Review

MOLECULAR METABOLISM

Not so hot: Optimal housing temperatures for mice to mimic the thermal environment of humans

J.R. Speakman [1,2,*], J. Keijer [3]

ABSTRACT

It has been argued that mice should be housed at 30 °C to best mimic the thermal conditions experienced by humans, and that the current practice of housing mice at 20–22 °C impairs the suitability of mice as a model for human physiology and disease. In the current paper we challenge this notion. First, we show that humans routinely occupy environments about 3 °C below their lower critical temperature (T_{lc}), which when lightly clothed is about 23 °C. Second, we review the data for the T_{lc} of mice. Mouse T_{lc} is dependent on body weight and about 26–28 °C for adult mice weighing >25 g. The equivalent temperature to that normally experienced by humans for most single housed adult mice is therefore 23–25 °C. Group housing or providing the mice with bedding and nesting material might lower this to about 20–22 °C, close to current standard practice.

Keywords Mouse; Human; Lower critical temperature; Thermoneutral; Thermoregulation; Ambient temperature

1. INTRODUCTION

The mouse is the model of choice for understanding the genetic basis of human disease. Recommendations on the housing temperature cover a substantial margin, being between 20 and 26 °C [8], 20 and 24 °C [22] or 19 and 23 °C [7]. Most mouse facilities however are operated at an ambient temperature of 20–22 °C, which is set primarily to match the comfort requirements of animal husbandry staff [27]. Mice have a different thermoregulatory response curve from humans, and the argument has been made that this housing temperature is not optimal to provide the best model for human metabolism or disease. In particular, it is argued that humans normally live at thermoneutral temperatures, while the thermoneutral zone of the mouse is at 30 °C, so laboratory mice at 20–22 °C are routinely under mild to moderate cold stress, because they are 8–10 °C colder than the equivalent temperature in humans [4,5,11,36,47]. It has been suggested that this persistent cold stress profoundly affects mouse physiology in ways that impair its suitability as a model for human physiology and disease [27]. The recommendation has therefore been made that studies of mice should optimally be made at 30 °C, within the mouse thermoneutral zone, to best facilitate comparisons to humans ([4,5,11,31,36]—but see [49] for some practical problems with this recommendation).

Perhaps the best recent example, among metabolic studies, of the importance of ambient temperature in determining a significant outcome variable was the finding that the effects of genetic ablation of the uncoupling protein 1 (UCP-1) were strongly dependent on ambient temperature. Enerbäck et al. [10] showed that UCP-1 KO mice on a mixed genetic background of C57BL/6 and sv129 mice, when housed at 21 °C, were cold intolerant but did not become any more obese than wild type mice when fed a high fat diet. When these UCP-1 KO mice were back-crossed onto a pure B6 background, however, they were actually resistant to weight gain when raised on a high fat diet at 21 °C, relative to wild type mice that had intact UCP-1 [30]. At 27 °C this difference was abolished [30]. Moreover, when UCP-1 KO mice on a pure B6 background were observed at 30 °C, they became obese, even when fed chow, and substantially more obese than wild-type mice when fed a high fat diet [12]. Hence there was a complete spectrum of responses in these mice, from protection against high fat diet induced obesity at 21 °C, to no effect at 27 °C and finally susceptibility to obesity at 30 °C. A less publicised example was the observation that ovariectomised mice become obese [52] but this effect was attenuated at 30 °C [6]. However, there are many previous examples, notably from the fields of immunology and parasitology that show ambient temperature is a key variable influencing the ability of mice to fight off infections or mount a response to lipopolysaccharide injections (reviewed in [27]). Temperature also affects chemical toxicity. One example is the U shaped curve of the lethal dose of salicylate at different temperatures, with a minimum around 25 °C [2]. Various other compounds show either increased or decreased toxicity with increasing temperature. Moreover, core body temperature can be differently affected by, for example, ethanol, depending on the environmental temperature [13,32]. Indeed temperature affects many aspects of mouse physiology, reproduction and behaviour [44,53]. Clearly housing temperature affects the outcome of many experiments, and analysis at different ambient temperatures may reveal important aspects of mechanisms that studies at single temperatures cannot, as is exemplified by the different responses to a high fat diet of mice without UCP-1, at different ambient temperatures [10,12,30]. A key

