PDV Trial

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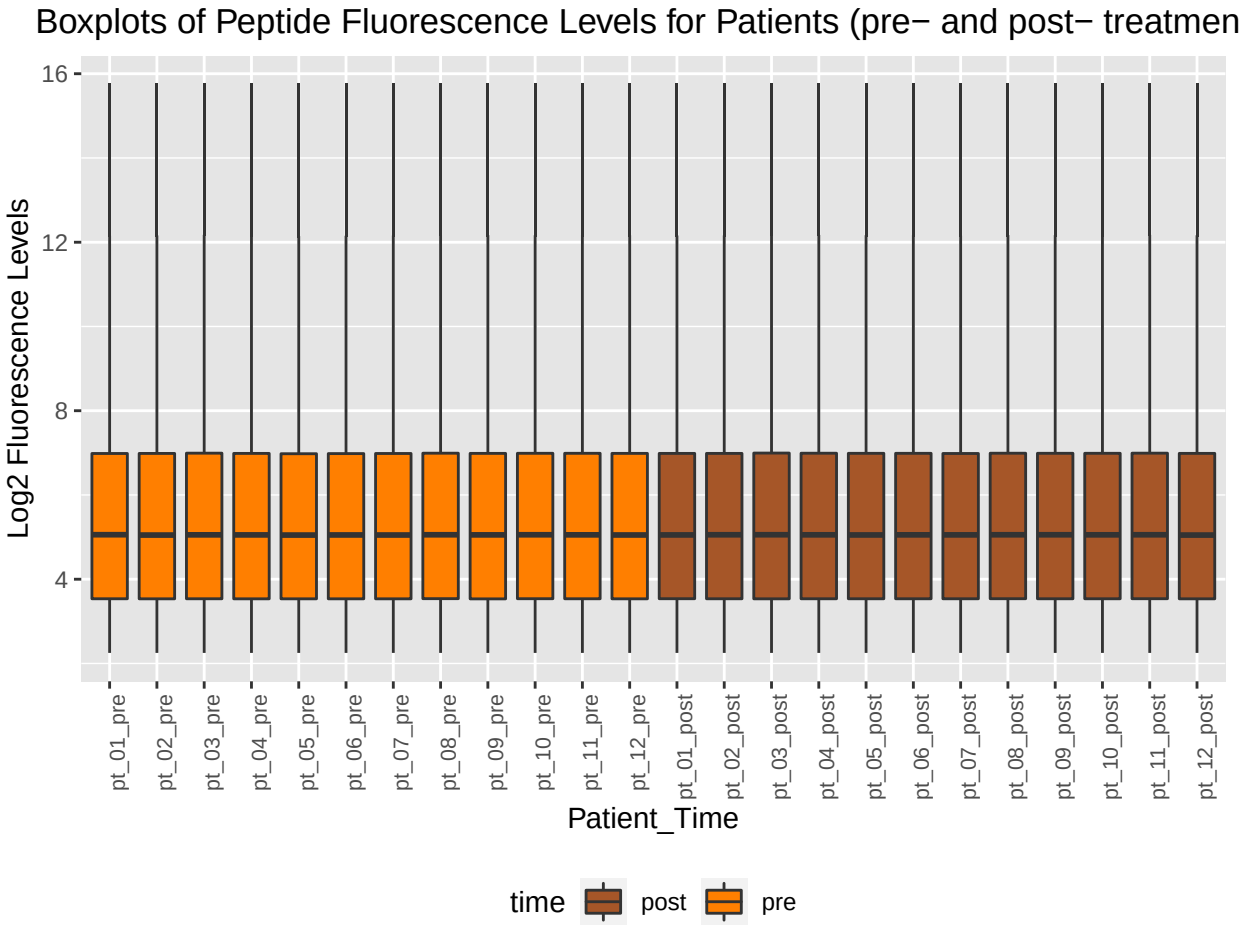
1 Introduction

This is a trial of PAP vaccine + GM-CSF in all 12 patients with later stage disease. The samples are labeled with PDV, and we have samples from pre-treatment and 6 months only. The objective is to sort-of "validate" what we reported in the JITC paper [Potluri et al., 2020], looking to see if there are significant changes pre to post, and whether these overlap with what was previously identified.

