



Exploration of the Transcriptome of the Adenoid Cystic Carcinoma Patient-derived Xenograft



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Background

- Adenoid cystic carcinoma (ACC) is a cancer that frequently impacts the head and neck
- ACC accounts for approximately 1% of all head and neck cancers
- In the United States, there are 1200 new salivary gland ACC cases each year
- One model that is used to study ACC is the patient derived xenograft (PDX), where investigators transplant primary ACC patient tumors into immunodeficient mice
- MYB, MYBL1, NFIB are all genes as they are all commonly found as a partner in a fusion transcript within ACC
- SOX4, NOTCH1, and EN1 are genes that have been found to be highly expressed within ACC based off microarray and RT-PCR studies of primary tumor
- Virtually no investigations have utilized RNA sequencing to characterize the transcriptome of the ACC PDX model to reevaluate its utility as a research model

Aim

- Determine genes that are differentially expressed between ACC Patient-derived xenograft (ACC PDX) tissue and normal salivary gland (NSG) tissue
- Assess the validity of the ACC PDX model by comparing differential expression results to validated hallmarks of the ACC tumor

Methods

- We analyzed sequencing reads from ten ACC PDX models and six NSG tissue samples.
- We utilized the pseudo aligner Kallisto to quantify transcripts in both the ACC PDX model and NSG
- Then, we utilized DESEQ2 to complete a differential expression analysis

