



# +++ ENVIGO

Research models  
and services

Fighting mice

## Fighting mice Considerations regarding aggression in mice

### Background information

While mice can be socially harmonious, there are times when they can display aggression. This applies to mice in nature or in captivity. When mice are group housed in the laboratory, aggression can be triggered which, up to a certain level, can be regarded as normal or natural. However, when aggressive interactions between cage mates cause severe injury and stress in the animals, it leads to negative effects both on the well-being of the animals (both dominant and subordinate) and on the validity of experimental results.<sup>1,2</sup> Although mostly associated with males, females can also exhibit aggressive behavior.

### Recognizing aggression

Fighting between mice is often noted by specific signs of injury such as the presence of skin wounds on the back and tail, or as more general signs such as weight loss.<sup>3</sup>

Multiple cage mates can be injured, while one (dominant) animal may remain unharmed. Behavioral observations show animals performing threats, attack bites on the back and flank, often while vocalizing. The pattern of aggression in male mice consists of a series of bursts that are separated by periods of relative inactivity. The most prominent reaction to aggressive acts is an escape leap that becomes full flight in which fleeing opponents are chased. Frequently attacked mice display a defeat posture with limp forelimbs, upward angled head and retracted ears.<sup>4</sup>

Females defending their pups will mainly strike at head and snout.<sup>4</sup> Aggression can also be exhibited as excessive barbering or whisker biting, shown as bald spots on cage mates. This last type of aggression is mainly seen in female animals.

### Potential causes of aggression

Causality can be found in both management and genetics.

Under laboratory conditions housing is usually arranged by gender, which contrasts the social organization of wild mice, as freely living (house-) mice are organized in a structure with one dominant male, several females, juveniles and probably a few subordinate males. The dominant male defends the territory of the group especially against other adult males. Under laboratory conditions, several adult males are often forced to cohabitate.<sup>4,5</sup> Once male mice reach sexual maturity, territorial aggression increases.<sup>7</sup> Exposure to female odors promotes aggression as males will compete for breeding opportunities.

Classic selection and strain comparisons show the heritability of aggressive behavior, and point to the influence of several genes. It can affect both inbred as well as outbred strains.<sup>4</sup> Swiss outbred mice are known to be highly aggressive.<sup>4</sup> Some inbred strains are genetically predisposed to high levels of aggression (SJL, BALB/c).<sup>2,6</sup>

### Prevention of aggression

Some preventive measures can be taken to minimize triggering aggressive behavior.

Cage cleaning can increase aggression in male groups due to the disruption of odors that normally define their social environment.<sup>8</sup> Providing nesting material and transferring odor cues (non-soiled nesting material) during cage cleaning reduces aggression in some strains, but can increase aggression in others. Shelters may influence aggressive behaviour, depending on i.e. number, size and design.<sup>1,3,9,10</sup>

Males should not be exposed to male urine when temporarily removed from their social groups and contamination of home cages with different scents should be avoided, for example, by cleaning cages thoroughly and ensuring that soiled substrate cannot fall into other cages.<sup>11</sup>

It is not per se necessary to house male mice individually. Studies describe that male mice prefer each other's company to individual housing.<sup>8</sup> Groups of three were found to have the most stable dominance hierarchy and show the least aggression between cage mates.<sup>12</sup> As unfamiliar mice are less tolerant to each other than acquainted ones, it is recommended not to disturb the social groups.<sup>1</sup>

Aggression is also a common response to unpredictable situations, such as experimental or husbandry procedures to which an animal cannot anticipate (e.g. cage cleaning or human approach). In these instances, an animal may direct its energy into aggression against nearby animals.<sup>1</sup>

### Preventive measures

Policy of Envigo RMS is to house male mice strains, where there may be a concern about aggression, in smaller, stable groups from a young age and not mix these animals during husbandry procedures. These animals are packed for transportation per cage and not mixed. Envigo applies this practice based on the experience gained with them for various mouse stocks and strains globally. Envigo advises housing male animals as they are received in their shipping cohorts.

