

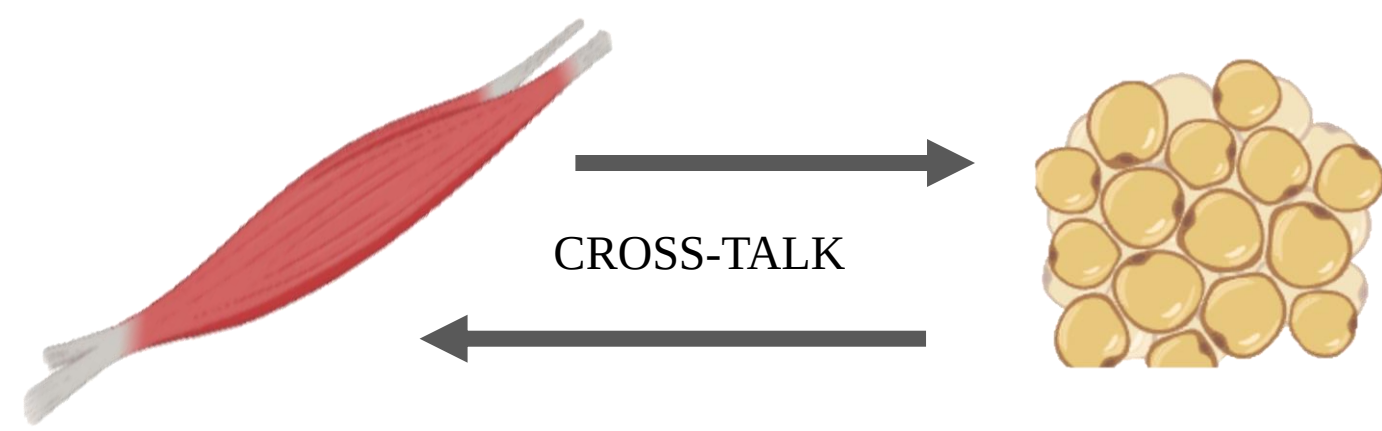
Changes in mRNA Expression Profiles of Follistatin-Like (FSTL) Family Members in Muscle and Adipose Tissues of Obese Diabetic Patients

Sheila Jafari¹, Reza Afrisham¹

¹ Department of Medical Laboratory Sciences, School of Allied Medical Sciences, Tehran University of Medical Sciences, Tehran, Iran

