Dexamethasone Response in Airway Smooth Muscle Cells

Your Name

Your Lab / Department, Institution

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Research question

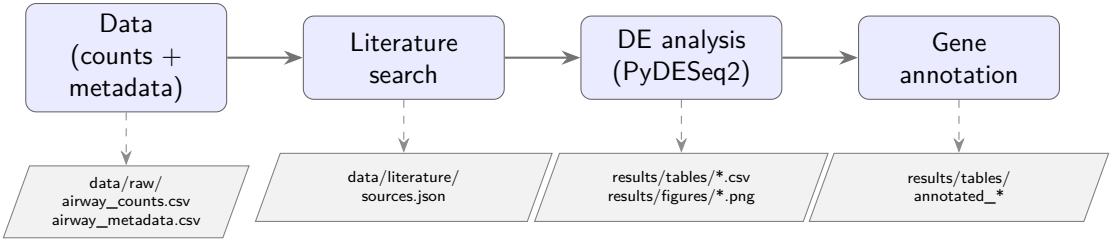
Question / goal

How does dexamethasone treatment change gene expression in human airway smooth muscle cells compared to untreated cells?

Objectives

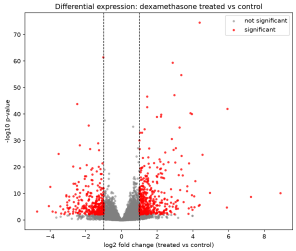
- Run a differential expression analysis (PyDESeq2) comparing dexamethasone-treated vs. untreated cells across 4 donor cell lines
- Use a simple single-factor statistical design (`~dex` only — donor cell line not included as a covariate), Benjamini–Hochberg adjusted $p < 0.05$, $|\log_2 FC| > 1$
- Check results against Himes et al. (2014), which flagged CRISPLD2 as a headline dexamethasone-responsive gene

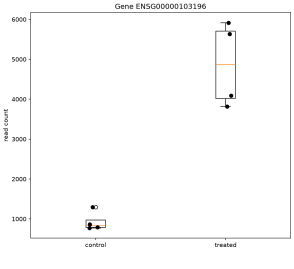
Method



Raw counts (GSE52778, 8 samples / 4 donor lines) → DESeq2, design `~dex`, BH padj < 0.05 → Ensembl/UniProt annotation of top hits.

Results: two views





Left: volcano plot of all tested genes; dashed lines mark $|\log_2 FC| = 1$, red points are significant (BH padj $<$ 0.05 and $|\log_2 FC| > 1$).
Right: CRISPLD2 (ENSG00000103196) normalized counts by treatment — a cysteine-rich secretory protein implicated in lung development, flagged by Himes et al. (2014) as the headline dexamethasone-responsive gene.

Results: top DE genes

Gene	log2FC	Description
Upregulated		
SPARCL1	+4.37	SPARC like 1 (calcium ion binding)
PER1	+2.86	Period circadian regulator 1
MAOA	+3.34	Monoamine oxidase A
DUSP1	+2.97	Dual specificity phosphatase 1
STOM	+1.43	Stomatin
PHC2	+1.44	Polyhomeotic homolog 2
ZBTB16	+5.93	Zinc finger and BTB domain containing 16
SAMHD1	+3.85	SAM and HD domain containing DNTPase 1
Downregulated		
ARHGEF2	−1.03	Rho/Rac guanine nucleotide exchange factor 2
KCTD12	−2.49	Potassium channel tetramerization domain containing 12

Top 10 genes by adjusted p-value (BH, all padj $\ll 0.05$), grouped by direction; order within each group follows that significance ranking.

Conclusions

Achieved

A differential expression analysis identifying the top dexamethasone-responsive genes in airway smooth muscle cells.

- This is a simple, single-factor design (`~dex`); no correction for other covariates, no pathway/GO enrichment yet
- Next steps:
  - More complex statistical design (`~cell + dex`)
  - Pathway/enrichment analysis (e.g. clusterProfiler) on the full hit list
  - Literature/functional follow-up on genes beyond CRISPLD2

References I

Himes, B.E. et al. (2014). *RNA-Seq Transcriptome Profiling Identifies CRISPLD2 as a Glucocorticoid Responsive Gene that Modulates Cytoskeleton Function in Airway Smooth Muscle Cells*. PLoS ONE, 9(6), e99625. doi:10.1371/journal.pone.0099625