Treatment sensitivity between cell lines

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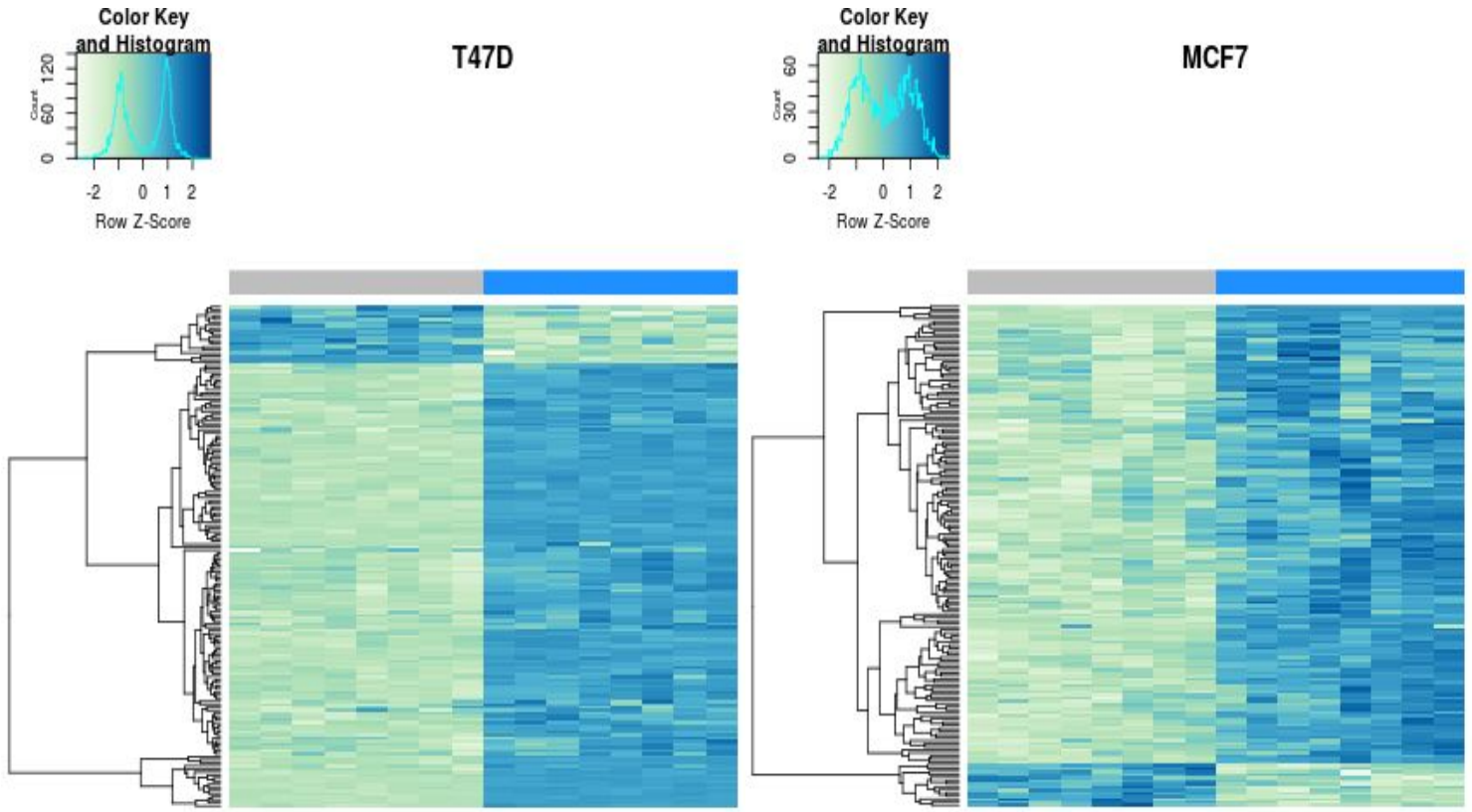
Callback: Responses to progesterone are different



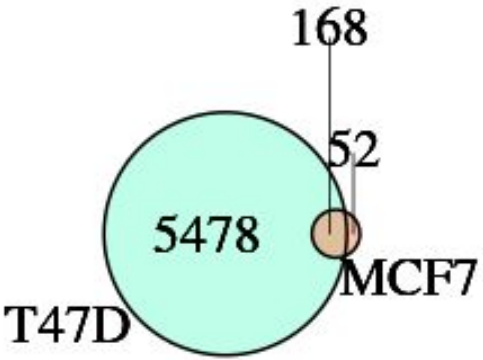
- Differences between cell lines are significantly larger than the differences between untreated / treated conditions.