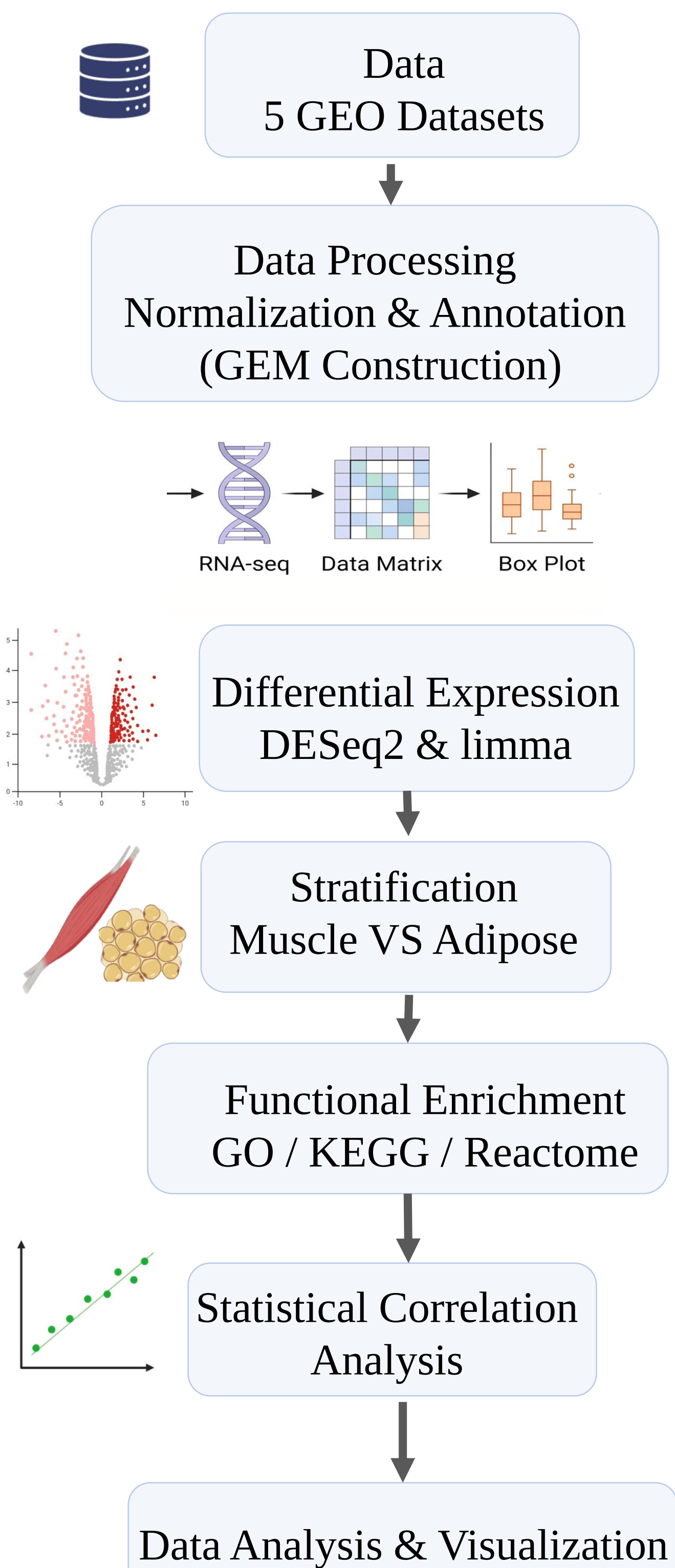
1. INTRODUCTION & AIM

- T2DM is associated with chronic inflammation, insulin resistance and adipose tissue dysfunction.
- FSTL family proteins (FSTL1-5) are secreted glycoproteins with roles in muscle-adipose cross-talk and metabolic regulation.
- Aim: Bioinformatically evaluate FSTL gene expression profiles in skeletal muscle and adipose tissue from lean, normal-weight (NW), obese non-diabetic (OW), and obese T2DM (OW-T2DM) individuals.



