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Understanding Nanog's role in cell differentiation

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Introduction

- Pluripotency and differentiation are crucial cellular states for normal development and disease control.
- Master transcription factors, such as Nanog, Sox2, and Oct4, play a critical role in pluripotency, but their function in differentiation is not entirely clear.
- This study aims to investigate Nanog's role in differentiation using mouse embryonic stem cells as a model.

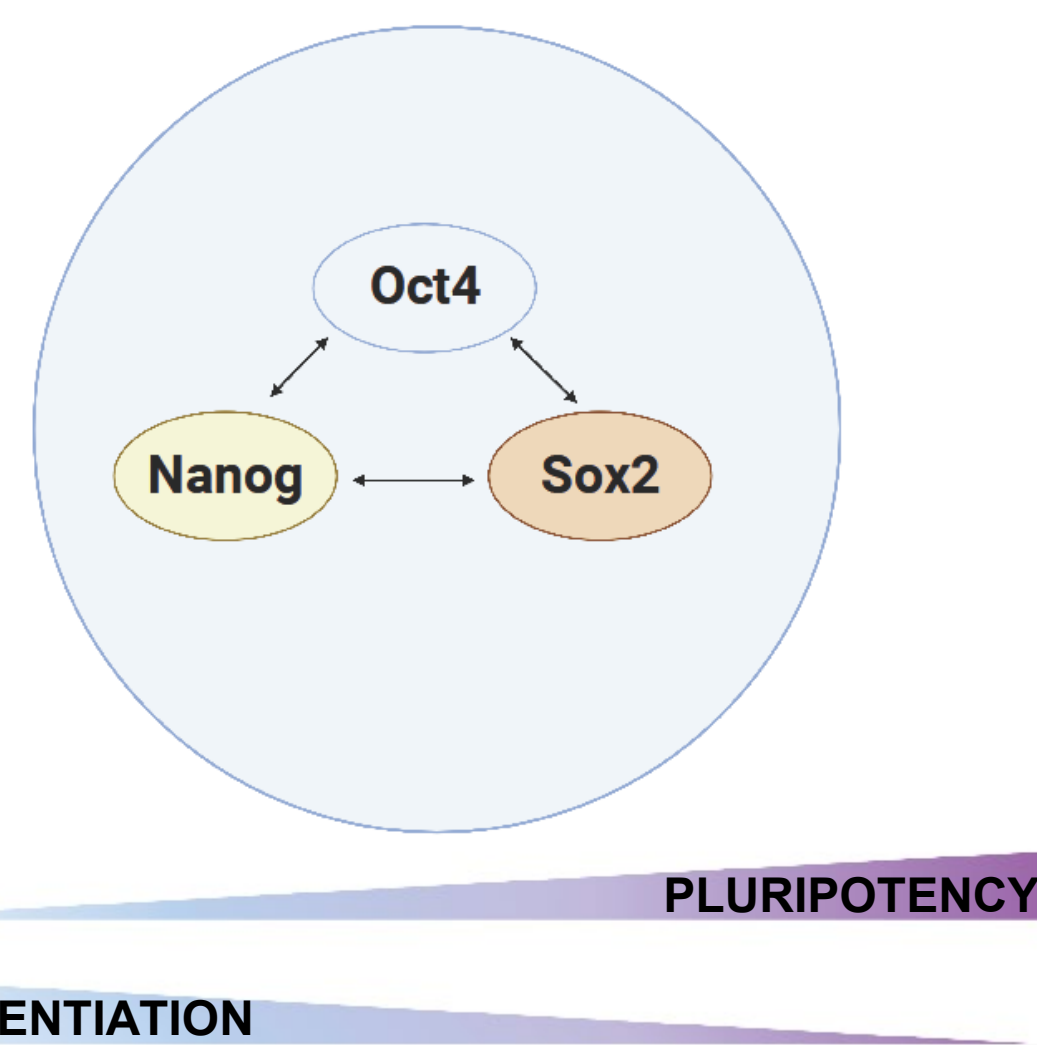


Figure 1. Diagram showing the master pluripotent transcription factors

Methods

- Mouse embryonic stem cells were treated with retinoic acid for 24 hours.
- Gene expression and Nanog ChIP-Seq data were obtained from NCBI sequence read archive database (Accession ID: SRP079975)¹.
- Functional analysis and motif discovery were also performed.

