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Title: Assessing Social Dominance in Mouse Models Using the Tube Test

Authors and Affiliations:

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Author Questionnaire

- 1. Microscopy:** Does your protocol require the use of a dissecting or stereomicroscope for performing a complex dissection, microinjection technique, or something similar? **No**

- 2. Software:** Does the part of your protocol being filmed include step-by-step descriptions of software usage? **No**

- 3. Filming location:** Will the filming need to take place in multiple locations? **Yes**
If **Yes**, how far apart are the locations? [Click to enter distance between locations.](#)

Current Protocol Length

Number of Steps: 9

Number of Shots: 20

Introduction

Videographer: Obtain headshots for all authors available at the filming location.

- 1.1. **Stephanie Fox:** The goal of my research is to find new therapies Frontotemporal dementia caused by progranulin mutations. We found that the tube test correlates with social dominance deficits and is a good outcome measure for preclinical screening of potential therapeutics.

1.1.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.3.1*

What advantage does your protocol offer compared to other techniques?

- 1.2. **Andrew Arrant:** The tube test is simple to perform and analyze. It can be used repeatedly on the same mice for longitudinal testing of age or treatment effects. Finally, we know the neural circuits that drive tube test behavior, which helps interpret results.

1.2.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.4.1*

What new scientific questions have your results paved the way for?

- 1.3. **Erik Roberson:** We used the tube test as a primary outcome measure in preclinical studies of therapeutic strategies for progranulin insufficiency in mouse models. Results provide support for both anti-sortilin antibodies and progranulin gene therapy, for clinical trials in patients with frontotemporal dementia due to progranulin mutations.

1.3.1. INTERVIEW: Named talent says the statement above in an interview-style shot, looking slightly off-camera. *Suggested B-roll: 2.6.1*

Videographer: Obtain headshots for all authors available at the filming location.

Ethics Title Card

This research has been approved by the Institutional Animal Care and Use Committee (IACUC) at the University of Alabama at Birmingham

Protocol

2. Standard Tube Test to Identify a Social Dominance Phenotype

Demonstrator: Stephanie Fox

- 2.1. To begin, obtain the PVC tubing with a length of 30.5 centimeters [1].
 - 2.1.1. WIDE: Talent picking up the PVC tubing from the workbench.
- 2.2. Place all cages containing mice of the same sex to be tested on a cart [1]. Transport the cages to the testing area [2].
 - 2.2.1. Talent placing multiple cages of mice on a cart.
 - 2.2.2. Talent pushing the cart towards the testing area.
- 2.3. Place the two cages for the first match on the testing surface [1]. Remove the lids and place them beside each cage [2].
 - 2.3.1. Talent placing two cages on the testing surface.
 - 2.3.2. Talent removing the lids and positioning them beside the cages.
- 2.4. Locate the two mice to be tested [1]. Hold one mouse in each hand, corresponding to its assigned side of the tube [2]. After identifying the first mouse, gently hold its tail and keep it in the cage while searching for the second mouse [3].
 - 2.4.1. Talent picking up the first mouse from the cage. Videographer's NOTE: This was a close up shot
 - 2.4.2. Talent holding a mouse in hand, aligning them with their assigned sides. Videographer's NOTE: 2.4.2, 2.4.3 and 2.5.1 were combined while shooting
 - 2.4.3. Talent holding the tail of the first mouse while searching for the second.
- 2.5. Simultaneously remove both mice from each cage [1] and gently place them with their heads at the entrance to the tube [2].
 - 2.5.1. Talent carefully removing the mice at the same time.
 - 2.5.2. Shot of placing the mice at the tube's entrance.
- 2.6. Maintain a grip on each mouse's tail to prevent premature contact [1].
 - 2.6.1. Shot of holding onto the tails of both mice to prevent early engagement. Videographer's NOTE: This was a close up shot
- 2.7. Once both mice have entered the tube, release the tails and step away from the tube [1].
 - 2.7.1. Talent releasing the tails and stepping back from the tube.

- 2.8. Observe the match and record the winner and loser [1]. A mouse is considered to have lost the match when two of its paws exit the tube and contact the testing surface [2]. After the match is over, return the mice to their home cages [3]. Clean the tube and the testing surface with 70% ethanol [4].
 - 2.8.1. Shot of the mice inside the tube. *Videographer: Please obtain multiple reusable shots for this step. It will be used again in 2.9.1*
 - 2.8.2. Shot of the loser mouse evicted from the tube.
 - 2.8.3. Talent carefully placing both mice back into their respective home cages.
 - 2.8.4. Talent wiping the tube with a paper towel soaked in ethanol.
- 2.9. Begin each round immediately after the preceding round [1]. Once all matches for one sex are completed, return the cages to the rack or cart [2-TXT]. After testing is complete, clean both the tubes and testing area with 2% chlorhexidine [3].
 - 2.9.1. ~~Reuse 2.8.1.~~ Shot of the mice inside the tube **Videographer's NOTE: A new shot of the mice inside the tube was taken. Do not reuse 2.8.1.**
 - 2.9.2. Talent placing the cage back in the rack or cart. **TXT: Test the mice of the opposite sex using the same procedure**
 - 2.9.3. Talent wiping the testing area with chlorhexidine soaked paper towel.

