

**Resident Intruder
IACUC Standard Procedure
Effective Date: July 27, 2021**

Description of Procedure:

The resident-intruder paradigm is used to monitor aggressive and exploratory behaviors that resemble the natural patterns of rodents in establishing and defending their territory ([Koodlhaas et al., 2013](#)). They are increasingly used in the study of drug effects on aggression as the polarization of offensive (resident) and defensive (intruder) patterns facilitates interpretation of drug effects on aggression, while non-agonistic behaviors can serve as controls for activity. Animals are housed individually in observation cages and on the day of testing, an unfamiliar mouse of similar body weight, age and sex is introduced into the home cage of the resident animal for 10 minutes. The number of offensive or exploratory interactions is recorded and scored manually. In the event of injurious or continuous attacks (>30sec) by either resident or intruder, testing will be terminated and animals removed from the experiment. Animals used in this paradigm must be placed in **Category E**.

Procedure Steps:

A) Experimental mice used as Intruders

Before conducting the test, researchers must identify potential aggressors in their subset of mice (often retired breeders) by placing a screener mouse directly into the home cage of the potential aggressor for 180 seconds. Up to three screening sessions, once daily, using different screeners on each subsequent day for each aggressor can be performed such that no aggressor defeats the same screener twice. Researchers will select aggressors for use in subsequent resident intruder experiments based upon two criteria: During three 180-s screening sessions, the aggressor must attack in at least two consecutive sessions; and the latency to initial aggression must be less than 60 seconds.

Once aggressor mice have been identified, they will be tested during the 10min exposure of the experimental mice into the aggressor's home cage. The aggression by the resident is video recorded and the latency to the first attack, the total number of attacks and the length of each attack are scored. The videos should be scored by individuals blind to genotype and treatment condition of each subject.

B) Experimental mice used as Residents

If the experimental mouse will be used as the Resident, he/she will be singly housed for at least 1 week prior to the test. On the day of the test, the intruder mouse will be introduced into the home cage of the experimental Resident. After 10 minutes of contact, test mice are separated and the intruder is then returned to his/her home cage. The interactions in the 10min-duration test are videotaped and later scored.

In both cases, intruder mice should be scored for signs of stress and subordination or aggression, including vocalization, flight response, and submissive or dominant postures.

Adverse effects: If the aggression leads to the development of multiple penetrating open wounds, the mouse will be immediately removed from the study and evaluated for possible treatment or euthanasia. If the aggressive interactions produce minor wounds, they will be treated with topical antibiotic ointment until the wounds heal; if not healed after 5 days, the mouse will be either euthanized or veterinary staff will be notified in order to evaluate him/her for treatment and possible euthanasia. For fight wounds that are more than minor contact LARC veterinary services.

Reference:

Koolhaas JM, Coppens CM, de Boer SF, Buwalda B, Meerlo P, Timmermans PJ. The resident-intruder paradigm: a standardized test for aggression, violence and social stress. *J Vis Exp.* 2013 Jul 4;(77)