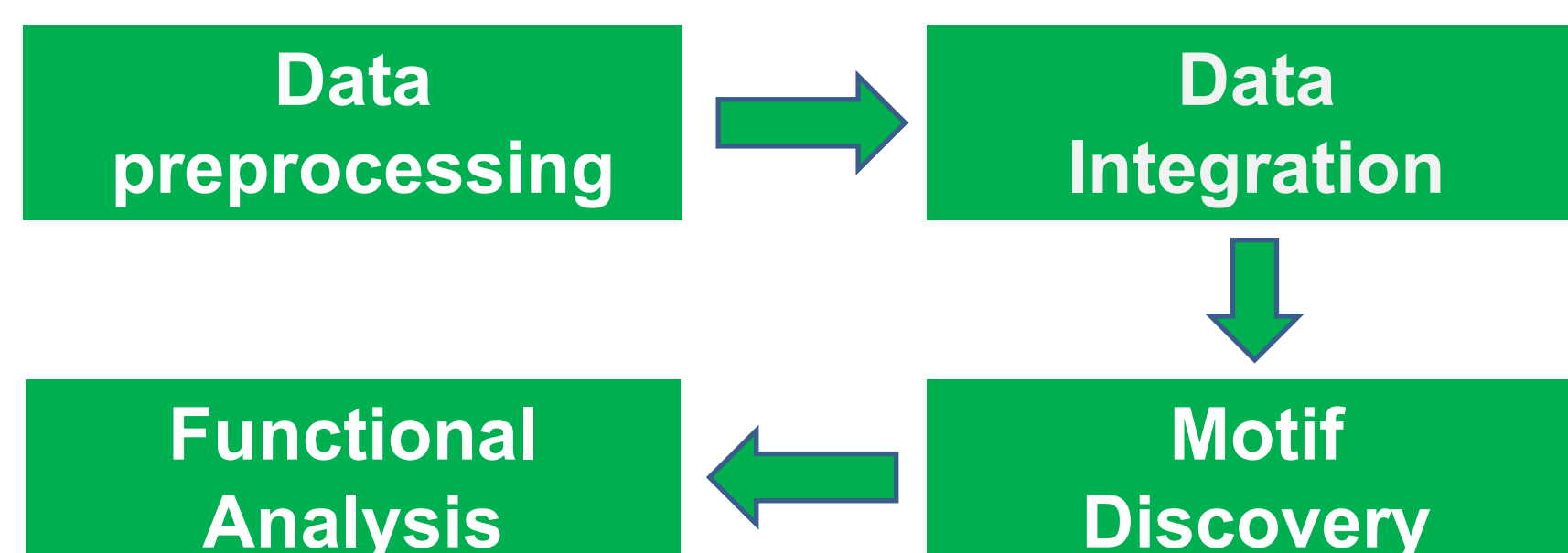


Figure 2. Analysis workflow

Results

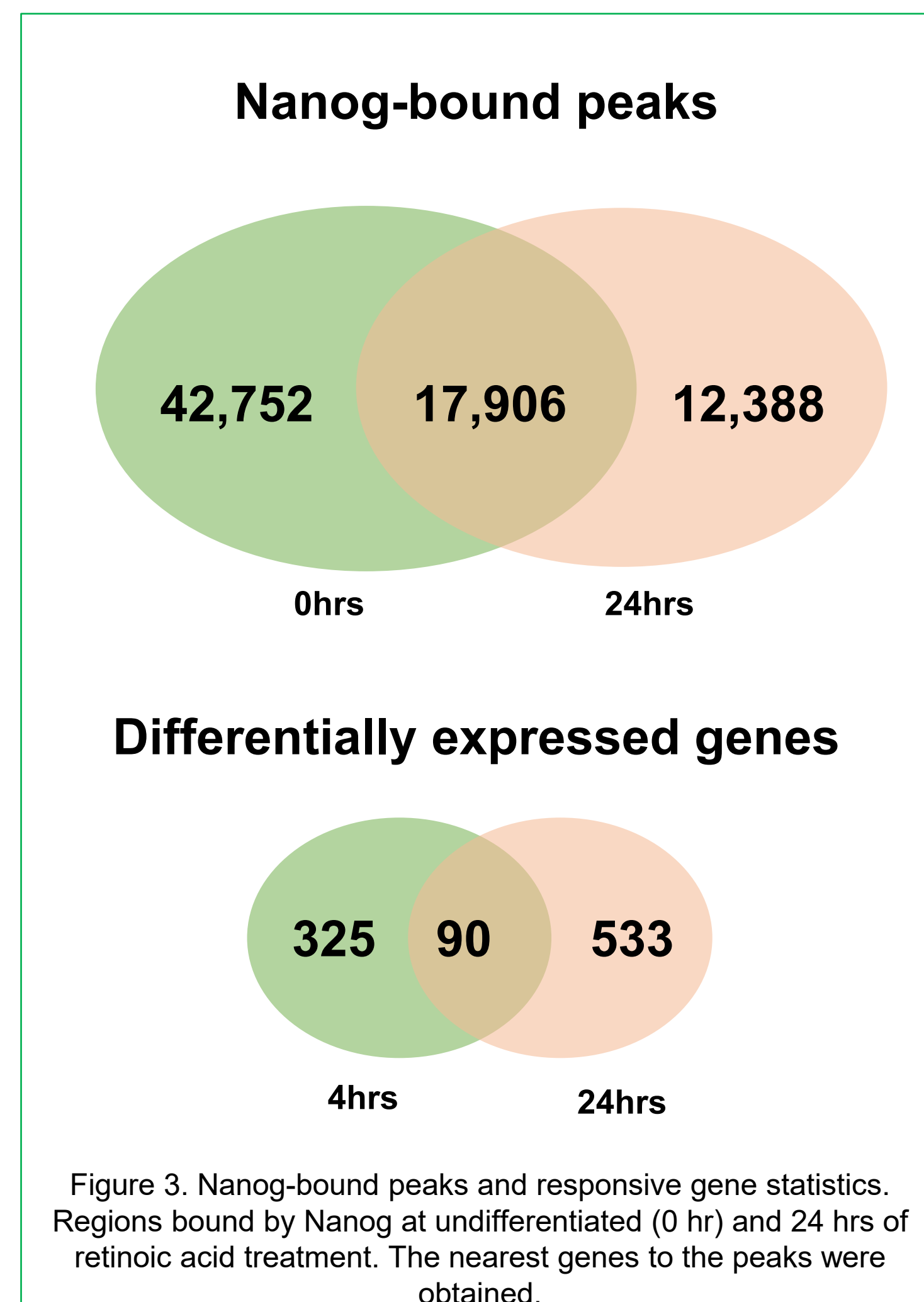


Figure 3. Nanog-bound peaks and responsive gene statistics. Regions bound by Nanog at undifferentiated (0 hr) and 24 hrs of retinoic acid treatment. The nearest genes to the peaks were obtained.

Enriched Motifs at 24hrs

Motif	Name	P Value
	LHX1	1e-113
	OCT4	1e-91
	KLF6	1e-87
	FLI1	1e-87
	NANOG	1e-50

Figure 5. Enriched motifs at 24hr identified by HOMER³. Most of Nanog motifs are lost at 24hrs and there is recruitment of new motifs, involved in mesodermal differentiation.