2. METHODS

Study Design: Bioinformatics analysis of 5 GEO transcriptomic datasets



3.Result

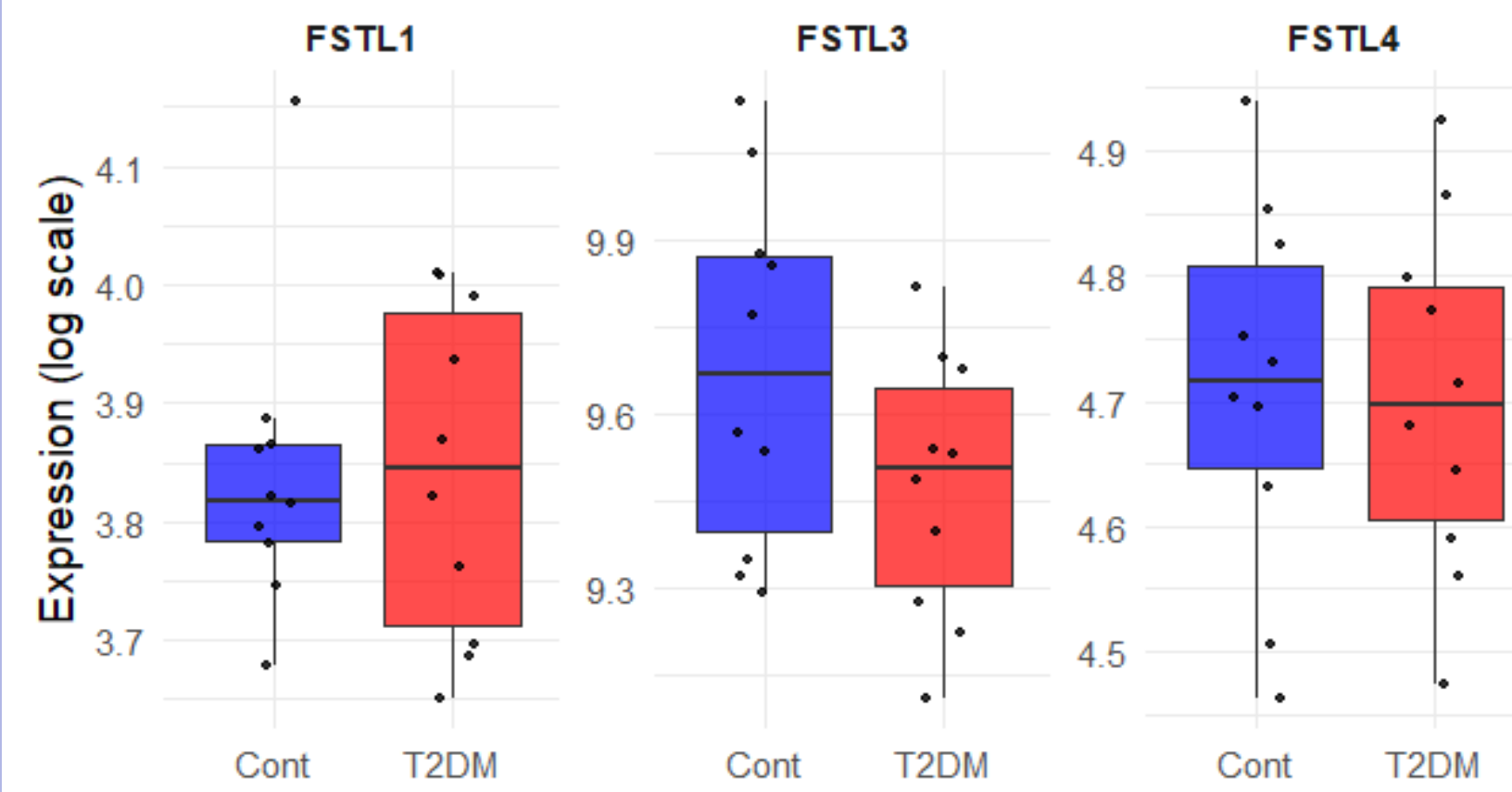


Figure 1. Microarray analysis comparing skeletal muscle samples from overweight individuals with type 2 diabetes mellitus (n = 10) and healthy controls (n = 10) revealed no statistically significant changes in the expression of *FSTL* family members

