1-S12 Symposium12

Toward clinical application of torpor: active hypometabolism research in mice

Genshiro Sunagawa

BDR, RIKEN

Some mammals enter a hypometabolic state either daily torpor (minutes to hours in length) or hibernation (days to weeks), when reducing metabolism would benefit survival. The metabolic rate drops to 1～30% of normal rates, and animals sacrifice their vital biological functions such as consciousness and mobility to save metabolism, which makes them look offline. The mechanisms for such hypothermia-resistance and hypometabolism-resistance is not understood.

Hibernators demonstrate deep torpor by reducing both the sensitivity (H) and the theoretical set-point temperature (T_R) of the thermogenesis system, resulting in extreme hypothermia close to ambient temperature (T_A). We have developed a stable torpor induction method for mice and evaluated minimal body temperature (T_B) and oxygen consumption rate (VO_2) of fasting-induced torpor in C57BL/6J mice (B6J) under various T_As. As in hibernators, H decreased 91.5% during daily torpor while T_R only decreased 3.79 ° C in mice (Sunagawa GA and Takahashi M, *Sci Rep*, 2016). Furthermore, we have found that C57BL/6N (B6N) has a higher metabolic rate during torpor than B6J (GA Sunagawa, 2018, *BioRxiv* 374975).

Interestingly, in both B6J and B6N mice strains, H is decreased as hibernators, but T_R remains relatively unchanged during daily torpor. To investigate whether the stable T_R during torpor is a common feature in mice, we have evaluated various inbred strains and found that in some strains, T_R may be reduced than B6J or B6N mice. Because T_R is suspected to be controlled centrally in mammals, we are attempting to control T_R by stimulating the central nervous system.