[1]Key State Laboratory of Molecular Developmental Biology, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Chaoyang, Beijing 100101, People's Republic of China [2]Institute of Biological and Environmental Sciences, University of Aberdeen, Aberdeen AB24 2TZ, Scotland, UK [3]Human and Animal Physiology, Wageningen University, Wageningen, The Netherlands

*Corresponding author at: Key State Laboratory of Molecular Developmental Biology, Institute of Genetics and Developmental Biology, Chinese Academy of Sciences, Chaoyang, Beijing 100101, People's Republic of China. Email: J.speakman@abdn.ac.uk (J.R. Speakman).

Received September 26, 2012 • Revision received October 10, 2012 • Accepted October 16, 2012 • Available online Month XX, 2012

http://dx.doi.org/10.1016/j.molmet.2012.10.002

 © 2012 Published by Elsevier GmbH.

Review

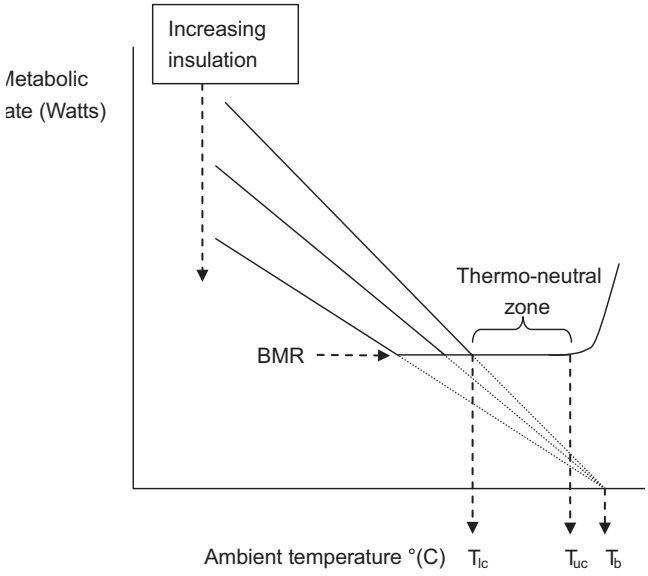

Figure 1: The classical Newtonian cooling model for an endotherm (after [40]).

question, however, is which ambient temperature allows for the most optimal translation of mouse data to humans and hence maximises the suitability of the mouse model (see also discussion of this issue with respect to temperatures at which experiments should be performed on rats: [39]).

The suggestion that mice should be housed at 30 °C is based on two main arguments. First, humans normally live almost continuously at thermoneutral temperatures, and second 30 °C in mice is thermoneutral. We challenge here the idea that mice should optimally be held at 30 °C to best mimic human thermal physiology. We agree that attempting to mimic human thermal physiology in the mouse is a good idea to maximise its utility as a model for human physiology and disease. Our argument is based on the derivation of equivalent ambient temperatures, relative to the thermoregulatory curves for humans and mice, which suggests to us that the optimal temperature to achieve this aim is not 30 °C.

The classic thermoregulatory curve for an endotherm is shown in Figure 1 (after [40]). The thermoneutral zone is the region where basal energy expenditure generates more than enough heat to balance heat losses due to the difference between ambient (T_a) and body temperatures (T_b). At the lower margin of this region (called the lower critical temperature or T_{lc}) heat requirements to maintain T_b and basal metabolic rate are exactly matched. At higher temperatures basal metabolic rate provides too much heat and this needs to be dissipated. Generally this is achieved by elevating evaporative water loss. At some upper critical temperature (T_{uc}) however other mechanisms need to be recruited and these paradoxically require an elevation of metabolism. Below T_{lc} metabolic rates must be higher than basal levels to balance heat loss, hence metabolic rate increases linearly as temperature declines and the gradient of this relationship reflects the degree of external insulation. Greater levels of external insulation lower the gradient of this line and hence also lower T_{lc}. These curves extrapolate on the x-axis to body temperature.