Results

3. Representative Results

- 3.1. Progranulin heterozygous mice exhibited lower social dominance compared to Progranulin wild-type mice at 9 to 16 months of age [1], with the low dominance phenotype being stable over repeated testing [2].
 - 3.1.1. LAB MEDIA: Figure 2A-D. *Video editor: Highlight all the data in black corresponding to "Grn+/+"*
 - 3.1.2. LAB MEDIA: Figure 2A-D. *Video editor: Highlight all the data in blue corresponding to "Grn+/-"*
- 3.2. Both male and female heterozygous mice exhibited lower social dominance in within-cage dominance hierarchy tests [1], whereas progranulin knockout mice did not display this abnormality [2].
 - 3.2.1. LAB MEDIA: Figure 3E. *Video editor: Highlight all the data in blue corresponding to "Grn+/-"*
 - 3.2.2. LAB MEDIA: Figure 3E. *Video editor: Highlight all the data in red corresponding to "Grn-/-"*
- 3.3. The heterozygous mice injected with a control Adeno-associated virus continued to show low social dominance [1], while the ones injected with a progranulin-boosting Adeno-associated virus no longer exhibited the low social dominance phenotype [2].
 - 3.3.1. LAB MEDIA: Figure 4A. *Video editor: Highlight the orange data.*
 - 3.3.2. LAB MEDIA: Figure 4D. *Video editor: Highlight the blue data.*

1. Progranulin

- **Pronunciation Link:** <https://www.howtopronounce.com/progranulin>
 - **IPA:** /proʊˈgrænjəlɪn/
 - **Phonetic Spelling:** proh-GRAN-yuh-lin[howtopronounce.com/7howtopronounce.com/7ru.howtopronounce.com/7merriam-webster.com/3merriam-webster.com/3merriam-webster.com/3en.wikipedia.org/2merriam-webster.com/2oed.com/2](https://www.howtopronounce.com/7howtopronounce.com/7ru.howtopronounce.com/7merriam-webster.com/3merriam-webster.com/3merriam-webster.com/3en.wikipedia.org/2merriam-webster.com/2oed.com/2)
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2. Heterozygous

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/heterozygous>
 - **IPA:** /ˌhetərəˈzaɪɡəs/
 - **Phonetic Spelling:** het-uh-roh-ZAI-guhs
-

3. Chlorhexidine

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/chlorhexidine>
 - **IPA:** /klɔːrˈhɛksəˌdiːn/
 - **Phonetic Spelling:** klor-HEK-suh-deen
-

4. Adeno-associated virus

- **Pronunciation Link:** <https://www.merriam-webster.com/medical/adeno-associated%20virus>
 - **IPA:** /ˌædɪnoʊ əˈsoʊsiɪtɪd ˈvaɪrəs/
 - **Phonetic Spelling:** AD-uh-noh uh-SOH-see-ay-tid VY-rus
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5. Ethanol

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/ethanol>
 - **IPA:** /ˈɛθəˌnɒl/
 - **Phonetic Spelling:** ETH-uh-nawl [lit.howtopronounce.com+1oed.com+1](https://www.howtopronounce.com+1oed.com+1)
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6. Phenotype

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/phenotype>
 - **IPA:** /ˈfiːnəˌtaɪp/
 - **Phonetic Spelling:** FEE-noh-type
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7. Genotype

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/genotype>

- **IPA:** /'dʒi:nə,taɪp/
 - **Phonetic Spelling:** JEE-noh-type
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8. Dominance

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/dominance>
 - **IPA:** /'dɑːmɪnəns/
 - **Phonetic Spelling:** DAH-muh-nuhns[howtopronounce.com](https://www.howtopronounce.com/dominance)+1[howtopronounce.com](https://www.howtopronounce.com/dominance)+1
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9. Hierarchy

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/hierarchy>
 - **IPA:** /'haɪə,rɑːrki/
 - **Phonetic Spelling:** HY-uh-rah-kee[howtopronounce.com](https://www.howtopronounce.com/hierarchy)
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10. Knockout

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/knockout>
 - **IPA:** /'nɔːk,əʊt/
 - **Phonetic Spelling:** NAHK-out[howtopronounce.com](https://www.howtopronounce.com/knockout)+5[oed.com](https://www.oed.com/knockout)+5[oed.com](https://www.oed.com/knockout)+5
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11. Homozygous

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/homozygous>
 - **IPA:** /,hoomə'zaɪgəs/
 - **Phonetic Spelling:** HOH-muh-ZAI-guhses[es.howtopronounce.com](https://www.howtopronounce.com/homozygous)
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12. Cart

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/cart>
 - **IPA:** /kɑːrt/
 - **Phonetic Spelling:** KAHRT
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13. Cage

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/cage>
 - **IPA:** /keɪdʒ/
 - **Phonetic Spelling:** KAYJ
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14. Ethanol

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/ethanol>
 - **IPA:** /'εθə,nɔl/
 - **Phonetic Spelling:** ETH-uh-nawl
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15. Chlorhexidine

- **Pronunciation Link:** <https://www.merriam-webster.com/dictionary/chlorhexidine>
- **IPA:** /klɔ:r'hεksə,di:n/
- **Phonetic Spelling:** klor-HEK-suh-deen