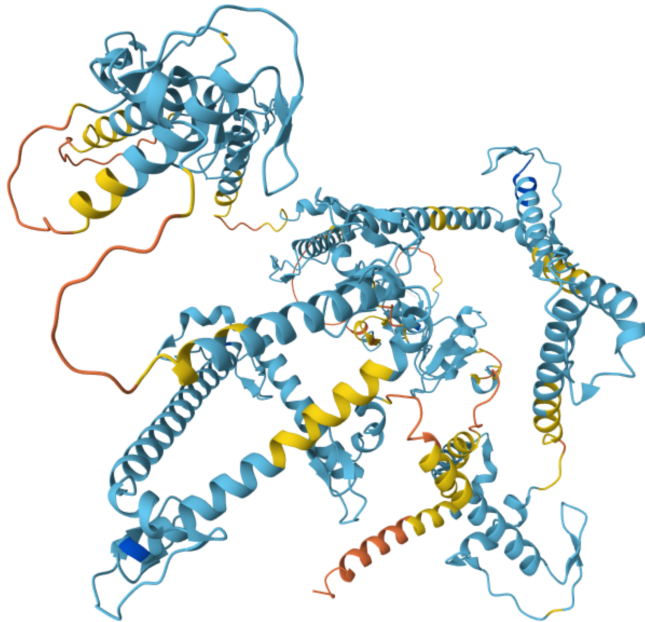




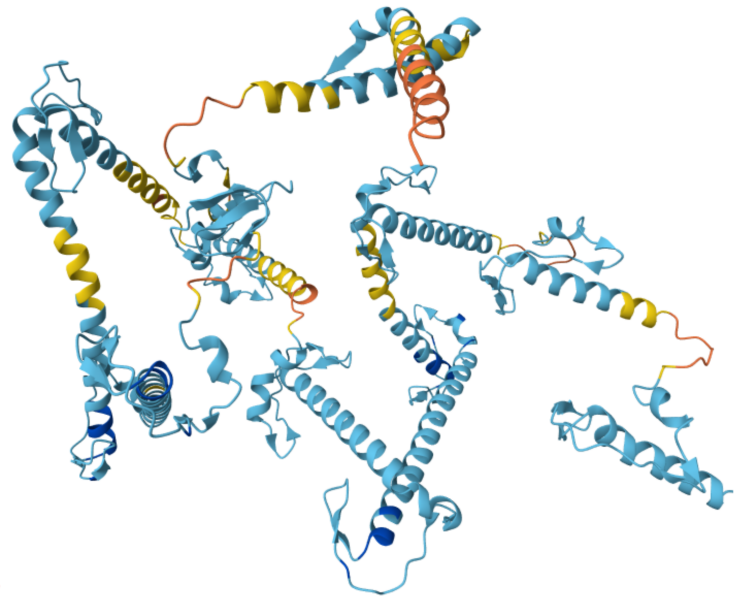
(A)

WT LEKTI



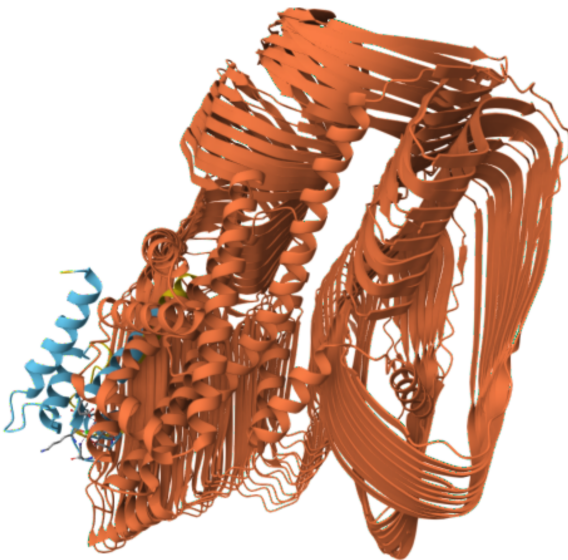
(B)