The thermoregulatory curve for naked humans has a lower critical temperature averaging about 28 °C (Table 1). Providing light clothing increases external insulation, lowers the gradient of the thermal response line and lowers the lower critical temperature. Light clothing such as would typically be worn indoors consisting of a long sleeved shirt or blouse (Clo = 0.2) and light trousers (Clo = 0.25) provide together 0.45 Clo units of insulation [54]. The effect of such clothing would be to lower the lower critical temperature by 5.1 °C (using the correction equation for clothing on T_{lc} in [28]). This results in a lower critical temperature of 22.9 °C. Humans, however, seldom operate at basal metabolic rate. Studies using doubly labelled water show that routinely our energy expenditure is about 1.6–1.8 × basal requirements [3,46]. If we lived at our lower critical temperature defined from basal metabolism, we would be under continuous mild heat stress, so we normally seek out cooler temperatures than thermoneutral, where our routine heat production is balanced by a thermal gradient that generates an equivalent heat loss. This is why buildings are regulated at 19–21 °C (about 3 °C below the lower critical temperature) rather than within the thermoneutral zone (which for a lightly clothed individual is 23–27 °C). The UK Workplace (Health, Safety and Welfare) regulations 1992, for example stipulate that rooms should ideally be maintained at 19–21 °C to provide a comfortable working environment. Although it is routinely stated that in mice 30 °C is thermoneutral (after [18]). Figure 1 emphasises that 'being thermoneutral' is not the same as being at the lower critical temperature. In fact Gordon [18] cites the thermoneutral zone as spanning from 26 to 34 °C in mice. A review of some estimates of T_{lc} in mice is shown in Table 2. There is a strong negative relationship between T_{lc} and body weight (Figure 2). For adult mice weighing > 25 g the T_{lc} is about 28 °C. The predicted T_{lc} for mice weighing 40 g is 25.7 °C. Consequently, if we want to keep mice at an equivalent temperature to that routinely occupied by free-living

Reference	T_{lc} (°C)
[9]	27
[21]	30
[51]	29
[41]	27
[15]	27
[38]	27
[28]	28.6
Average	28

Table 1: Some estimates of lower critical temperature (T_{lc}) in naked humans.

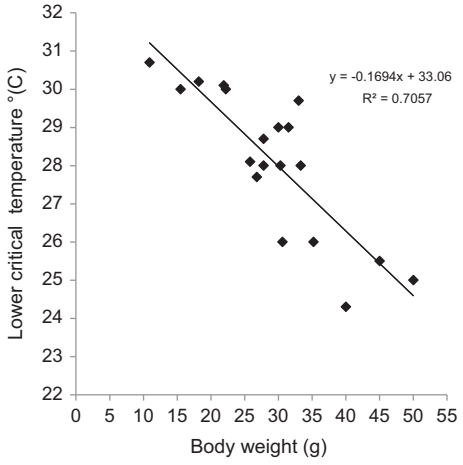

Figure 2: Lower critical temperatures of some mouse strains plotted against body weight. There was a strong and significant negative relationship (for data sources see Table 1).

 © 2012 Published by Elsevier GmbH.

MOLECULAR METABOLISM

Strain	BM (g)	T_{lc} (°C)	Reference
–	–	28.5	[48]
Hairless	–	29	[1]
–	–	25	[24]
Hairless	32.8	32	[35]
LACA	31.5	29	[37]
Wild	15.5	30.0	[26]
FVB	33.0	29.4	[29]
DTA-UCP	54.7	29.7	[29][a]
MF1	33.3	28.0	[45]
MH	30.3	28.0	[42]
ML	27.8	28.0	[42]
C3HeB/FeJ	27.8	28.7	[34]
Sma1 (+/−)	18.2	30.2	[34]
Sma1 (−/−)	10.9	30.7	[34]
TR-KO	22.2	30.0	[17]
Mixed	30.6	26.0	[17]
C57BL/6	30.0	29.0	[25][b]
Ob/Ob (6)[c]	~45	25.5	[25][b]
Ob/Ob (10)[c]	~50	25.0	[25][b]
Db/Db	40.0	24.3	[25][b]
Trpv1 KO	45.0	32.5	[14][d]
WT	40.0	31.5	[14][d]
C57BL/6[e]	21.9	30.1	[33]
C57Bl/6	26.8	27.7	[33]
C57BL/6[f]	25.8	28.1	[33]
MF1	35.2	26.0	[43]