- MCF7 has a copy number loss of the progesterone receptor gene, also evidenced by a fold change of ~2.5 in PR expression levels.

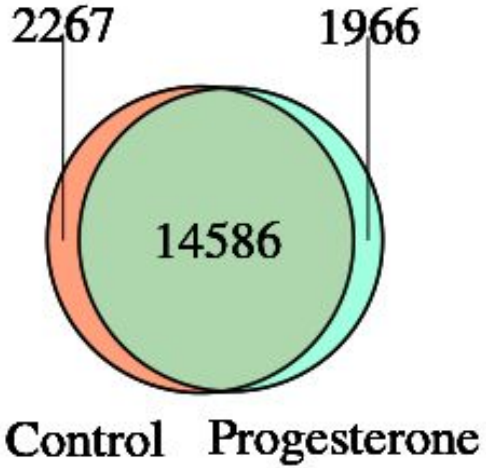
- Is this the sole factor driving response to progesterone treatment?

Driving differences between cell lines

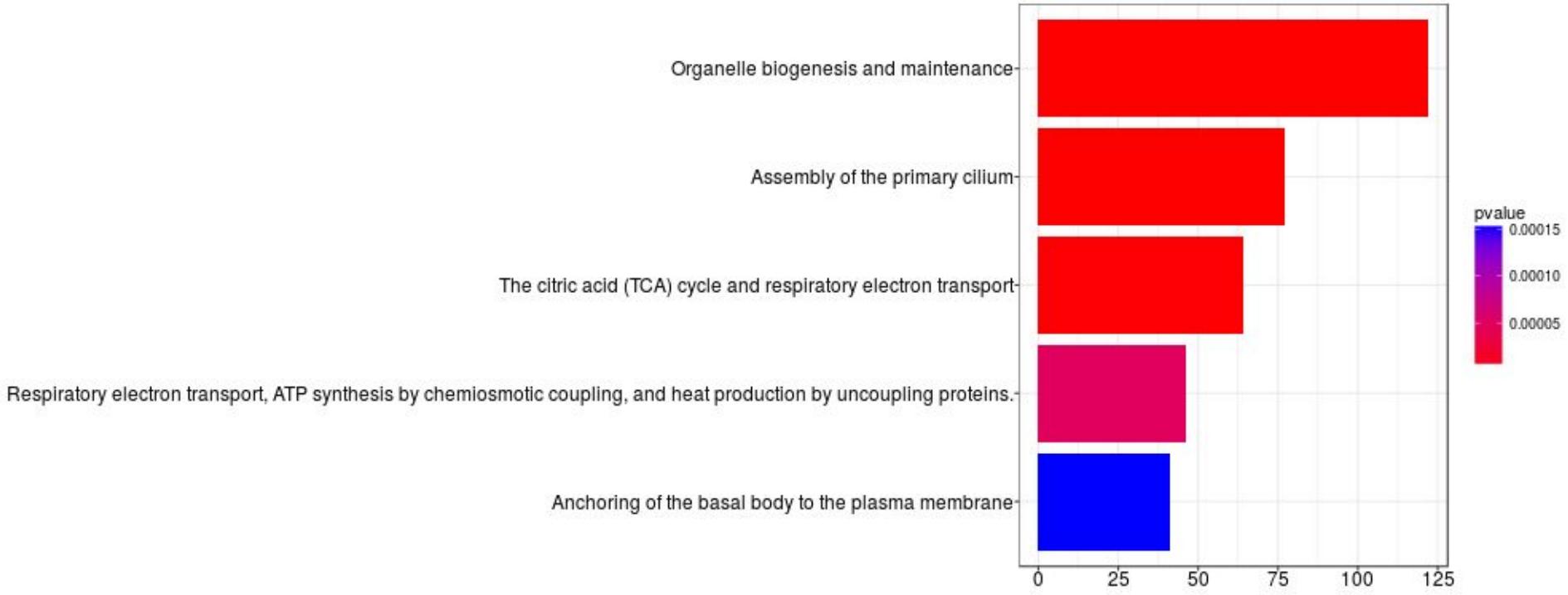
Differential expression when treated with progesterone



