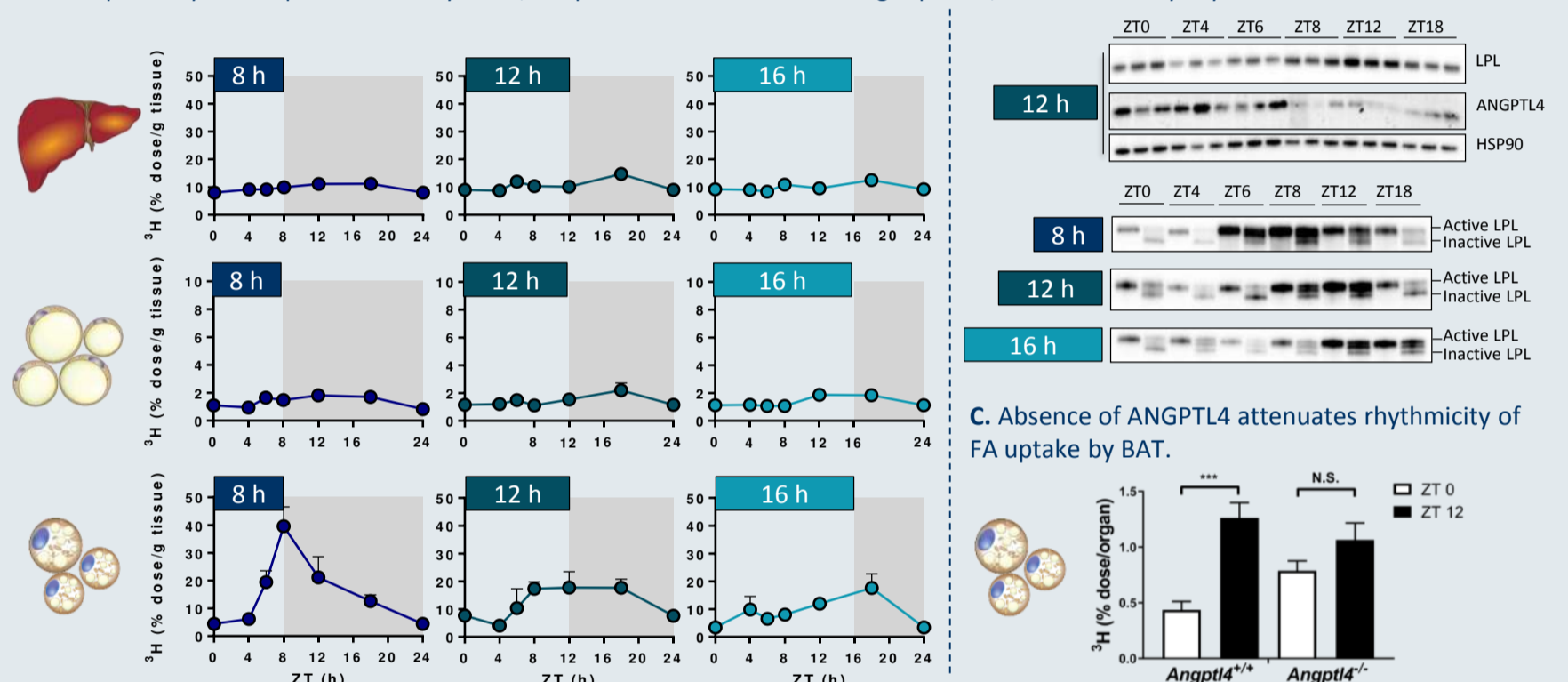
Offspring from nonagenarian siblings (n=19), and their partners as controls (n=18), were recruited from the Leiden Longevity Study. Participants received three isocaloric meals at 9:00h, 12:00h and 18:00h. Venous blood was drawn every 30 min.

### Results

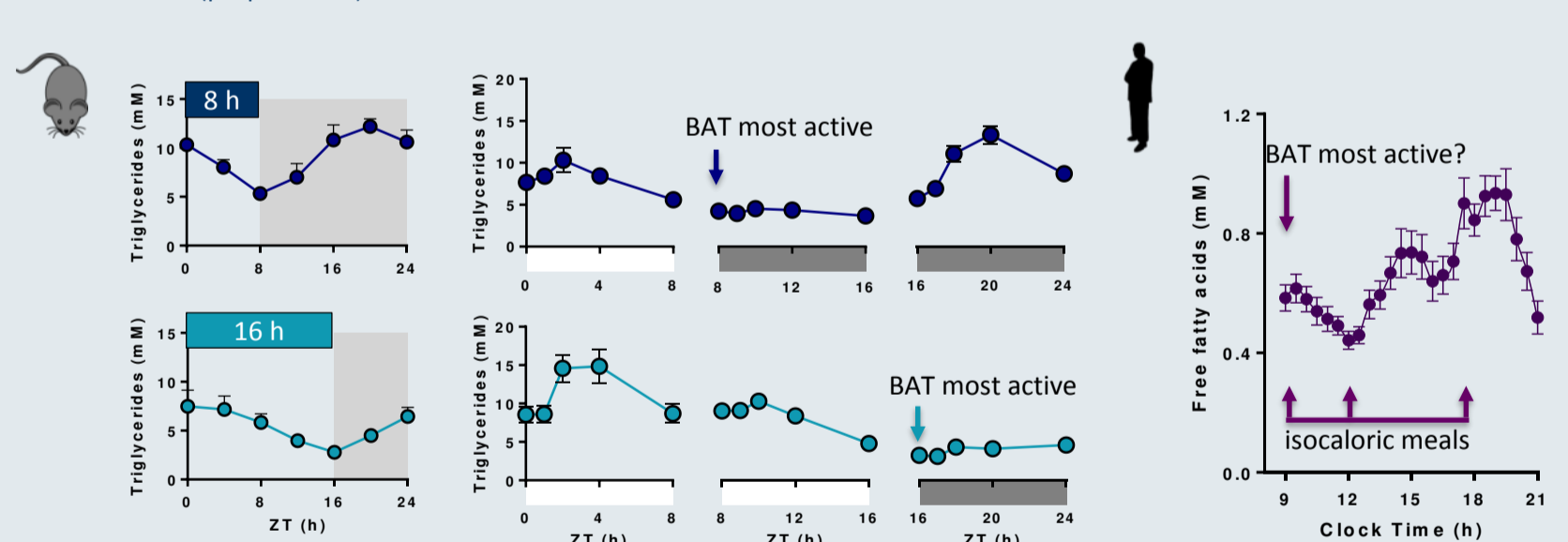
#### A. Prolonged light exposure decreases the uptake of TG-derived FA specifically by the BAT depots, resulting in body weight gain<sup>4</sup>.