Table 2: Some estimates of lower critical temperatures (T_{lc}) in different mouse strains. [a] UCP diphtheria toxin A mice with impaired thermoregulatory function. [b] Precise weights not given. [c] (6) and (10) refer to weeks old. [d] Measured using the thermal camera method. Not comparable to other data. [e] Under caloric restriction. [f] Fed rapamycin.

humans (3 °C lower than T_{lc}), this equates to an ambient temperature of 23–25 °C.

While this calculation is arithmetically equivalent it assumes that the thermal responses of mice and humans are proportionally the same. That is it assumes a reduction of temperature by 3 °C has the same impact on a mouse as a human. Another way to approach this calculation is to calculate how much of a reduction in ambient temperature below the lower critical temperature in the mouse would be necessary to increase the metabolic rate from basal to 1.7 × basal (the average level of energy expenditure in free living humans: [3,46]). Using the published thermoregulation curves in some of the papers cited in Table 2 we have made this calculation and the results are shown in Table 3. These data suggest that to increase metabolic rate to 1.7 × BMR the temperature would need to be on average about 6.3 °C below the lower critical temperature. Consequently, this might suggest it would be most appropriate to keep mice weighing 25–40 g at ambient temperatures of 19.4–21.7 °C. However, this is probably an overestimate because the value of 1.7 × BMR for humans is based on our total daily energy demands, including periods when we are physically active and outdoors, while the temperature we regulate our buildings at (3 °C below lower critical) is geared towards balancing heat production during light activities such as sitting, computer use, preparing and having lunch and visiting the rest-room etc. If we use a value of 1.3–1.4 × BMR for these activities [50] then the equivalent reduction in ambient temperature below lower critical temperature, to generate a 1.3–1.4 fold increase in metabolism, is a reduction by 2.7–3.6 °C. This suggests the estimate of 23–25 °C as an equivalent temperature at which solitary mice should be housed to mimic humans is probably appropriate.

[1]		6.0 °C
[48]		5.0 °C
[24]		8.0 °C
[37]		9.5 °C
[29]		4.4 °C
[34]		6.0 °C
[17]		7.0 °C
[26]		7.5 °C
[42]	high	6.1 °C
	low	5.5 °C
[43]		4.0 °C
Mean		6.27 °C
Sd		1.62 °C

Table 3: Approximate reductions in ambient temperature below the lower critical temperature that would be necessary to achieve an increase in metabolism from basal to 1.7 × basal in various studies of mice. For details of studies and strains refer to Table 2.

The estimates of T_{lc} for mice are based on respirometry measurements of solitary mice in respirometry chambers. Two common aspects of housing that are normally absent in such measures might further lower this estimate of the optimal housing temperature to mimic human physiology. First, mice that are group housed can huddle together to lower their thermoregulatory requirements [19,20]. This effectively lowers the T_{lc}, in part because of the reduced combined surface area [23]. Similarly, providing mice with bedding or nesting material acts as additional insulation which shifts the position of the thermoregulatory response line (see Figure 1) also lowering the T_{lc} [20]. This might further lower the optimal temperature. However, it is difficult to estimate to what extent, since mice will adapt their behaviour to the environmental temperature. Depending on the temperature, they will or will not bury themselves in bedding and nesting material or huddle together [16,20]. Consequently, this may suggest that the optimal housing temperature for comparison to humans of 3 °C below T_{lc} (23–25 °C) may be further decreased to as low as 20–22 °C with the availability of deep bedding, nesting material and/or group housing.