Results

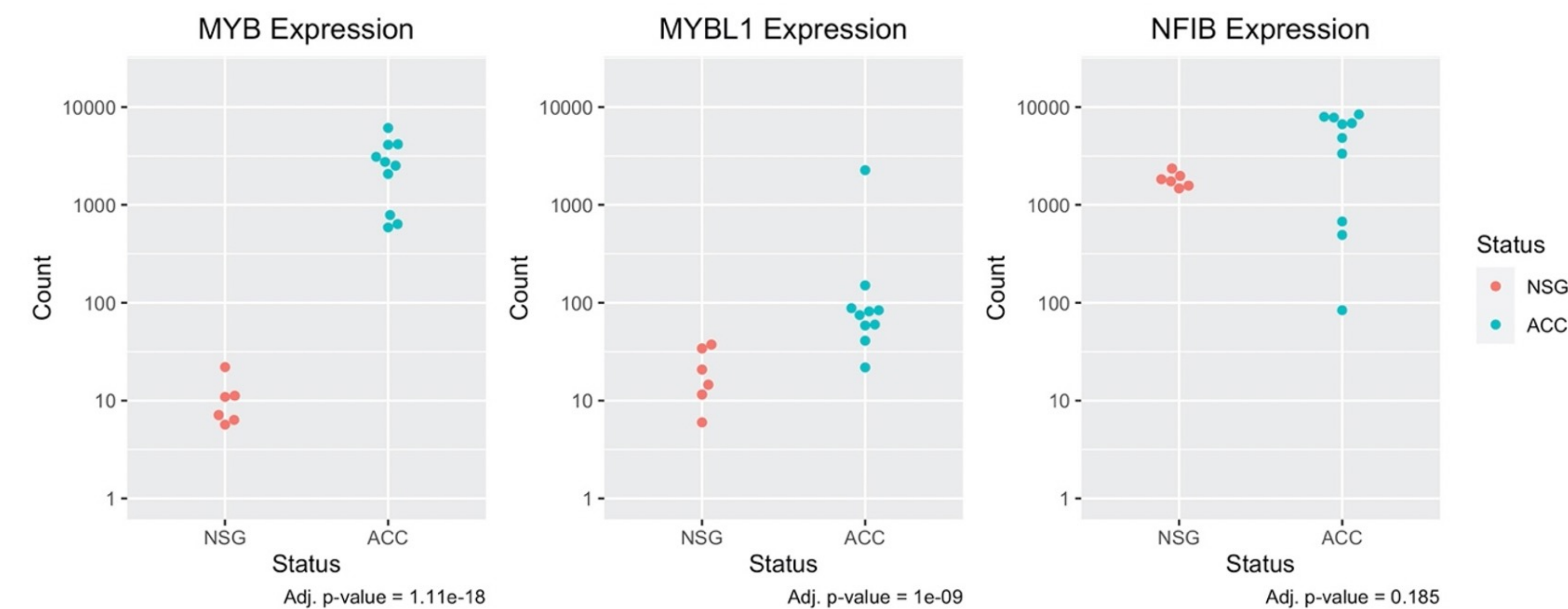


Figure 1: Quantification of transcript count for the fusion genes: MYB, MYBL1 and NFIB

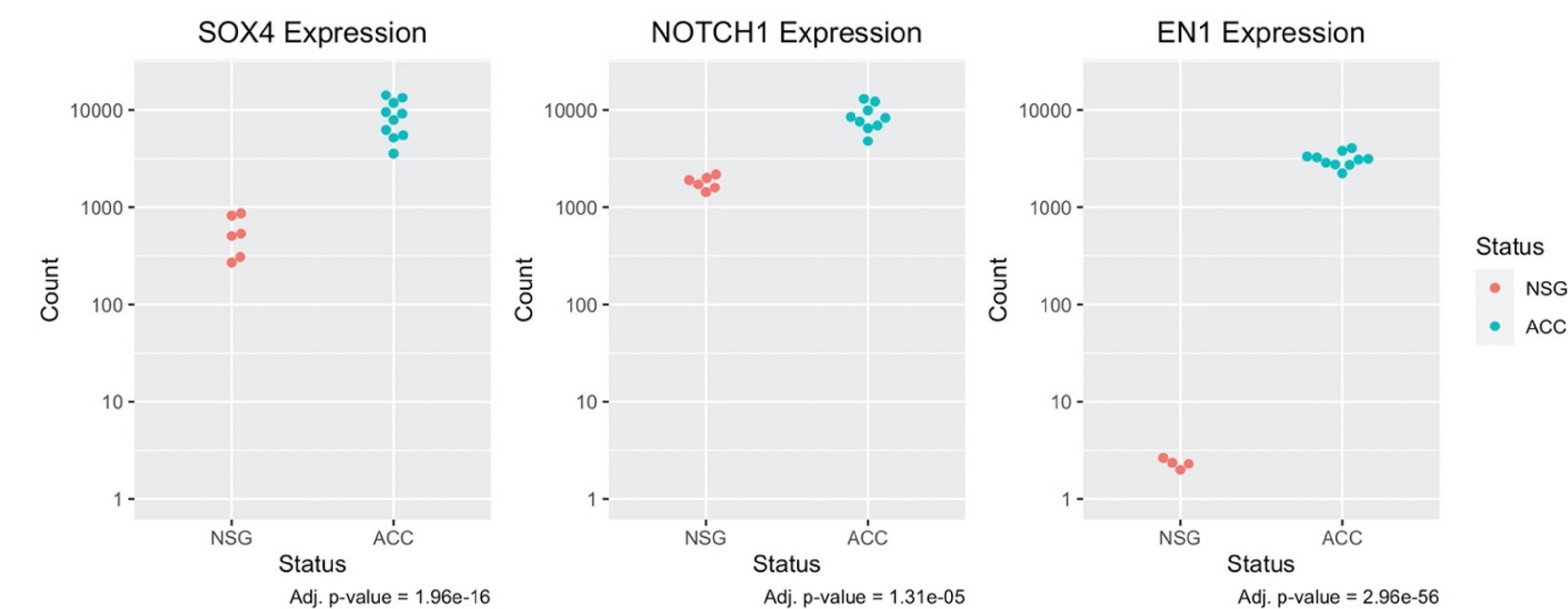


Figure 2: Quantification of transcript count of the hallmarks of ACC tumors: SOX4, NOTCH1 and EN1 genes