c.2468dup; p.Lys824Glu fs4 LEKTI



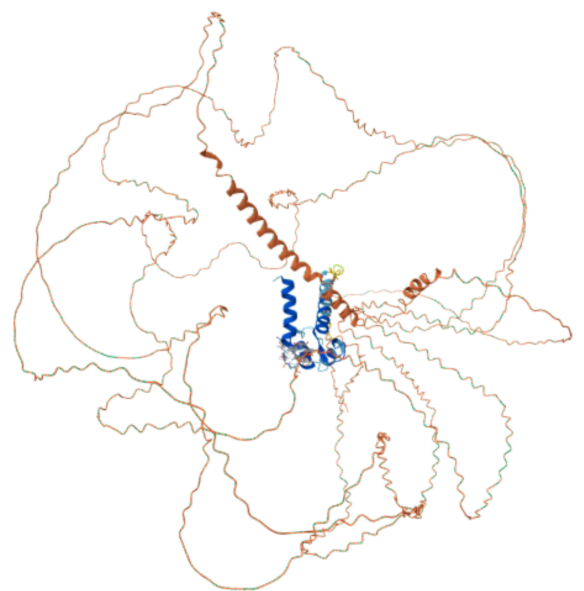
(C)

WT FLG

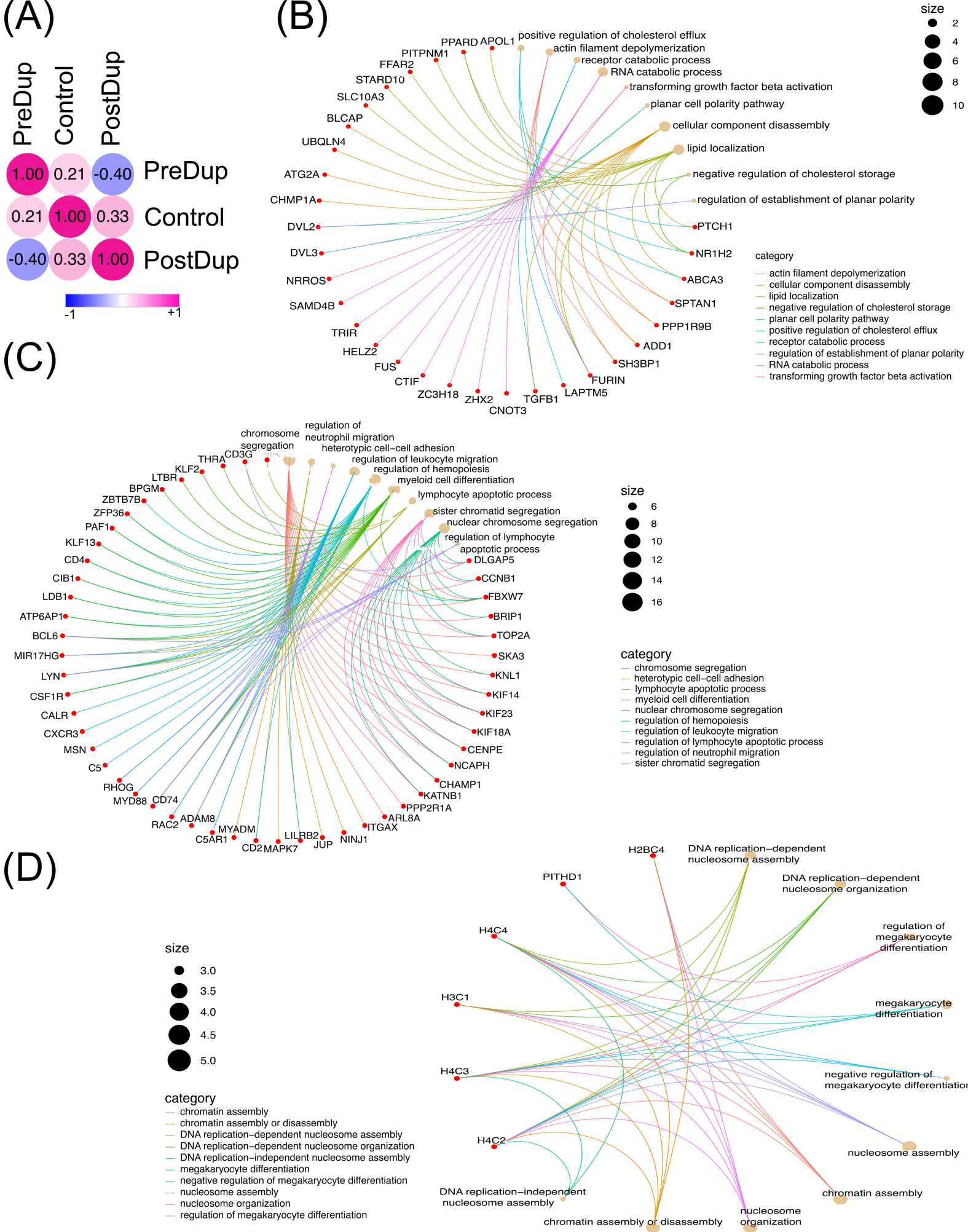


(D)