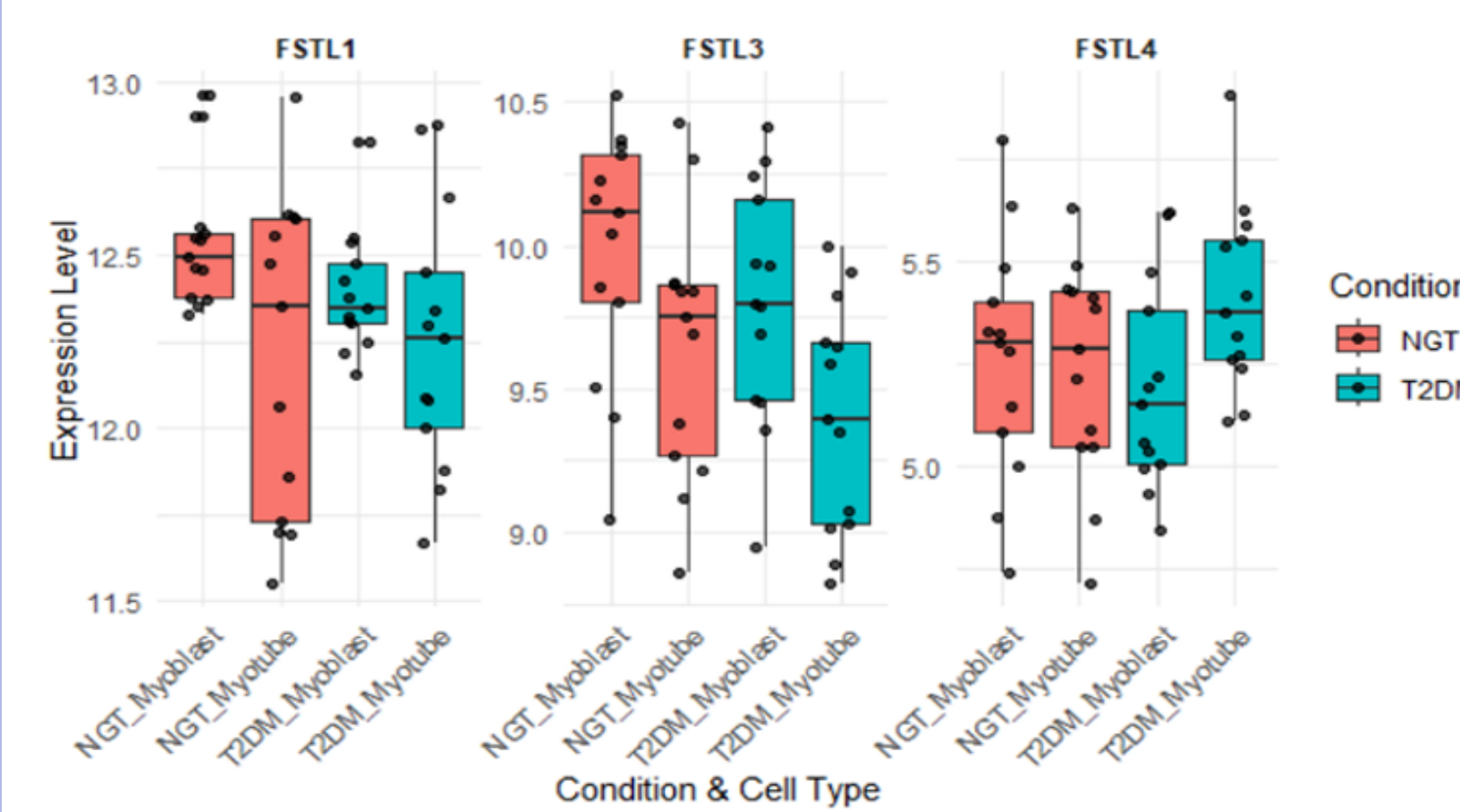


Figure 2. Comparison between myotubes and myoblasts from NW-NGT (n=13) and OW-T2DM (n=13). For both *FSTL3* and *FSTL1*, the differentiation of myotubes to myoblasts was associated with reduced expression in both T2DM and NGT.