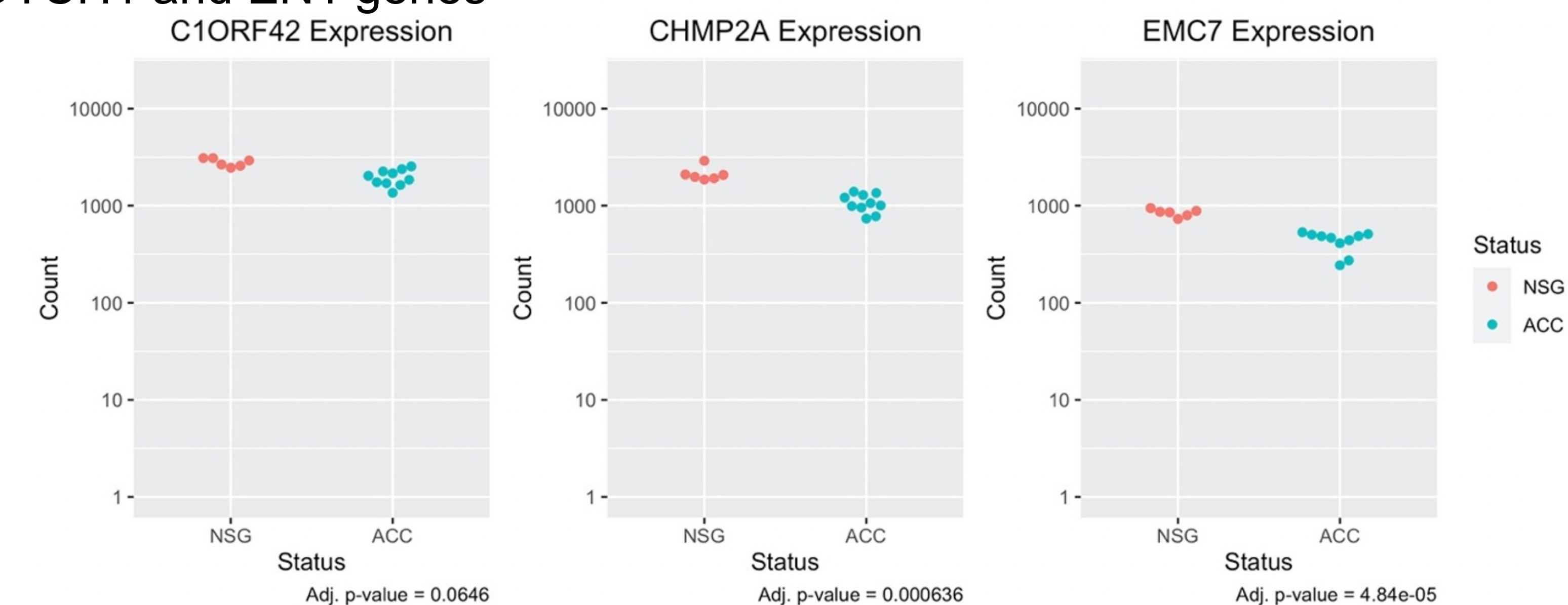


Figure 3: Quantification of transcript count for the housekeeping genes: C1ORF42, CHMP2A and EMC7

Limitations

- Batch and sample status were confounded based on the experimental design of the original sequencing experiment
- Additionally, many housekeeping and cancer related genes had high basal expression in NSG tissue; This may be due to low RNA quality that was a result of a high number of duplication events or contamination of the samples during preparation

Conclusions

- Through differential expression analysis, we observed that of 18084 genes considered, 6993 genes were found to be differentially expressed between ACC PDX and NSG tissue (FDR <.05)
- MYB-NFIB is a gene fusion that has emerged as a defining molecular event of ACC. Through our differential expression analysis, we observed that MYB and its paralog MYBL1, were found to be differentially expressed. NFIB was not found to be differentially expressed.
- Several previously characterized cancer related ACC genes, were found to be differentially expressed between ACC PDX and NSG tissue
- Housekeeping genes were found to be elevated in NSG tissue

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