

## Response

### To best mimic human thermal conditions, mice should be housed slightly below thermoneutrality



We agree with Fischer et al 2019 [1] that there are some points of similarity between our data sets (our paper with data is [2], paper of Fischer *et al.* is [3]). Although rounding the PAL values at 30 °C to one decimal place tends to minimize the differences. However, we did not recommend a temperature of 27.2–29.1 °C, as is stated in the legend of Figure 2 (of [1]). These were the results of our 12 min readings, but it was not our recommendation. Our recommendation was: 'Given the observed ratio of DEE to BMR of 1.7 at 27.6 °C and 1.8 at 25.5 °C, we suggest that this is the best temperature range for housing C57BL/6 mice to mimic human thermal relations' [2].

To clarify how we reached this conclusion. We consider BMR of 1.7–1.8x most appropriate. Second, we think a 24 min reading is most appropriate, because this is similar to that used in human measurements of BMR. Since, the average at 1.8x BMR is 25.5 °C and the average at 1.7x BMR is 26.7 °C, this is what we advocated [2]. It is important to note that this is below thermoneutrality. Hence, we do not advocate thermoneutral as the best translational housing temperature as the suggestion there is agreement between our datasets implies. This also fits with the data showing that humans also routinely live below thermoneutrality, an argument this is ignored by Fisher, Cannon, and Nedergaard [1,3].

There are several further mistakes in Figure 2 (of [1]): Regarding the Zone proposed by Speakman and Keijer [4], it would be better to state this zone as 23–25 °C, since that is what we proposed (in [4]) for single housed mice, and that is what all the other zones in Figure 2 (of [1]) refer to. The extended zone down to 20–22 °C was for group housed mice in different housing conditions. The implication from the diagram is that we advocated 20–22 °C for single housed mice, which we did not. The new zone is also not the zone we proposed. This should be 25.5–27.6 °C, if it is to be called zone proposed by Keijer, Li and Speakman [2]. The zone advocated by Fischer et al. (2018), which is indicated as 28–30 °C, is also incorrect because they did not advocate that. They advocated 30 °C which was one of the only 2 temperatures they measured [1]. In conclusion, mice should be housed slightly below thermoneutrality to best mimic humans thermal conditions.

### CONFLICTS OF INTEREST

None declared.

## REFERENCES

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Available online 28 May 2019