Resident Intruder
IACUC Standard Procedure
Effective Date: February 2024

UCSF Office of Research
Institutional Animal
Care and Use Program

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 (Koolhaas 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. It can also be used to evaluate social stress. Animals are housed individually in observation cages and cages should not be changed for at least 1 week prior to testing. On the day of testing, an unfamiliar animal 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 (example interaction illustrations in Himmler et al., 2013). In the event of injurious or continuous attacks (>30sec) by either resident or intruder, trial will be terminated and animals separated. Animals used in this paradigm must be placed in **Category E**.

Procedure Steps:

Both intruder and resident animals should be scored for signs of stress and subordination or aggression, including vocalization, flight response, submissive or dominant postures, and latency to first attack.

A) Experimental animals used as Intruders
Before conducting the test, researchers must identify potential aggressors in their subset of animals (often retired breeders) by placing a screener animal 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 animals have been identified, they will be tested during the 10min exposure of the experimental animals into the aggressor's home cage. Offense (aggressive) behaviors should be quantified. 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 animals used as Residents
If the experimental animal 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 animal will be introduced into the home cage of the experimental Resident. After 10 minutes of contact, test animals are separated and the intruder is then returned to his/her home cage. The interactions in the 10 min-duration test are videotaped and later scored.

IACUC Protocol:
Section G. (Procedures): Specify the maximum frequency and total number of testing sessions that an individual resident or intruder animal will undergo.

Section J. (Adverse Effects): State that the trial will be stopped if aggression results in penetrating wounds. If any animal receives more than superficial wounds or minor scratches, immediately notify LARC veterinary services. The animal will be immediately evaluated for treatment or possible euthanasia. If the wound is minor (superficial, scratches), animal may be treated with topical antibiotic ointment until wounds heal; if not healed after 5 days, veterinary staff will be notified to re-evaluate for further treatment or possible euthanasia. Animals that cause repeated serious wounds may need to be excluded from experiments.

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)

Himmler, B. T., Pellis, V. C., Pellis, S. M. Peering into the Dynamics of Social Interactions: Measuring Play Fighting in Rats. J. Vis. Exp. (71), e4288, doi:10.3791/4288 (2013).