2. SUMMARY

The argument that to best mimic human physiology in mouse studies we should set the thermoregulatory conditions so that the metabolism of the two species is well matched makes a lot of sense. However, comparing the thermoregulatory curves of humans and mice, combined with the temperatures routinely selected by humans, suggests that the optimal temperature to achieve this is in the range from 23 to 25 °C for single housed mice, and around 20–22 °C for group housed mice. Keeping mice at 30 °C as has been recently advocated probably does not mimic well the situation in humans.

Conflict of interest. None declared.

REFERENCES

[1] Benedict, F.G., and Fox, E.L., 1933. Der Energieumsatz normaler und haarloser Mause bei verschiedener Umgebungstemperatur. Pflügers Archiv für die gesamte Physiologie 231:455.

[2] Beynene, A.C., Gartner, K., and van Zutphen, L.F.M., 2001. Standardization of animal experimentation. In: Van Zutphen, L.F.M., Baumans, V., Beynene, A.C. (Eds.), Principles of laboratory animal science, Second revised ed. Elsevier, Amsterdam, The Netherlandsln: Van Zutphen, L.F.M., Baumans, V., Beynene, A.C. (Eds.), Principles of laboratory animal science, Second revised ed. Elsevier, Amsterdam, The Netherlands, p. 103–10.

[3] Black, A.E., Coward, W.A., Cole, T.J., and Prentice, A.M., 1996. Human energy expenditure in affluent societies: an analysis of 574 doubly-labelled water studies. European Journal of Clinical Nutrition 50:72–92.

[4] Cannon, B., and Nedergaard, J., 2009. Thermogenesis challenges the adipostat hypothesis for body-weight control. Proceedings of the Nutrition Society 68:401–407.

[5] Cannon, B., and Nedergaard, J., 2011. Nonshivering thermogenesis and its adequate measurement in metabolic studies. Journal of Experimental Biology 214:242–253.

[6] Chandler, A.R., Messina, M.M., and Overton, M.J., 2007. Thermoneutrality attenuates body weight gain in ovariectomised female mice. FASEB Journal 21:A460.

[7] Code of practice for the housing of animals used in scientific procedures, HMSO, London, 1989 44pp.

[8] Committee for the update of the guide for the care and use of laboratory animals, Institute for Laboratory Animal Research Guide for the care and use of laboratory animals (eighth ed.), National Research Council of the National Academies, The National Academies Press, Washington, DC. 2011. www.nap.edu.

[9] DuBois, E.F., 1936. Basal metabolism in health and disease, Lea and Febiger, Philadelphia.

[10] Enerbäck, S., Jacobsson, A., Simpson, E.M., Guerra, C., Yamashita, H., Harper, M.E., et al., 1997. Mice lacking mitochondrial uncoupling protein are cold-sensitive but not obese. Nature 387:90–94.

[11] Even, P.C., and Nadkarni, N.A., 2012. Indirect calorimetry in laboratory mice and rats: principles, practical considerations, interpretation and perspectives. American Journal of Physiology—Regulatory, Integrative and Comparative Physiology 303:R459–R476.

[12] Feldmann, H.M., Golozoubova, V., Cannon, B., and Nedergaard., J., 2009. UCP1 ablation induces obesity and abolishes diet-induced thermogenesis in mice exempt from thermal stress by living at thermoneutrality. Cell Metabolism 9:203–209.

[13] Finn, D.A., Bejanian, M., Jones, B.L., Syapin, P.J., and Alkana, R.L., 1989. Temperature affects ethanol lethality in C57BL/6, 129, LS and SS mice. Pharmacology Biochemistry and Behavior 34:375–380.

[14] Garami, A., Pakai, E., Oliveira, D.L., Steiner, A.A., Wanner, S.P., Almeida, M.C., et al., 2011. Thermoregulatory phenotype of the Trpv1 mouse: thermoeffector dysbalance with hyperkinesis. Journal of Neuroscience 31:1721–1733.

[15] Garland, H.O., 1985. Altered temperature. In: Case, R.M., Evans, D.E. (Eds.), Variations in human physiology. Manchester University Press, Manchester, UK, p. 111–33.

