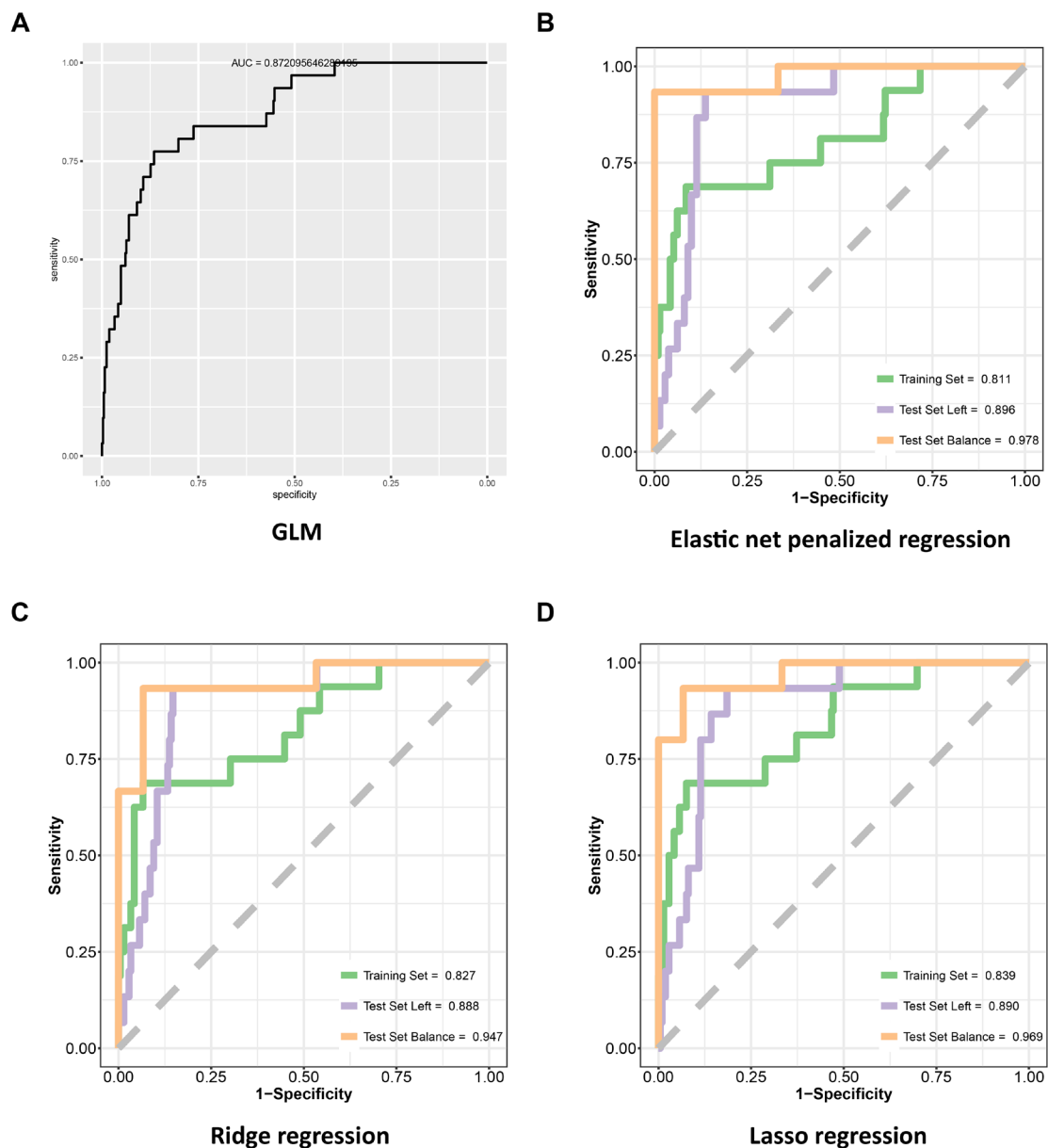


RESPONSE LETTER TO REVIEWER 1 ON REMAINING ISSUES

Dear Reviewer. This time, we have some good news to share. Following the first revision strategy described earlier, we abandoned the re-normalization step and used E-MTAB-4321 alone to train and validate the PFS model. The model's efficiency recovered to a higher level, showing satisfactory AUCs. Unlike the first version, we used the logarithmic matrix of original count data for ssGSEA analysis instead of using the re-normalized expression matrix. We built four models (GLM, elnet, lasso, and ridge regression) and evaluated them by AUCs in predicting the PFS status of all samples (n=454), or training set (n=228), test set containing all remaining samples (n=226), and test set containing balanced positive and negative samples (n=30). Appendix Figure 6 shows their performance.



Appendix Figure 6. ROCs of four model-building strategies in predicting the PFS status of NMIBC patients from E-MTAB-4321 dataset.

All models reflect good and close abilities in predicting the early progression of NMIBC patients. We choose the ridge model because it includes all nine candidate immune cells in the final model. In this way, our article is more like a meta-analysis article in the feature selection step containing integrated evidence from multiple data sources. The model-building step does not include the re-normalization of transcriptomics data anymore, so we modified our discussion about the importance of the procedure. Meanwhile, we emphasized the importance of selecting an appropriate meta-analysis method to filter candidate features from multiple analyses sequenced by different platforms. Corresponding modification could be found in Line 326-335, 352-354. Please find the revised manuscript and figures in our latest submission. We hope the results in this version were qualified for publication in the *Frontiers in genetics*.

Furthermore, we keep trying re-normalization methods (e.g., FSQN, rank-in) for further research needs and are willing to publish the results in new branches in Gitee and Github repositories. We thank the Reviewer again for helping us improve our article's rigor and quality. Biological statistics indeed is a sophisticated and elegant work, and we are pleased to practice and improve through this and further studies.