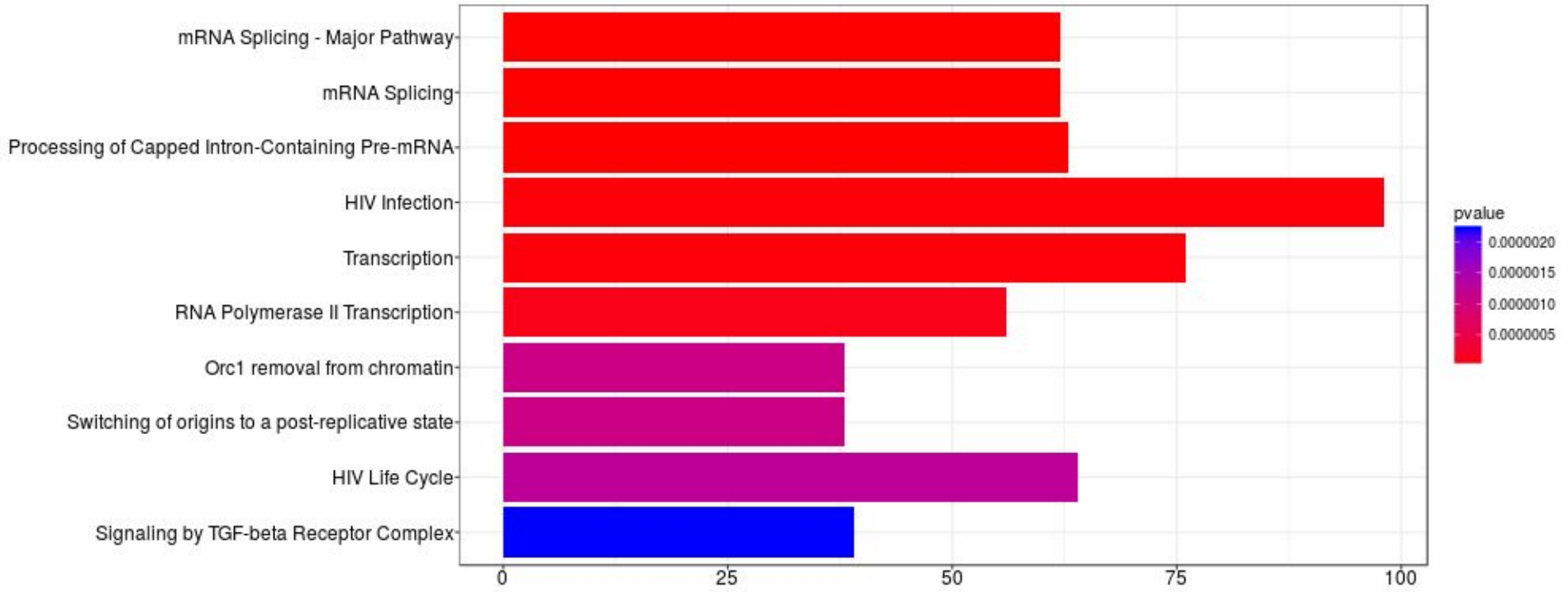
Differential expression between cell lines



T47D: Upregulated pathways



T47D: Downregulated pathways



- Most genes that are differentially expressed between cell lines stay so after treatment with progesterone

- 245 genes change “allegiance” after treatment (mostly upregulated)
  - These are related to the RHO GTPase pathway which is indicative of cancer progression
  - 243 of these are differentially expressed in the T47D cell line, only 18 in MCF7

