F30/F31/F32/F33 Review

Applicant:

# Overall Impact

Reviewers will provide an overall impact score to reflect their assessment of the likelihood that the fellowship will enhance the candidate’s potential for, and commitment to, a productive independent scientific research career in a health-related field, in consideration of the following scored and additional review criteria. An application does not need to be strong in all categories to be judged likely to have a major impact. *See BIOTRAIN 720 review criteria rubric for guidance in evaluating proposals and writing critiques.*

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| Overall Impact/Merit *Write a paragraph summarizing the factors that informed your Overall Impact score.* |
| The medial preoptic area (POM) is a crucial regulator of social and sexual behavior in vertebrates. This area has been shown to be especially important for zebra finches to learn courtship behavior. While it is known that connections from POM to ventral tegmental area (VTA) and midbrain dopaminergic neurons (A11) are important for singing, what neuron types form this circuitry and how they impact behavior is still unclear. In aim 1, the applicant will use RNA sequencing to identify what genes are expressed after directed vs undirected singing. In aim 2, the applicant will use a transient GABA agonist to observe how POM inhibition influences directed and undirected singing. If successful, this project will greatly deepen our understanding of POM circuitry and its influence on behavior. Concerns largely center on the lack of details about how the RNA sequencing data and the behavior data will be analyzed. |

# Review Criteria

Reviewers will consider each of the review criteria below in the determination of the candidate’s qualifications, scientific and technical merit of the proposed research, candidate’s training potential, and institutional environment and commitment to training.

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| 1. Significance |
| **Strengths**   * It is impressive for the applicant to go all the way from RNA sequencing to behavior and link the two together * Hypotheses are clearly supported by the literature * Lab has experience in studying how POM circuitry influences motor learning * Development of numerous innovative techniques   **Weaknesses**   * Lack of a global framework that can generalize the findings beyond sexual motor learning in songbirds. How the findings will relate to motor learning across species, and whether the findings can be generalized to non-sexual motor learning, is unclear. * The last three paragraphs explain the approach clearly but do not elaborate on the significance of the project. * The authors relate “extrinsic” vs “intrinsic” motivation to directed and undirected singing, respectively. However, this parallel is not convincing since it does not fully align with the original definition of “extrinsic” and “intrinsic” motivation from the human motivation literature. Even when birds learn to sing by themselves, it could be argued that they are still extrinsically motivated to learn this behavior for successful courtship in the future. |

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| 2. [Innovation](http://grants.nih.gov/grants/peer/critiques/rpg_D.htm%23rpg_03) |
| **Strengths**   * Use of novel RNA sequencing techniques * Study how the POM functions on a cell-type basis * Use of novel machine learning methods   **Weaknesses**   * None |

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| 3. Approach |
| **Strengths**   * Preliminary data supports the validity of the RNA sequencing. In Aim 1, they were able to show retrograde labeling from the VTA to POM. * Preliminary data supports that GABA agonist in POM hinders both directed and undirected singing. * Multiple collaborations to assist with the variety of methods used. * Clear backup plans for both Aim 1 and Aim 2.   **Weaknesses**   * In Aim 1, it is not clear why group 1 sings for 30 minutes while group 2 sings for 10 minutes. * Each group has 5 birds, and it’s assumed that this sample size will be enough to distinguish differences in RNA expression between the groups. How much variability in gene expression there is across different cells and different birds within one condition is unclear. Since this sequencing will be performed on a large array of genes, it would be good to know how the authors will handle possible type II errors. * How the VAE analysis will be performed is not described. It is also unclear how we will be able to infer the amount of learning from this unsupervised analysis. |

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| Resubmission |
| Comments (if applicable): |