[16] Gaskill, B.N., Rohr, S.A., Pajor, E.A., Lucas, J.R., and Garner, J.P., 2009. Some like it hot: mouse temperature preferences in laboratory housing. Applied Animal Behaviour Science 116:279–285.

[17] Golozoubova, V., Gullberg, H., Matthias, A., Cannon, B., Vennström, B., and Nedergaard, J., 2004. Depressed thermogenesis but competent brown adipose tissue recruitment in mice devoid of all hormone-binding thyroid hormone receptors. Molecular Endocrinology 18:384–401.

[18] Gordon, C.J., 1993. Temperature regulation of laboratory rodents. Cambridge University Press, Cambridge, UK.

[19] Gordon, C.J., Becker, P., and Ali, J.S., 1998. Behavioral thermoregulatory responses of single- and group-housed mice. Physiology & Behavior 65:255–262.

[20] Gordon, C.J., 2004. Effect of cage bedding on temperature regulation and metabolism of group-housed female mice. Comparative Medicine 54:51–56.

[21] Hardy, J.D., and Dubois, E.F., 1937. Differences between men and women in their response to cold. Proceedings of the National Academy of Sciences of the United States of America 26:389–398.

[22] Havenaar, R., Meijer, J.C., Morton, D.B., Ritskes_Hoitinga, J., and Zwart, P., 2001. Biology and husbandry of laboratory animals. In: Van Zutphen LFM, Baumans V, Beynene AC (Eds.), Principles of laboratory animal Science, 2nd revised edition. Amsterdam The Netherlands: Elsevier; 2001. p. 19–76.

[23] Hayes, J.P., Speakman, J.R., and Racey, P.A., 1992. The contributions of local heating and reducing exposed surface-area to the energetic benefits of huddling by short-tailed field voles (Microtus-agrestis). Physiological Zoology 65:742–762.

[24] Herrington, L.P., 1940. The heat regulation of small laboratory animals at various environmental temperatures. American Journal of Physiology 129:123–139.

[25] Högberg, H., Engblom, L., Ekdahl, A., Lidell, V., Walum, E., and Alberts, P., 2006. Temperature dependence of O_2 consumption; opposite effects of leptin and etomoxir on respiratory quotient in mice. Obesity 14:673–682.

[26] Hussein, H.K., 1991. Effect of temperature and body size on the metabolic rate of Egyptian house mice (Mus musculus) and the roof rat (Rattus rattus). Journal of the Islamic Academy of Sciences 4:249–252.

[27] Karp, C.L., 2012. Unstressing intemperate models: how cold stress undermines mouse modelling. Journal of Experimental Medicine 209:1069–1074.

[28] Kingma, B., Frijns, A., and van Marken Lichtenbelt, W., 2012. The thermoneutral zone: implications for metabolic studies. Frontiers in Bioscience e4.

[29] Klaus, S., Münzberg, H., Trüloff, C., and Heldmaier, G., 1998. Physiology of transgenic mice with brown fat ablation: obesity is due to lowered body temperature. American Journal of Physiology 274:R287–R293.

[30] Liu, X.T., Rossmeisl, M., McClaine, J., and Kozak, L.P., 2003. Paradoxical resistance to diet-induced obesity in UCP-1 deficient mice. Journal of Clinical Investigation 111:399–407.

[31] Lodhi, I.J., and Semenkovich, C.F., 2009. Why we should put clothes on mice. Cell Metabolism 9:111–112.

[32] Malcolm, R.D., and Alkana, R.L., 1983. Temperature dependence of ethanol lethality in mice. Journal of Pharmacy and Pharmacology 35:306–311.

[33] Manning-Geist B. Oral rapamycin does not mimic caloric restriction in mice. Unpublished thesis. Willamsburg College. Supervisor Swoap S, 2011. (accessed online).

[34] Meyer, C.W., Klingenspor, M., Rozman, J., and Heldmaier, G., 2004. Gene or size: metabolic rate and body temperature in obese growth hormone-deficient dwarf mice. Obesity Research 12:1509–1518.

[35] Mount, L.E., 1971. Metabolic rate and thermal insulation in albino and hairless mice. Journal of Physiology 217:315–326.