c.1501C>T; p.Arg501* FLG

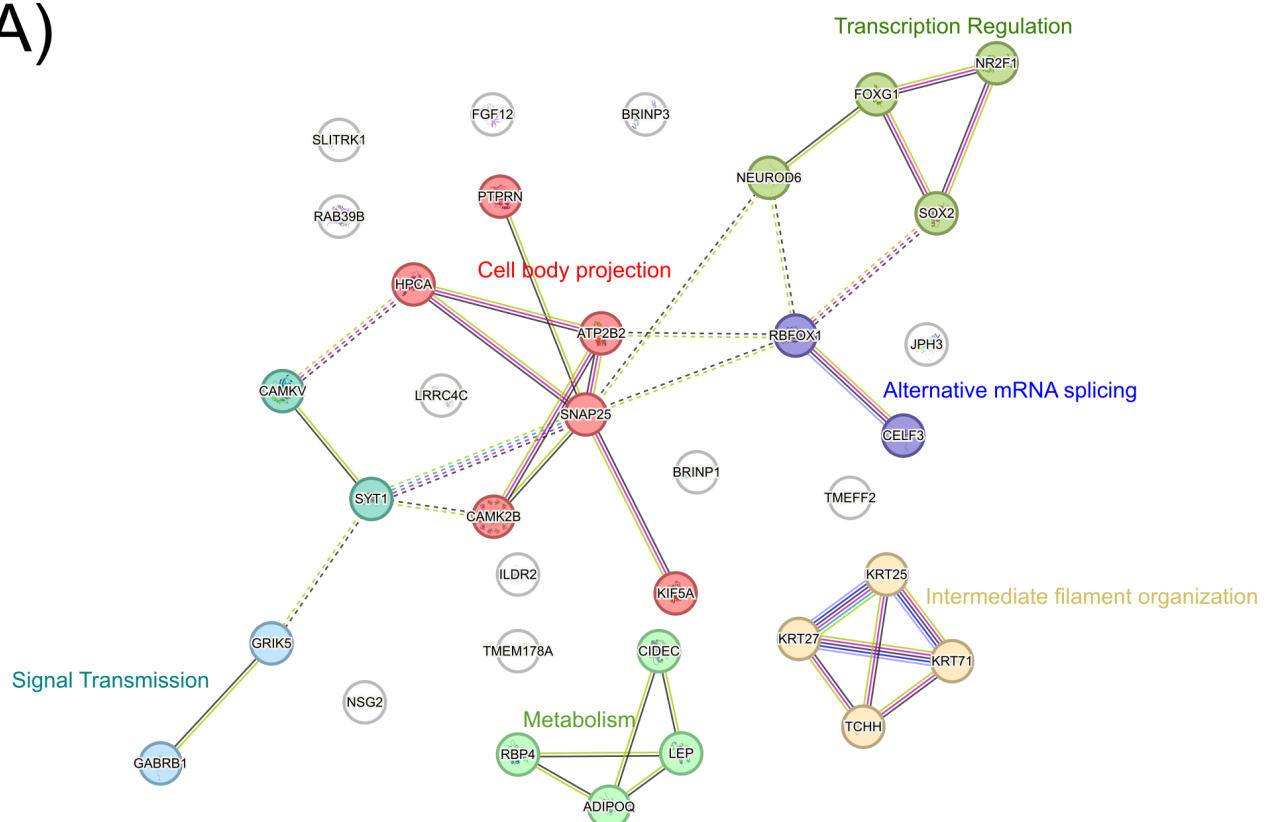


Supplementary Figure 1. AlphaFold3-predicted protein structures, colored according to the predicted confidence (pLDDT) score as indicated in the legend at the top of the page. (A) Wild-type (WT) Lympho-epithelial Kazal-type-related inhibitor (LEKTI) predicted protein structure; (B) c.2468dup; p.Lys824Glu fs4 Lympho-epithelial Kazal-type-related inhibitor (LEKTI) predicted 3D protein structure; (C) Wild-type (WT) Filaggrin (FLG) protein configuration; (D) Predicted c.1501C>T; p.Arg501* Filaggrin (FLG) 3D protein configuration.

