Are lab mice too cold? Why it matters for science

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Roswell Park Cancer Institute MD/PhD student checking his mice in the incubator. Credit: Guanxi (Christina) Qiao

A typical mouse laboratory is kept between 20 and 26 degrees C, but if the mice had it their way, it would be a warm 30 degrees C. While the

mice are still considered healthy at cooler temperatures, they expend more energy to maintain their core temperature, and evidence is mounting that even mild chronic cold stress is skewing results in studies of cancer, inflammation, and more. Researchers review the evidence April 19 in *Trends in Cancer*.

"Most people only look at results from experiments at standard lab temperatures," says Bonnie Hylander, an immunologist at the Roswell Park Cancer Institute. "They're not necessarily aware that if you repeat the experiments with mice at a different temperature, you might get a different outcome."

There are multiple reasons to keep a mouse lab cool. Researchers don gowns, gloves, and masks to work with the animals, which makes the lower temperature more comfortableand also cuts down on the smell. The National Research Council, which publishes guidelines for housing mice, gives the 20-26 degrees C range and recommends that the animals have nesting material. But when mice are constantly trying to generate enough heat to stay warm, the chill causes their heart rate and metabolism to change, and they eat more food to make up the energy.

A few years ago, Hylander and Elizabeth Repasky, an immunologist at the Roswell Park Cancer Institute, along with their colleagues, began investigating the effects of cold stress on the mouse immune system's ability to fight tumors. As the team revealed in 2013, lab mice do a better job of fighting cancer naturally when they're nice and warm. Tumors grew slower and were less likely to metastasize compared to mice kept at standard lab temperatures. The warmer mice also responded better to chemotherapies.

Concerned about the implications for drug research and selection, Hylander and Repasky started digging into a growing body of research on mouse housing temperature in other fields. Now, they're sounding the

alarm.

Studies in fields ranging from obesity research to neurobiology have shown that housing temperature can alter study results in mice. "While animal physiologists have recognized the potential of this problem for some time, we were surprised that essentially no work was done on cancer models. We thought it was very important to highlight how many other areas of biomedical research, some related to cancer, are influenced by standard housing temperatures," says Repasky. "We're concerned that too many publications in which results differ, either between labs in various countries or within the same lab, may be due to environmental conditions."

But the answer isn't necessarily just turning up the thermostats. "Working at a thermoneutral temperature for mice isn't very pleasant for people," Hylander says. "It's hot, and it's hard for people to work very long when they're overheated."

As a first step, Hylander and Repasky recommend that researchers report the ambient temperature used in their colonies and simply be aware that the cage positions, the number of mice per cage, and the type of disease being modeled can influence the degree of cold stress.

For a more direct approach, Hylander suggests that researchers try pilot experiments at warmer temperatures to see how the difference affects experimental outcomes. This could be accomplished by either keeping mice in incubators or giving the animals more nesting material (in the wild, mice ward off cold temperatures by building nests).

"We're not saying one housing temperature is better than another," Repasky emphasizes. "The different temperatures are simply resulting in differences in experimental outcomes, which could be important. I think a lot more research is needed to optimize the use of mice for testing

therapies that will be useful in people."

More information: *Trends in Cancer*, Hylander and Repasky: "Thermoneutrality, Mice and Cancer: A Heated Opinion" dx.doi.org/10.1016/j.trecan.2016.03.005

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