[36] Overton, J.M., 2010. Phenotyping small animals as models for the human metabolic syndrome: thermoneutrality matters. International Journal of Obesity 34:S53–S58.

[37] Pertwee, R.G., and Tavandale, L., 1977. The effects of Δ^9-tetrahydrocannabinol on the rates of oxygen consumption of mice. British Journal of Pharmacology 60:559–568.

[38] Rintamäki, H., 2007. Human responses to cold. Alaska Medicine 49 (Suppl. 2), 29–31.

[39] Romanovsky, A.A., Ivanov, A.I., and Shimansky, Y.P., 2002. Molecular biology of thermoregulation. Selected contribution: ambient temperature for experiments in rats: a new method for determining the zone of thermal neutrality. Journal of Applied Physiology 92:2667–2679.

[40] Scholander, P.F., Hock, R., Walters, V., Johnson, F., and Irving, L., 1950. Heat regulation in some arctic and tropical mammals and birds. Biological Bulletin 99:237–258.

[41] Scholander, P.F., Lange Andersen, K., Krog, J., Vogt Lorentzen, F., and Steen, J., 1957. Critical temperature in Lapps. Journal of Applied Physiology 10:231–234.

 © 2012 Published by Elsevier GmbH.

MOLECULAR METABOLISM

[42] Selman, C., Lumsden, S., Korhonen, T., Bunger, L., Hill, W.G., and Speakman, J.R., 2001. Thermoregulatory responses of two mouse Mus musculus strains selectively bred for high and low food intake. Journal of Comparative Physiology B 171:661–668.

[43] Speakman, JR. Measuring energy metabolism in the mouse—theoretical, practical and analytical considerations. Frontiers in Physiology, (in press).

[44] Speakman, J.R., and Krol, E., 2005. Limits to sustained energy intake IX: a review of hypotheses. Journal of Comparative Physiology B 175: 375–394.

[45] Speakman, J.R., and Rossi, F.P., 1999. No support for socio-physiological suppression effect on metabolism of paired white mice (Mus sp.). Functional Ecology 13:373–382.

[46] Speakman, J.R., and Westerterp, K.R., 2010. Associations between energy demands, physical activity and body composition in adult humans between 18 and 96 years of age. American Journal of Clinical Nutrition 92:826–834.

[47] Swoap, S.J., Li, C., Wess, J., Parsons, A.D., Williams, T.D., and Overton, J.M., 2008. Vagal tone dominates autonomic control of mouse heart rate at thermoneutrality. American Journal of Physiology Heart and Circulatory Physiology 294:H1581–H1588.

[48] Terroine, E.F., and Trautmann, S., 1927. Influence de la temperature exterieure sur la production calorique des homeothermes et loi des surfaces. Annales de Physiologie et de Physicochimie Biologique 3:422.

[49] Tschöp, M.H., Speakman, J.R., Arch, J.R.S., Auwerx, J., Brüning, J.C., Chan, L., et al., 2012. A guide to analysis of mouse energy metabolism. Nature Methods 9:57–63.

[50] Vaz, M., Karaolis, N., Draper, A., and Shetty, P., 2005. A compilation of energy costs of physical activities. Public Health Nutrition 8:1153–1183.

[51] Winslow, CEA., and Herrington, LP., 1949. Temperature and human life, Princeton University press, Princeton.

[52] Witte, M.M., Reshuehr, D., Chandler, A.R., Mehle, A.K., and Overton, J.M., 2010. Female mice and rats exhibit species specific metabolic and behavioural responses to ovariectomy. General and Comparative Endocrinology 166 (S1), 520–528.

[53] Yamauchi, C., Fujita, S., Obara, T., and Ueda, T., 1983. Effects of room temperature on reproduction, body and organ weights, food and water intakes, and hematology in mice. Experimental Animals 32:1–11.

URL1: The engineering toolbox. Values of insulation in clo units for various items of clothing. 〈http://www.engineeringtoolbox.com/clo-clothing-thermal-insulation-d_732.html〉 [accessed 06 08 12].

 © 2012 Published by Elsevier GmbH.