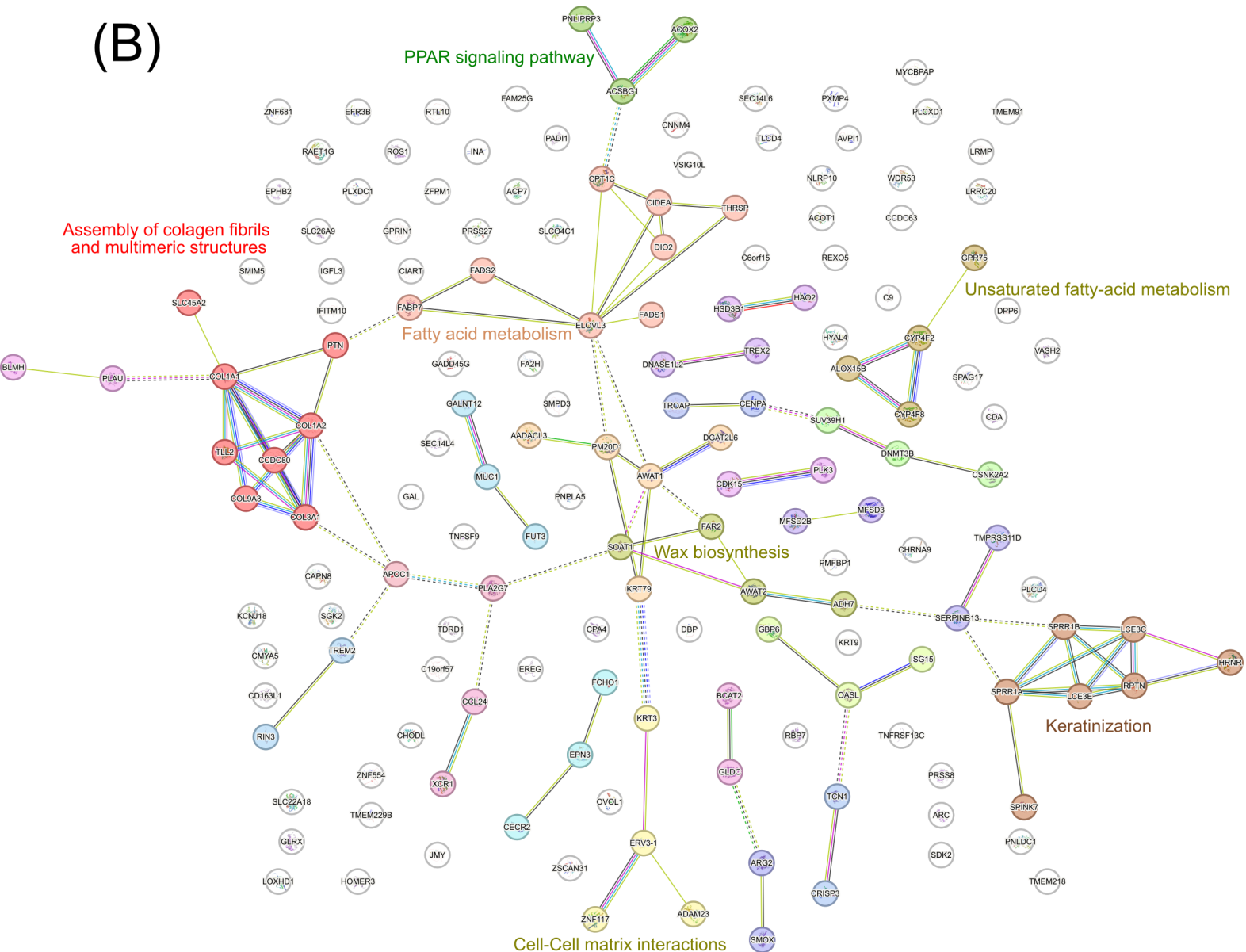


Supplementary Figure 2. Correlation and functional clustering analysis of blood transcriptomic profiles. (A) Spearman correlation matrix of transcriptomic profiles across controls (healthy control samples), pre-Dupilumab (PreDup), and post-Dupilumab (PostDup) samples. Scale: -1 (blue) negative correlation; +1 (magenta) positive correlation. (B) CNETplot showing enriched Gene Ontology (GO) Biological Process (BP) terms for cluster 1. (C) CNETplot displaying enriched GO BP terms for clusters 5 and 10. (D) CNETplot illustrating enriched GO BP terms for clusters 17 and 18; dot size: number of contributing genes, dot colors: red - genes; neutral - pathways/processes.

(A)