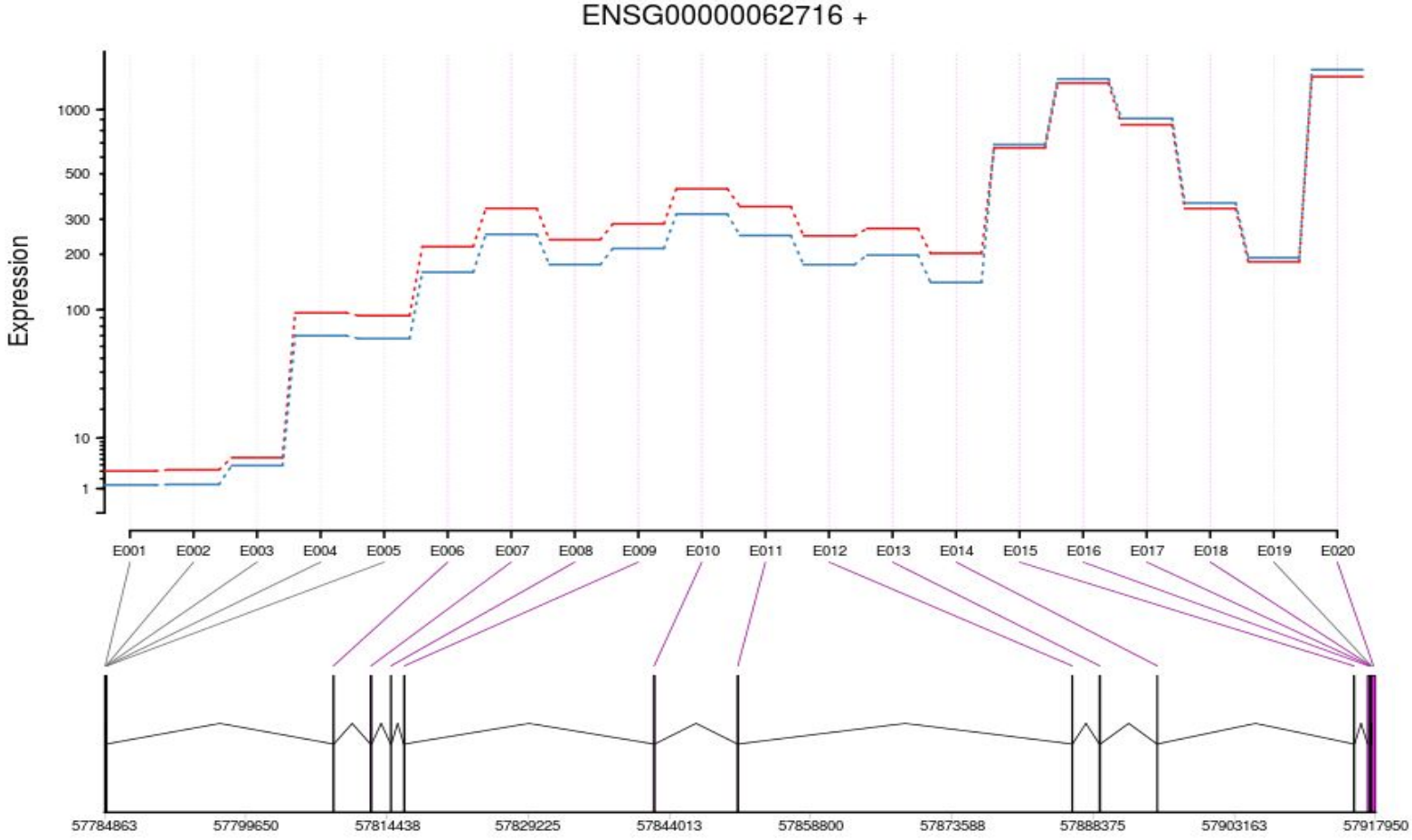
- The genes which are differentially regulated in **both** T47D and MCF7 have roles in signal transduction; involved in **no** Reactome pathways

Can isoform differences affect expression levels?

- Identify differentially expressed **exons** using DEXSeq and use these to identify differences in transcript levels

- Test groups:
  - Genes differentially expressed after treatment in T47D & MCF7
  - Genes with inter-cell line difference conserved after treatment
  - Genes with difference not conserved after treatment

- Results:
  - Some inferred differential expression of isoforms, but marginal and seemingly non-related.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Expression
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500
300
200
100
10
1
E001
E002
E003
E004
E005
E006
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E009
E010
E011
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E019
E020
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57799650
57814438
57829225
57844013
57858800
57873588
57888375
57903163
57917950

Are genes related to the PR-complex differentially expressed between the cell lines?

Are genes related to the PR-complex differentially expressed between the cell lines?

- 7 / 9 genes are differentially expressed between controls of T47D and MCF7
- 9 / 9 are differentially expressed between cell lines after progesterone treatment
- Again, isoform analysis show no relevant results

Integration with ChIP-seq binding data

Distance from TSS (kb)	T47D	MCF7
10	3	1
20	4	1
30	7	2

Conclusions

- Cell lines are overall fairly different, with a large set of genes being differentially expressed between them
- This difference mostly remains after treatment with progesterone
- In particular, genes related to the disease condition are more sensitive to progesterone treatment in T47D, but in conflict with expectations
- Integration of sequencing hints at general bias towards one cell line for significant genes