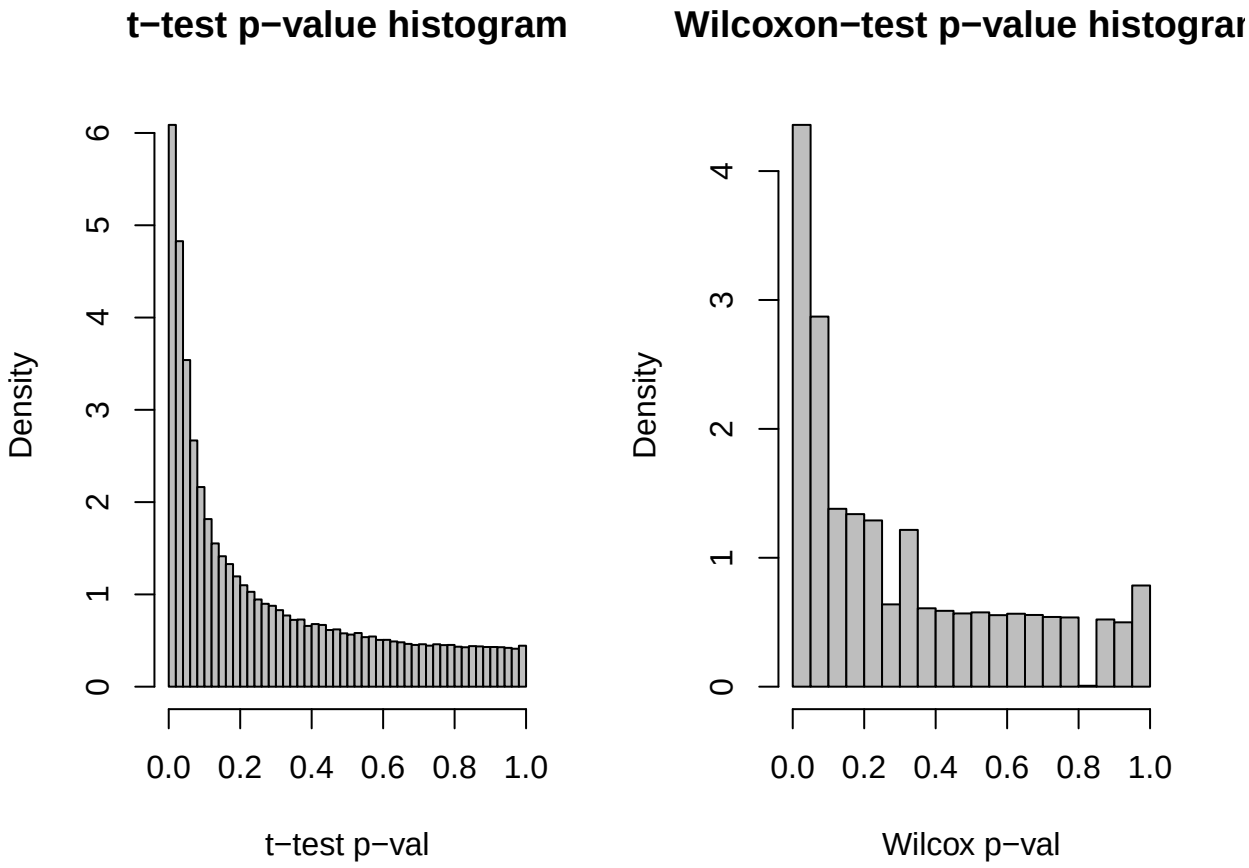
We applied a log2 transformation of the peptide fluorescence data, and we verified that the peptide array data were normalized accordingly via the boxplots of log2 fluorescence level of all peptides.



2 Statistical Test

We deploy peptide-level t-tests and Wilcoxon tests on the difference (post - pre) between log2(fluorescence) to identify changes in peptide-level antibody response among all 12 patients.

We plot the p-value histograms.



Applying the Benjamini-Hochberg (BH) method [Benjamini and Hochberg, 1995] on the t-test p-values to control FDR, we tabulate peptide counts at various FDR thresholds:

FDR threshold	0.15	0.16	0.17	0.18	0.19	0.2	0.21	0.22	0.23	0.24	0.25
Peptide counts	0	0	28956	36624	42691	48095	52436	55961	59612	62849	65923