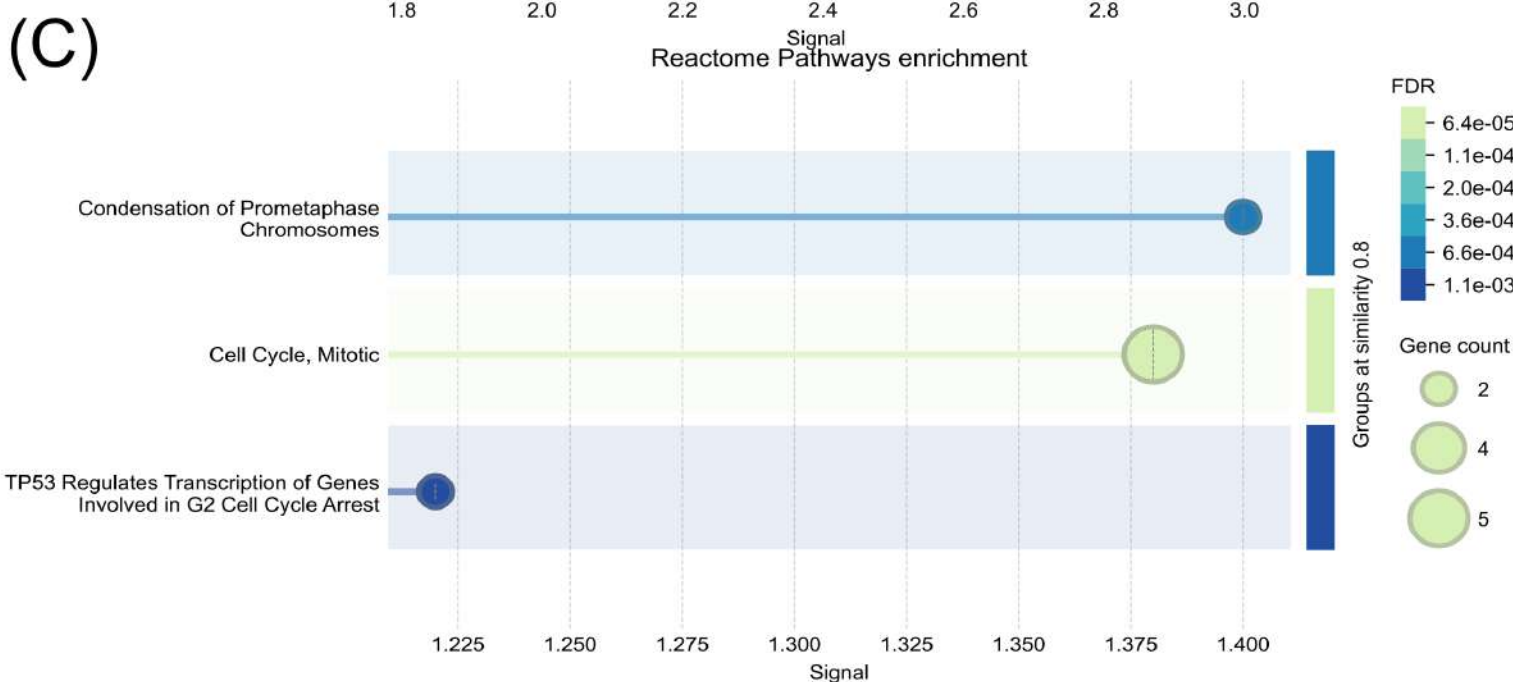