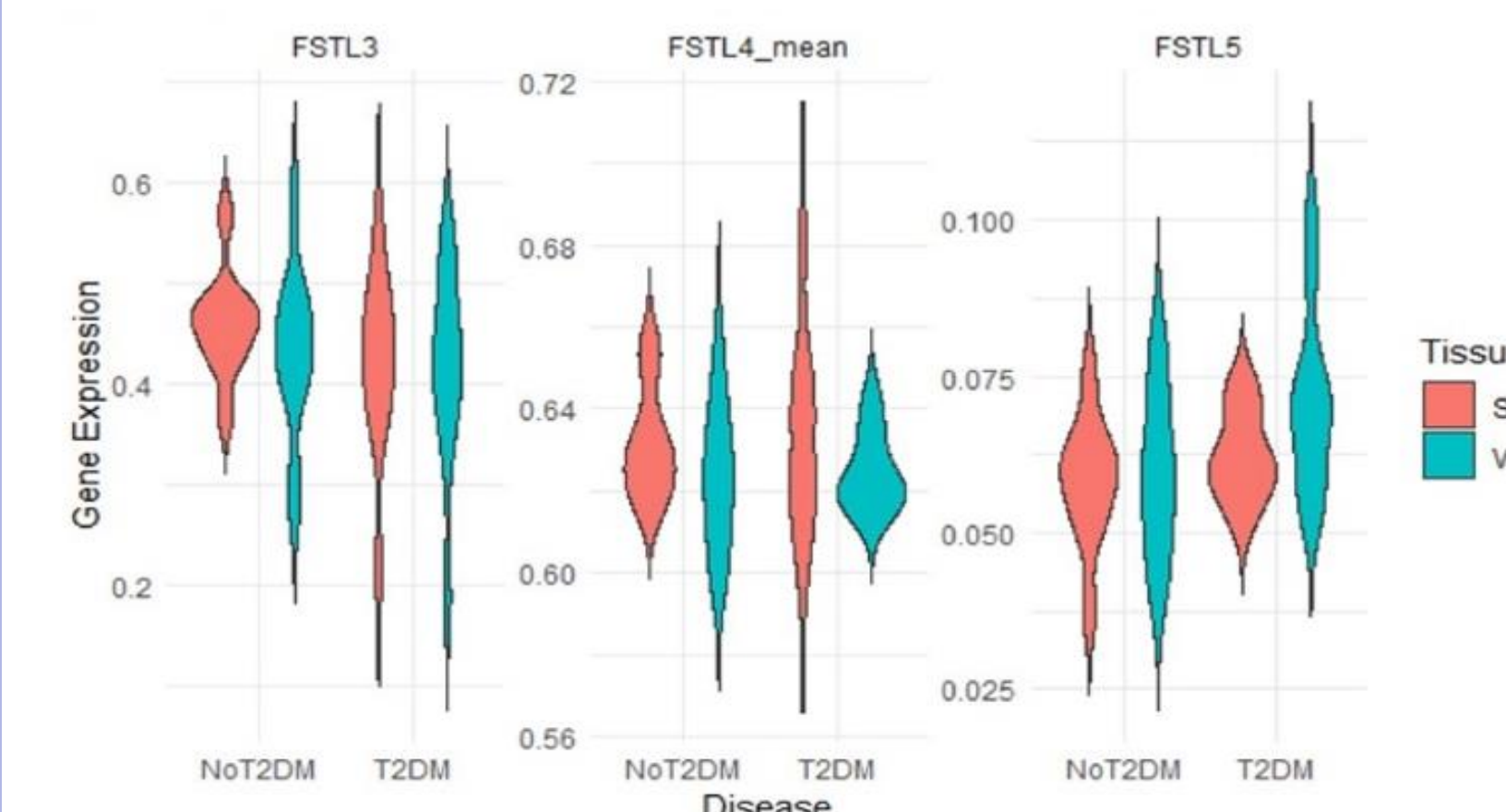


Figure 3. Expression of *FSTL* Genes by disease and tissue. Violin plots show gene expression level distribution for *FSTL3*, *FSTL4*, and *FSTL5* in subcutaneous adipose tissue (SAT) vs. visceral adipose tissue (VAT) in T2DM cases vs. controls.

