6.047/6.878 TERM PROJECT PROPOSAL EVALUATION FORM.

Proposal Title: Use of transcriptomic and epigenetic classifiers to discover novel sex differences in human tissues

Reviewer Role: #1. Primary

Please use this review form to evaluate each proposal.

Reviewers will provide an overall impact score to reflect their assessment of the likelihood for the project to exert a sustained, powerful influence on the research field(s) involved, in consideration of the following five scored review criteria, and additional review criteria. An application does not need to be strong in all categories to be judged likely to have major scientific impact.

Overall Impact. ***What is the expected impact of this proposal, weighed by how likely it is to succeed. This requires originality, challenge, and relevance, but also that the aims are actually accomplished, so a high score also requires that they are likely to succeed.***

Brief summary of proposal (Primary Reviewers only, 1 paragraph, 2-3 sentences):

The project aims to use RNA-seq and epigenetic data, gathered from GTEx, Blueprint, and CEEHRC to determine defining characteristics that discriminate between men and female autosomes. These features will then be used to search for functional pathways that may be differently regulated between males and females. These features, hypothesized to be genes, will also be evaluated on the differences of their promoter regions that correspond with motifs for estrogen and androgen binding sites.

Summary of your assessment (Most salient points of the review, all reviewers):

Project idea is thorough and interesting for a term project. However, later successes depend on previous success in Aim 1, and lack of alternative plans may inhibit progress. Knowledge of the biological basis behind the project seems sufficient to carry out the project.

Overall score (1-9, 9=best): 6

DETAILED REVIEW CRITERIA

Primary reviewers can be more thorough, and secondary reviewers can be more brief.

All reviewers will consider each of the five review criteria below in the determination of scientific and technical merit, and give a separate score for each.

Please note, your stated scores will not impact the grade of the student whose proposals you are reviewing. On the contrary, constructive criticism can help improve their proposals.

1. Significance/Challenge: ***If the application succeeds, what is the expected advance in the field. Is the problem tackled sufficiently complex and interesting for a term project? For your own proposals, you should balance challenge and probability of success. Please note that a score of 5 should still correspond to a feasible proposal for a term.***

Score (1-5, 5=best): 4

Strengths

- Significance is quite convincing and interesting, advancing knowledge in sex differences that may have immediate impact on treatments.

- Success will yield a new view of sex, and how differences by sex may be apparent in many other areas of biological function, including autosomes (previously believed to be sex-independent).

Weaknesses

- Decent chance of success, dependent on the discriminators in Aim 1 successfully identifying characteristics that differentiate male and female.

2. [Relevance](#) *Is the work proposed relevant to the class material? Are techniques presented in the class used, or extended, are the topics relevant to the biological problems presented in the class.* Note: If the investigators are engaged in a similar activity (e.g. UROP), have they defined clear boundaries of what will be achieved in the context of the class.

Score (1-5, 5=best): 4

Strengths

- Relevant use of RNAseq data and epigenetic data from various lectures.

- Methods use (including Naïve Bayes) were discussed in class and in homework assignments.

Weaknesses

- Uncertain how the project differs from UROP or other research, due to the mention of the lab's unpublished results – is this work distinct from the research that is currently being conducted in the lab? The name of the lab should also be mentioned.

3. [Innovation/Originality](#) *Are the methods proposed original, or are existing methods applied to original problems? Is the literature cited sufficiently enough to show that the investigators have a good grasp of the state of the field, so that they can show how their work relates to it. If there are closely related papers, do they show how their proposed work differs?*

Score (1-5, 5=best): 3

Strengths

- New analysis of biological differences in male and female autosomes.

- Many of the methods have been validated and used previously, but are applied in a new domain and question.

Weaknesses

- Lack of cited papers (in this section) on the work that has been achieved, even if none of the approaches have been focused on autosomal biological features.

- Since autosomes may be randomly passed from parent to child, how can the differences in autosomes be attributed to sex differences?

4. [Approach](#). *This is about the "precision of dragon-slaying". No matter how big the challenge they're tackling, are they meticulous about how they will address it, the potential*

issues that may be most trickiest or most difficult, and how they will go about them, and what they will try to do if it doesn't work. Are the methods well laid out, and are the necessary datasets available? Is there a plan for testing the methodologies by simulation or gold standard datasets. Will they be able to interpret their results? Is there a plan for validation of the results? Even if all the other scores are very strong, this score determines the overall potential for success of the project.

Score (1-5, 5=best): 3

Strengths

- Very detailed into which datasets will be used, and how those datasets will be used.

- Aim 1 has concrete methodology for success without too much difficulty. However, these is a possibility that none of the classifiers will perform well.

Weaknesses

- Doesn't specify how the results will be validated.

- Later aims depend on earlier aims; if earlier aims don't yield results as significant as desired, this could impede progress on other fronts.

- Should have a discussion on what alternative approaches may be used if the primary method does not appear to be effective.

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5. Presentation/Timeline. **Are the investigators explaining their ideas clearly, and providing enough background and information for the reviewers to assess the work. Please point to specific parts that were unclear, or should have been expanded. Is a detailed timeline presented for achieving the work?**

Score (1-5, 5=best): 4

Strengths

- Presentation is very clear with diagrams illustrating the techniques that will be used.

Weaknesses

- Timeline is appropriate but quite brief and lacking in detail. Lack of alternative plans as well.

- Expand on Aim 3 in the presentation. How will the potential new classifier help discover differentials in the areas listed in the final slide?