**Even though preventive measures are taken it may be impossible to completely remove aggression between mice in the present way of housing laboratory mice.**<sup>13</sup>

### What can you do?

- + Order male animals young (e.g. at 4 wks) and keep in small stable groups (3-5 animals) after arrival
- + House male animals preferably per shipping compartment and do not mix animals from different compartments
- + Newly grouped animals will establish a new hierarchy and close observation is needed to intervene at an early stage should aggression occur
- + House males in social groups before adulthood
- + Avoid housing males near female cages and avoid (indirect) exposure to female scent (e.g. gloves, equipment)
- + Avoid unpredictable stimuli

- + Avoid contamination of the home cage with other male scents (e.g. bedding falling in)
- + Transfer clean nesting material to the new cage to retain some familiar scent and allow territory re-marking at a lower, less stressful level
- + Wash the cage when removing bedding
- + Familiarize animals with other scents used in procedures

### Summary

Aggression is a natural occurring phenomenon, but can interfere with welfare of the animals and validity of test results. Be alert, so preventive measures can be taken, such as using small groups, use nesting material which is transferred at cage cleaning and prevent mixing of the animals and unpredictable situations.

### References

1. PLP Van Loo, LFM Van Zutphen, V Baumans, Male management: coping with aggression problems in male laboratory mice. *Lab Anim* 2003;37:300-13.
2. C Hunt, C Hambly, Faecal corticosterone concentrations indicate that separately housed male mice are not more stressed than group housed males, *Physiology & Behavior* 87(2006), 519-526.
3. EK Kaliste, SM Mering, HK Huuskonen, Environmental Modification and Agonistic Behavior in NIH/S Male Mice: Nesting Material Enhances Fighting but Shelters Prevent It, Volume 56, Number 3, June 2006, pp. 202-208(7).
4. KA Miczek, SC Maxson, EW Fish, S Faccidomo, Aggressive behavioral phenotypes in mice, *Behavioural Brain Research* 125 (2001) 167-181.
5. SS Arndt, MC Laarakker, HA van Lith, FJ Van der Staay, E Gieling, AR Salomons, J van't Klooster, F Ohl Individual housing of mice — Impact on behaviour and stress responses, *Physiology & Behavior* 97 (2009) 385-393.
6. J Hurst, Making sense of scents: reducing aggression and uncontrolled variation in laboratory mice, 2005 <http://www.nc3rs.org.uk/news.asp?id=164>.
7. T Kikusui, Y Mori, Behavioural and Neurochemical Consequences of Early Weaning in Rodents, *Journal of Neuroendocrinology* 21, 2009, 427-431.
8. PLP Van Loo, AC de Groot, LFM Van Zutphen, V Baumans, Do male mice prefer or avoid each other's company? Influence of hierarchy, kinship and familiarity, *Journal of Applied Animal Welfare Science* 4, 2001, 91-103.
9. V Marashi, A Barnekow, E Ossendorf, N Sachser. Effects of different forms of environmental enrichment on behavioral, endocrinological, and immunological parameters in male mice. *Horm Behav* 2003;43:281-92. PLP Van Loo, E Van der Meer, CLJJ Kruitwagen, JM Koolhaas, LFM Van Zutphen, V Baumans Long-term effects of husbandry procedures on stress-related parameters in male mice of two strains, *Lab Anim* 2004 38: 169-177.
10. JC Lacey, RJ Beynon, JL Hurst, The importance of exposure to other male scents in determining competitive behavior among inbred male mice, *Applied Animal Behaviour Science* 104 (2007) 130-142.
11. H Würbel, Ideal homes? Housing effects on rodent brain and behaviour, *Trends in Neuroscience* April 2001, Vol.24 No.4.
12. A Bisazza, Social organization and territorial behaviour in three strains of mice. *Bollettino Zoologica* 48, 1981 157-167.
13. EM Weber, JA Dallaire, BN Gaskill, KR Pritchett-Corning, JP Garner, Aggression in group-housed laboratory mice: why can't we solve the problem? *Lab Anim* 2017 46(4): 157-161.

## Contact us

North America 800.793.7287 EU and Asia [envigo.com/contactus](http://envigo.com/contactus) [info@envigo.com](mailto:info@envigo.com)

++++  
ENVIGO