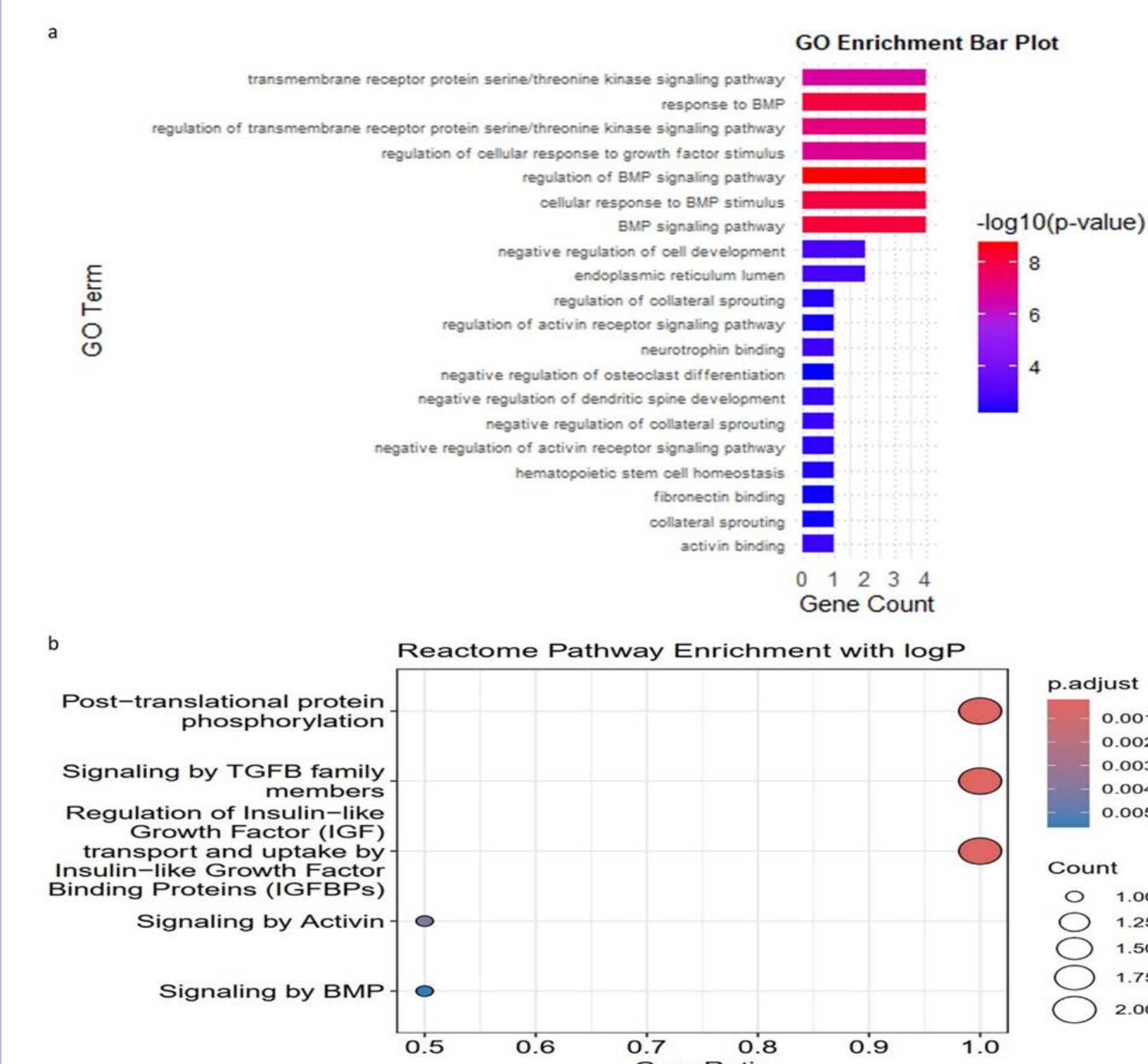


Figure 4. Gene Ontology (GO) and Reactome pathway enrichment analysis of *FSTL*-related genes. (a) GO enrichment bar plot of the most important biological processes involved in *FSTL* gene expression. (b) Reactome pathway enrichment analysis highlighting key signaling pathways involving *FSTL*-related genes.

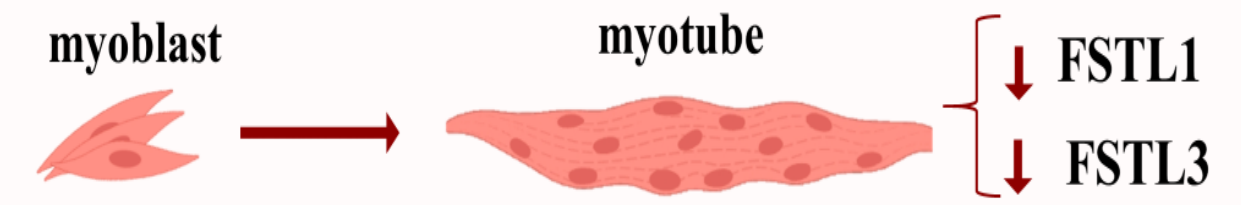
4. Discussion

1 SKELETAL MUSCLE



• No significant differences in FSTL gene expression in OW-T2DM vs. NW individuals.