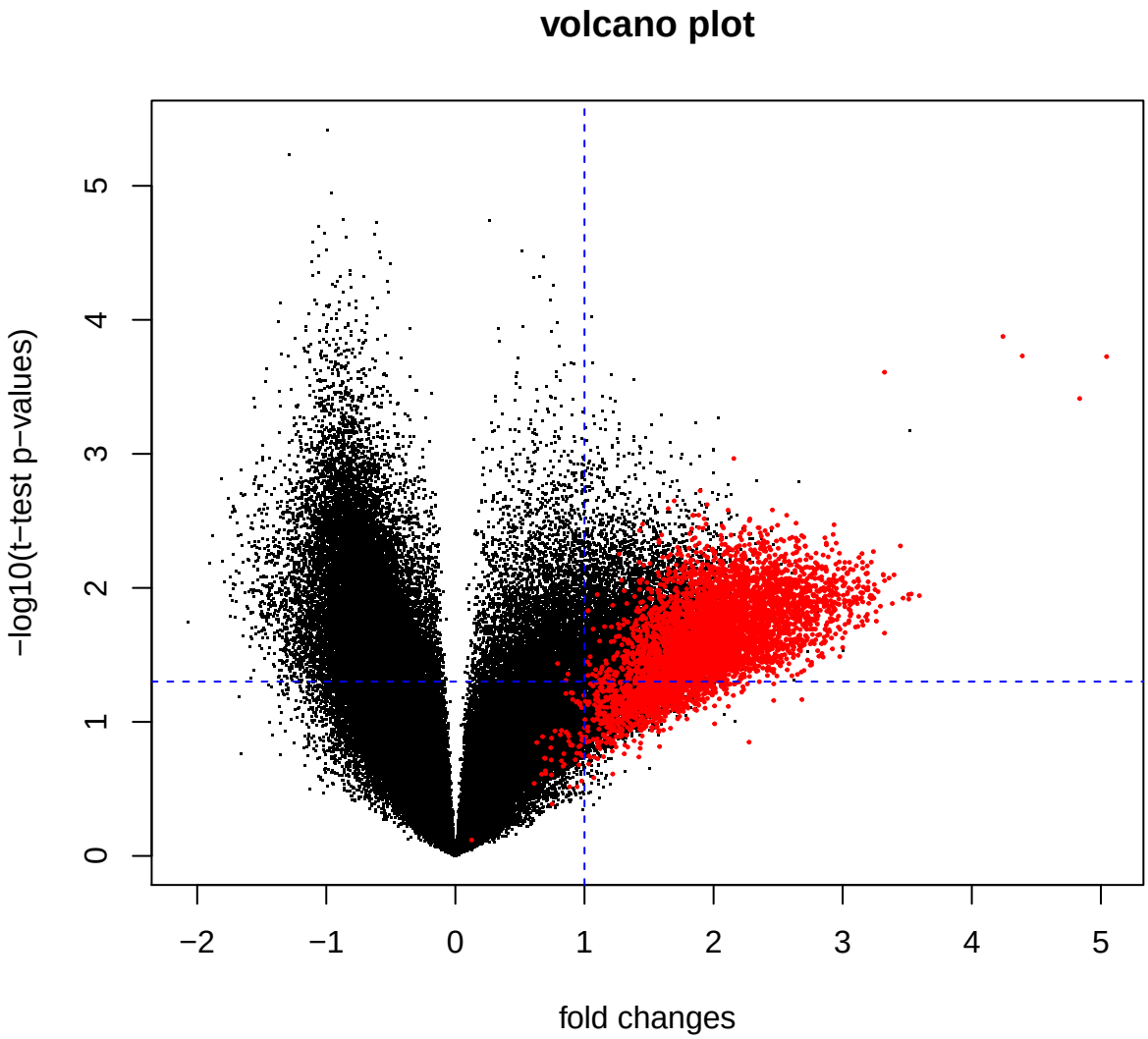
We also tabulate the peptide counts at various FDR thresholds based on BH-adjusted Wilcoxon p-values.

FDR threshold	0.15	0.16	0.17	0.18	0.19	0.2	0.21	0.22	0.23	0.24	0.25
Peptide counts	0	0	17246	26972	32713	38671	45131	45166	51613	58029	58029

The histograms of p-values suggest that there might be some signal of antibody response changes among the 12 patients, but none of the 177,604 peptides are significant at 10% FDR. This could be due to the small sample size (12 patients) of the PDV trial.

3 Comparison with JITC paper

In the JITC paper [Potluri et al., 2020], we have identified 5680 significant peptides. We shall superimpose these 5680 peptides (represented by red dots) on top of the volcano plot (-log10(p-value) vs effect estimate) for this PDV trial. The effect estimate in this case is simply the difference (post - pre) between log2(fluorescence).



The horizontal blue dashed line represents $-\log_{10}(0.05)$ whereas the vertical blue dashed line represents unit fold-change. From the preceding volcano plot, we observe that most (81.44 %) of all the JITC-identified peptides fall on the top right quadrant of the volcano plot (small raw p-values <= 0.05 with at least one-fold increase in peptide activity in this PDV trial). In fact, 98.98 % of all the JITC-identified peptides display at least one-fold increase in peptide activity in this PDV trial (represented by the red dots on the right side of the vertical dashed line). This corroborates with our reported results in the JITC paper.

References

Yoav Benjamini and Yosef Hochberg. Controlling the false discovery rate: A practical and powerful approach to multiple testing. *Journal of the Royal Statistical Society. Series B (Methodological)*, 57(1):289–300, 1995.

Hemanth K. Potluri, Tun Lee Ng, Michael A. Newton, Jin Zhang, Christopher A. Maher, Peter S. Nelson, and Douglas G. McNeel. Antibody profiling of patients with prostate cancer reveals differences in antibody signatures among disease stages. *Journal for ImmunoTherapy of Cancer*, 8(2), 2020. doi: 10.1136/jitc-2020-001510.