#### B. FA uptake by BAT in particular is rhythmic, adapts to the duration of the light period, and is driven by rhythms in LPL and ANGPTL4<sup>5</sup>.



#### D-E. Circadian BAT activity imposes a rhythm in fasted and postprandial triglyceride levels of mice (blue/green curves) and possibly also in humans (purple curve)<sup>5</sup>.



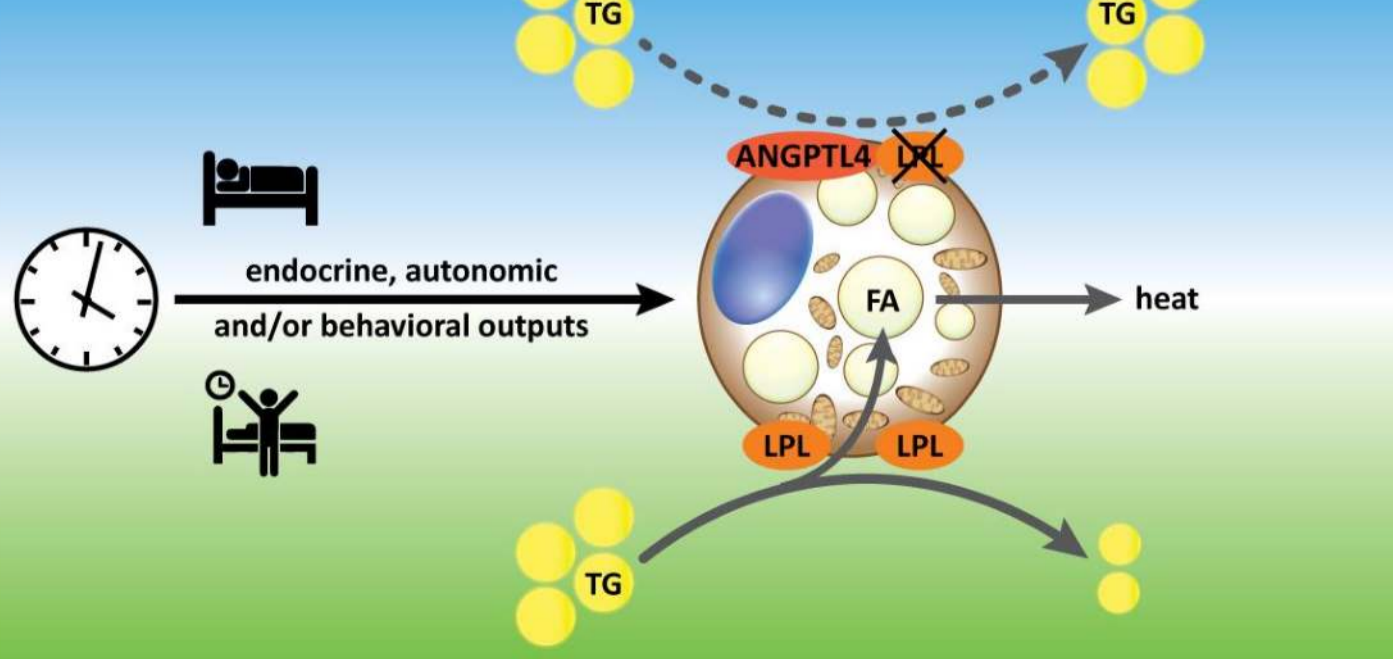
### Conclusion

- Prolonged light exposure affects the uptake of TG-derived FA by BAT specifically, leading to weight gain.
- BAT shows a high amplitude diurnal rhythm in the uptake of TG-derived FA, likely mediated by LPL and ANGPTL4, with highest uptake at the onset of the dark period.
- Circadian BAT activity determines differences in (postprandial) TG metabolism throughout the daily light-dark cycles in mice and possibly also in humans.

### Implications

BAT activity is highest at waking, accompanied by low postprandial lipid excursions. We anticipate that restriction of food intake to the early wakeful period improves metabolic health mediated by circadian BAT activity.

### Work model



### References

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- Chappuis, S. et al. *Mol. Metab* 2, 184-193 (2013).
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