

	Reviewer 1	Reviewer 2	Reviewer 3	
Ultrasonic Voclaization	5	3	4	Write on Mouse vocalization
Monogamous Rodents	6	4	6	

Reviewer 1

Abstract #1 Title (Abbreviated): **“Mouse Ultrasonic Vocalizations”**

Background

Strengths: All the relevant issues are sufficiently addressed.

Weaknesses: However, it requires some re-writing as well as reorganization of each section to make it sound more cohesive. It also has some conflicting descriptions about the functional relationship between Egr-1 and FoxP2, which needs to be better sorted out to help understand the abstract.

Hypothesis

Strengths:

Weaknesses: The hypothesis can be improved in clarity by offering more insights into the functional relationship between FoxP2 and Egr-1. In addition, it is quite shallow in depth. It does not represent a significant advancement from the existing literature.

Specific Aims

Strengths: All the experiments proposed are designed well to address the hypothesis.

Weaknesses:

Abstract #1 Overall Evaluation: This abstract is too shallow in depth, and the student needs to develop a more significant hypothesis out of the existing body of literature.

Abstract #1 Score (1=best; 10=worst): 5

Abstract #2 Title (Abbreviated): **“Monogamous Rodents”**

Background

Strengths: The problems are clearly brought forth based on the existing body of literature.

Weaknesses: The obvious functional relationship between GR as a possible regulator of the 5'-regulatory region of V1aR doesn't seem to be appreciated by the author. This may reflect the lack or insufficiency of his clear understanding of the gene expression control processes.

Hypothesis

Strengths: The student is able to present the eventual benefit of the proposed study, which is commendable.

Weaknesses: However, once again, the hypothesis is very shallow in depth.

Specific Aims

Strengths: All the experiments are designed appropriately to address the hypothesis.

Weaknesses: Some of the experiments can clearly be further improved. For instance, GFP-V1aR can be co-expressed using a vector with IRES.

Abstract #2 Overall Evaluations: As with the first abstract, this one also suffers from the lack of depth in the hypothesis.

Abstract #2 Score (1=best; 10=worst): 6

Reviewer 2

Abstract #1 Title (Abbreviated): Mouse Ultrasonic Vocalizations

Background

Strengths: Clearly written and factually correct. Interesting extension of language related gene expression into mouse brain

Weaknesses:

Hypothesis

Strengths: Testable hypothesis.

Weaknesses:

Specific Aims

Strengths: Experiments are doable.

Weaknesses: (1) Homozygous mice die, so hets will be used – may not decisively answer the question. Striatal conditional knockout assumes this is the only important structure involved. (2) why not analyze vocalizations in the *egr* KO mice as well? (3) No evidence that mice can learn paternal patterns; if not, the remainder of the specific aim cannot be performed.

Abstract #1 Overall Evaluation: 3

Abstract #1 Score (1=best; 10=worst): 3

Abstract #2 Title (Abbreviated): Monogamous Rodents

Background

Strengths: Effect of neurohormones on bonding behavior is interesting and there is preliminary data implicating vasopressin in the ventral pallidum by blocking the receptor gene V1aR.

Weaknesses: Unclear whether variation between voles involves the levels of vasopressin, release, or level of receptor expression.

Hypothesis

Strengths: Specific and testable

Weaknesses: Selection of vasopressin gene receptor for analysis of genetic variation in regulatory region looks at only half of the signal – what about the promoter region of genes for synthesis or release of vasopressin itself? What about the rest of the gene?

Specific Aims

Strengths:

Weaknesses: (1) unclear how overexpression will affect general behavior and overall health of mouse. How will this be examined? (2) *In situ* hybridization is not sufficiently quantitative to answer the question. Is there a known antagonist? Specify how this will affect health of mouse (3) Glucocorticoids induce many genes – how will you determine a specific effect on vasopressin mediated behavior?

Abstract #2 Overall Evaluation: 4

Abstract #2 Score (1=best; 10=worst): 4

Reviewer 3

Abstract #1 Title (Abbreviated): Mouse Ultrasonic Vocalizations

Background

Strengths: Interesting topic. The link to human speech is interesting.

Weaknesses: If this is developed into a full proposal, it would be nice to see some discussion of the FOXP2 gene in chimps or other primates. Has the gene changed significantly to allow human speech? The reader needs more information to appreciate how diverse mouse vocalizations are. This is important because later you are going to try to experimentally alter the song, so how large of a repertoire do mice have to start with?

Hypothesis

Strengths:

Weaknesses: I didn't understand if you believe that FoxP2 is required for animals to hear/perceive vocalizations, appreciate their meaning, or physically produce vocalizations. If you already know that FoxP2 controls vocalization in humans and birds, isn't it a pretty safe bet it plays a similar role in mice? Maybe this is a too cautious/conservative model.

Specific Aims

Strengths:

Weaknesses: SA1: I was surprised that you plan to use Df FoxP2/+ mice for your experiments to avoid the lethal effects of homozygous nulls. What is the evidence that the gene is haploinsufficient for vocalization? The human KE family? Exactly what is the KE mutation? Does this KO/+ mouse stock have any gross behavior/mating phenotype? The conditional, tissue-specific KO sounds more promising. Do the viral transformations really work more than a few cell diameters from the injection needle? AIM3: It seems you need to do so much more than you outlined. Don't you need to identify adult males with different songs and see if they teach their particular version of song to offspring? Switch adult males and switch songs in foster sons? Maybe not supply a real male, but play recordings of different male vocalizations. Could you teach them the song from a different species? What are your controls? What other brain mutants would you test for learning vocalizations to show FoxP2 effects were specific?

Abstract #1 Overall Evaluation: This might lead to a successful proposal, but I think you need a stronger genetic component. It would be nice if the proposal were a bit more ambitious.

Abstract #1 Score (1=best; 10=worst): 4

Abstract #2 Title (Abbreviated): Monogamous Rodents

Background:

Strengths:

Weaknesses: It was not clear if the mice carrying prairie vole *V1aR* was a transgenic array, or a knock-in. This makes a difference in expression levels. What is the advantage for males to be monogamous? The significance of the short repeats seems shaky.

Hypothesis

Strengths: Clearly stated.

Weaknesses: Evidence for STR seems weak based on background.

Specific Aims

Strengths:

Weaknesses: In a full proposal you would need to be very clear about the time course for injecting transgenes into the animals brains, waiting for *V1aR* expression, any possible vasopressin treatment, behavioral assay, and then killing the animal to get brain sections. SA2: How specific are vasopressin antagonists? Glucocorticoid injections will do many things to the animals. How will you establish a direct link to the behavior under study?

Abstract #2 Overall Evaluation: This abstract does not have enough of a genetic component. I'm worried that injecting transgenes into brains of a few animals will be too variable from one animal to the next. Also, I worry that the drugs used will not be as specific as needed.

Abstract #2 Score (1=best; 10=worst): 6