

Dept. Animal Welfare and 3Rs

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Laboratory Animal Services Center

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Aggression in male mice

When laboratory mice are group housed, they display social behaviors similar to those seen in mice living in the wild^{1,2}. Especially male mice maintain a dominance hierarchy which can result in inter-male aggression (fighting, biting, chasing)^{3, 4}. Whereas some levels of aggression can be recognized as normal⁵, more escalated aggressive interactions may cause stress in both, the dominant and the subordinate male^{4, 6}. This leads to negative effects on the well-being of the animals (death, injuries often obvious only after a longer history of repeated and severe fighting^{7, 8}; weight loss etc.) and commonly results in single housing. Additionally, this stressful social condition may impact the validity of scientific data^{2, 9}. Therefore, male aggression is one of the major welfare concerns in mouse husbandry and presents a significant challenge for those working with male mice.

Aggressive mouse strains

Some mouse strains, inbred and outbred, have a predisposition to higher levels of aggression^{10, 11}, for example:

- SJL/J
- SAM mice
- FVB/N
- SWISS (CD-1)
- C57BL/6
- BALB/c
- NMRI
- Athymic nude (Outbred)

Measures to reduce aggression in male mice

For several important scientific reasons, it is not advisable or possible to work with female mice only. Also, it might not be possible to work only with docile strains. Therefore, several strategies should be implemented to keep male aggression at a low level:

Transport / Ordering

Since one well described cause for aggression in male mice is establishing social structures after being regrouped and aggression levels are normally lower in familiar, stable groups^{2, 12}, the preparation and transport process by the supplier can have a great impact. Therefore, when processing orders, LASC requests from suppliers that males will only be pooled in transport boxes if they originate from the same production cage. Further, every transport box will receive enrichment of various types to offer some sort of distraction during the transport, ideally also used but not soiled nest material is added.

As the aggressive behavior increases once males reach sexual maturity, it is advisable to order males of predisposed strains at an age of 3 - 4 weeks, allocate and house them in the same group composition and size (3 - 5 males per cage)^{2,8} as they will be housed during experiments and let them mature in the target facility¹³. If this is not possible, ordering of males in the same group composition and size as they will be housed after arrival / during experiments can reduce the risk of fighting, thus reducing the risk of losses, single-housing and negative effects on experimental



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results. Therefore, the Department Animal Welfare and 3Rs and LASC recommends specifying, at least for the above-mentioned strains, group size already during the order process.

Suppliers can have special transport conditions that can further restrict the group sizes in the transport boxes. This may be necessary to ensure to receive healthy animals and LASC has no influence on this. Also, please note that some sorts of transport boxes can be subdivided, others cannot. This can result in slightly higher costs as each transport box will be charged. After all, one should consider that higher costs for transportation will result in higher animal welfare, less single housing and sick notifications. Therefore, approving higher costs for transportation might in the long run reduce costs and other negative incidents.

Housing / Handling

There are several strategies for male mouse routine housing and care that can be applied to keep aggression at a low level: The maintenance of stable groups throughout the experiments, the reduction of stress by implementing gentle handling techniques like tunnel or cup handling, the transfer of used but not soiled nest building material during cage change as well as the processing of cages with males prior to cages with females have been reported to reduce aggression significantly ^{2, 4, 8, 13}. The department of Animal Welfare and 3Rs is happy to help you with designing a suitable housing and handling protocol for your projects.

References

- 1) Brown RZ. Social behavior, reproduction, and population changes in the house mouse (Mus musculus L.). *Ecological Monographs*. 23, 217-240 (1953).
- 2) Van Loo PLP, Van Zutphen LFM, Baumans V. Male management: coping with aggression problems in male laboratory mice. *Lab Anim* 2003;37:300–13.
- 3) Scott JP & Fredricson E. The causes of fighting in mice and rats. Physiol Zool. 24, 273-309 (1951).
- 4) Weber EM, Dallaire JA, Gaskill BN, Pritchett-Corning KR, & Garner JP. (2017). Aggression in group-housed laboratory mice: why can't we solve the problem? Lab animal. 46(4). 157-161.
- 5) Brown RZ. Social behavior, reproduction, and population changes in the house mouse (Mus musculus L.). *Ecological Monographs*. 23, 217-240 (1953).
- 6) Haemisch A, Gärtner K. Effects of cage enrichment on territorial aggression and stress physiology in male laboratory mice. *Acta Physiologica Scandinavica. Supplementum.* 1997 ;640:73-76.
- 7) Gaskill BN. et al. He's getting under my skin! Comparing the sensitivity and specificity of dermal vs subcuticular lesions as a measure of aggression in mice. Applied Animal Behaviour Science 183, 77–85, (2016).
- 3) Jirkof P, Bratcher N, Medina L, Strasburg D, Ebert P, & Gaskill BN. (2020). The effect of group size, age and handling frequency on intermale aggression in CD 1 mice. Scientific reports, 10(1), 1-13
- 9) Sherwin CM. The influences of standard laboratory cages on rodents and the validity of research data. Animal Welfare 13, 9–15 (2004).
- 10) Miczek KA, Maxson SC, Fish EW, Faccidom S. Aggressive behavioral phenotypes in mice, *Behavioural Brain Research* 125 (2001) 167–181.
- 11) Kappel S, Hawkins P, Mendl MT. To Group or Not to Group? Good Practice for Housing Male Laboratory Mice. *Animals (Basel)*. 2017;7(12):88. Published 2017 Nov 24. doi:10.3390/ani7120088
- 12) Envigo, Research models and services, Fighting mice. Considerations regarding aggression in mice. (2017)
- 13) Zidar J, Weber EM, Ewaldsson B, et al. Group and Single Housing of Male Mice: Collected Experiences from Research Facilities in Sweden. *Animals (Basel)*. 2019;9(12):1010. Published 2019 Nov 21. doi:10.3390/ani9121010