During myogenic differentiation
(both glycemic statuses)



2 ADIPOSE TISSUE

- FSTL1 ↑ Highly upregulated in obese and diabetic individuals
- FSTL3 ↑ Trend towards upregulation (non-significant)
- FSTL4 ↓ Lean-specific completely lost in both obese and diabetic adipose tissue
- FSTL5 ↓ Lean-specific, completely lost in both obese and diabetic adipose tissue

3 LIFESTYLE INTERVENTION

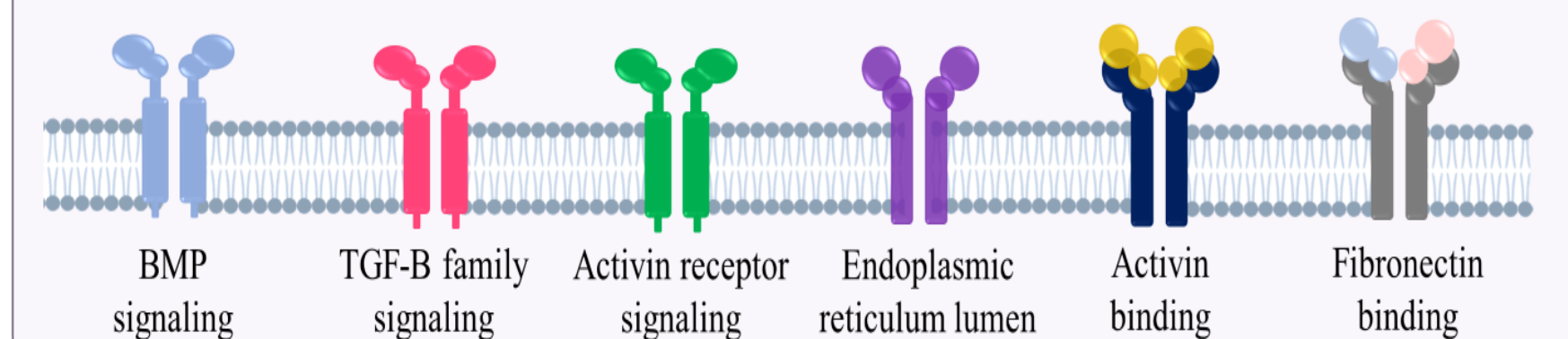


Intensive Lifestyle Therapy

FSTL1 responded to the intervention
FSTL3 responded to the intervention

4 FUNCTIONAL ENRICHMENT ANALYSIS

FSTL Family members are involved in:



5.CONCLUSIONS

- The FSTL family exhibits tissue- and condition-specific expression patterns.
- FSTL4 and FSTL5 are lean-specific, with complete loss in obese and diabetic adipose tissue.
- FSTL1 and FSTL3 are downregulated during myogenic differentiation; FSTL3 is further reduced in T2DM myotubes.
- These genes may serve as diagnostic markers or therapeutic targets in obesity-related T2DM.

6.REFERENCES

- Michalopoulou E, Thymis J, Lampsas S, Pavlidis G, Katogiannis K, Vlachomitros D, et al. The Triad of Risk: Linking MASLD, Cardiovascular Disease and Type 2 Diabetes; From Pathophysiology to Treatment. *Journal of Clinical Medicine*. 2025;14(2):428.
- Guerreiro VA, Carvalho D, Freitas P. Obesity, adipose tissue, and inflammation answered in questions. *Journal of obesity*. 2022;2022(1):2252516.
- Pervin S, Reddy ST, Singh R. Novel roles of follistatin/myostatin in transforming growth factor- β signaling and adipose browning: Potential for therapeutic intervention in obesity related metabolic disorders. *Frontiers in Endocrinology*. 2021;12:653179.

ACKNOWLEDGMENTS

The authors would like to thank the NCBI Gene Expression Omnibus (GEO) for providing access to the transcriptomic datasets analyzed in this study