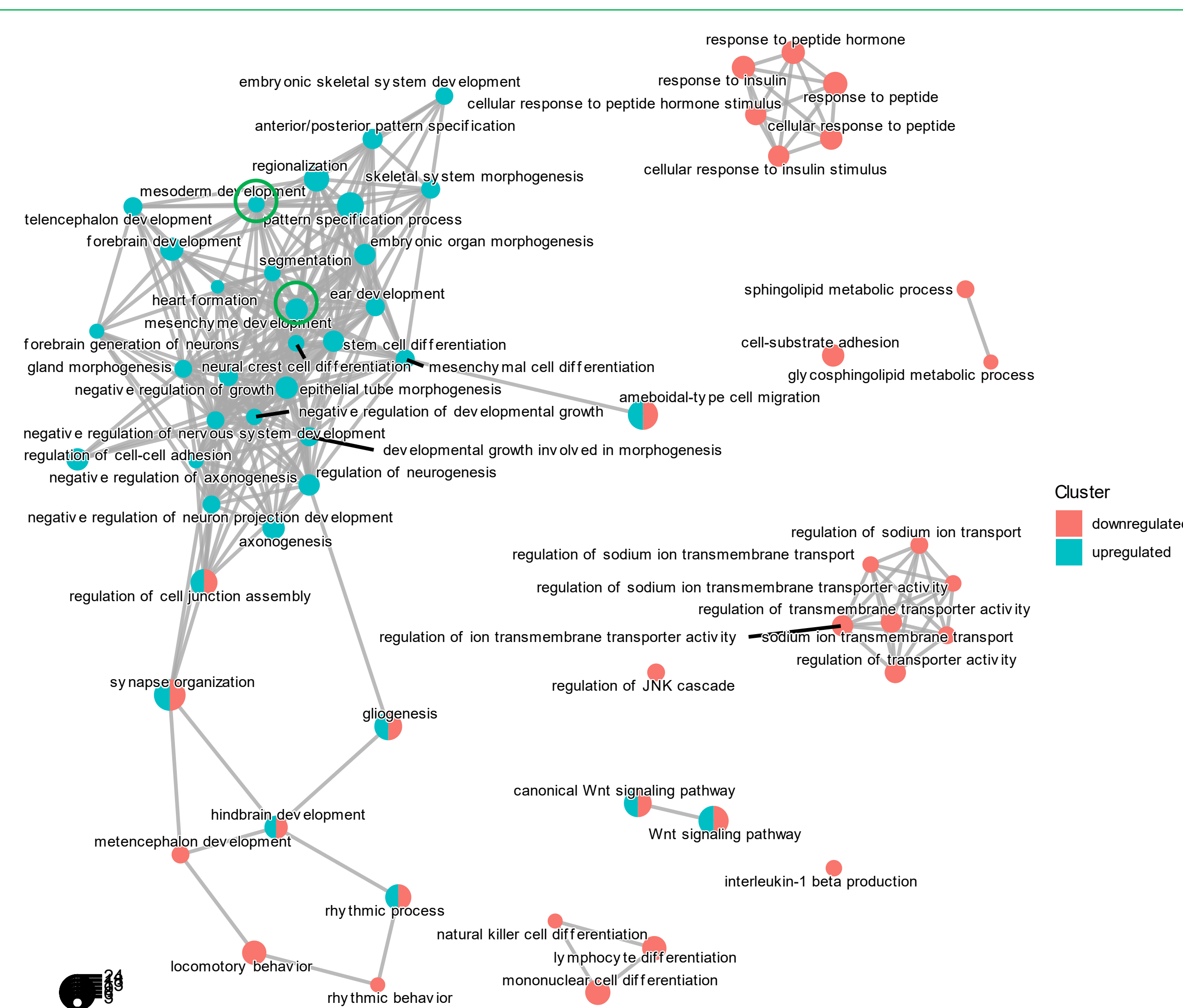
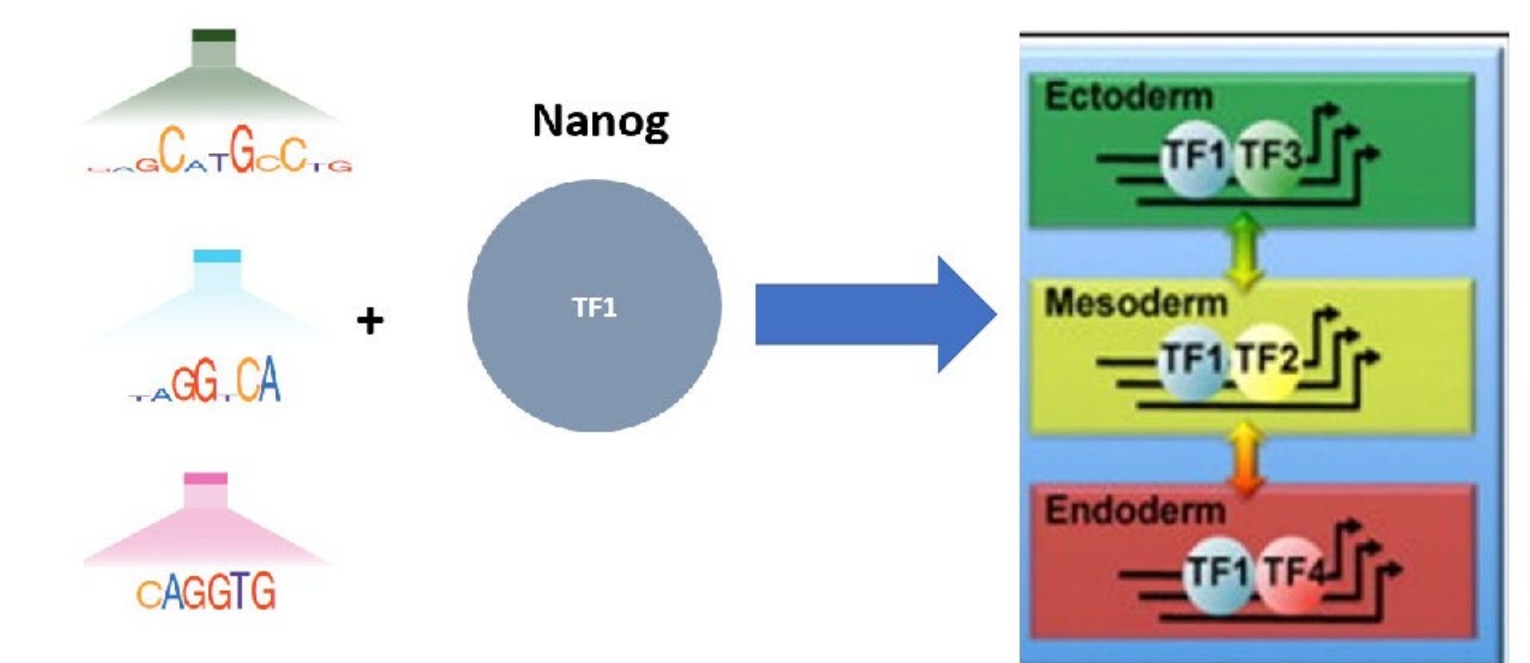


Figure 4. Functional enrichment analysis of differentially regulated genes at 4hrs of neuroectodermal differentiation using clusterProfiler². The enriched pathways of genes (325) closest to Nanog-bound peaks (42752) are mostly involved in mesodermal development.

Conclusions

- This study suggests Nanog regulates mesodermal differentiation through indirect recruitment by mesodermal transcription factors.
- Further research is necessary to understand Nanog's precise mechanism of involvement in differentiation.

Future Directions



- We propose that Nanog can act in a combinatorial fashion with other transcription factors to direct the lineage specificities of cells during development.

Figure 6: Proposed model and future direction.

Acknowledgments

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