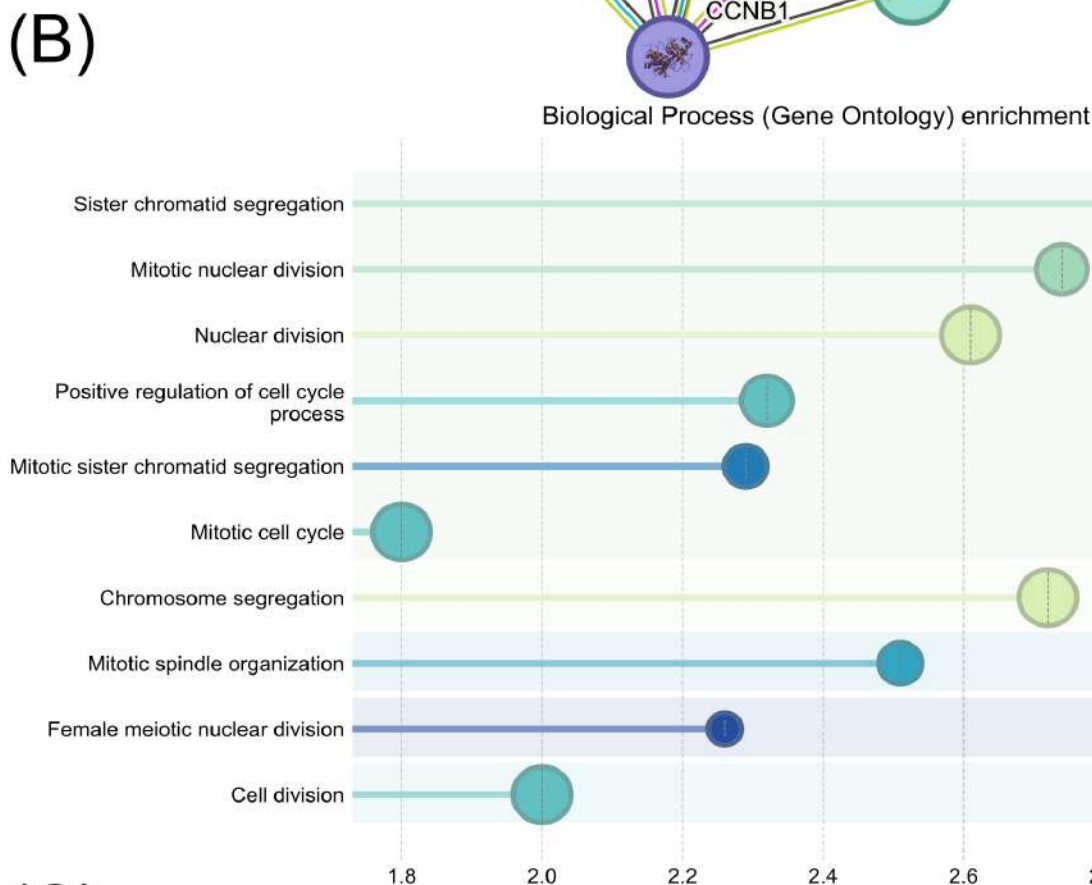
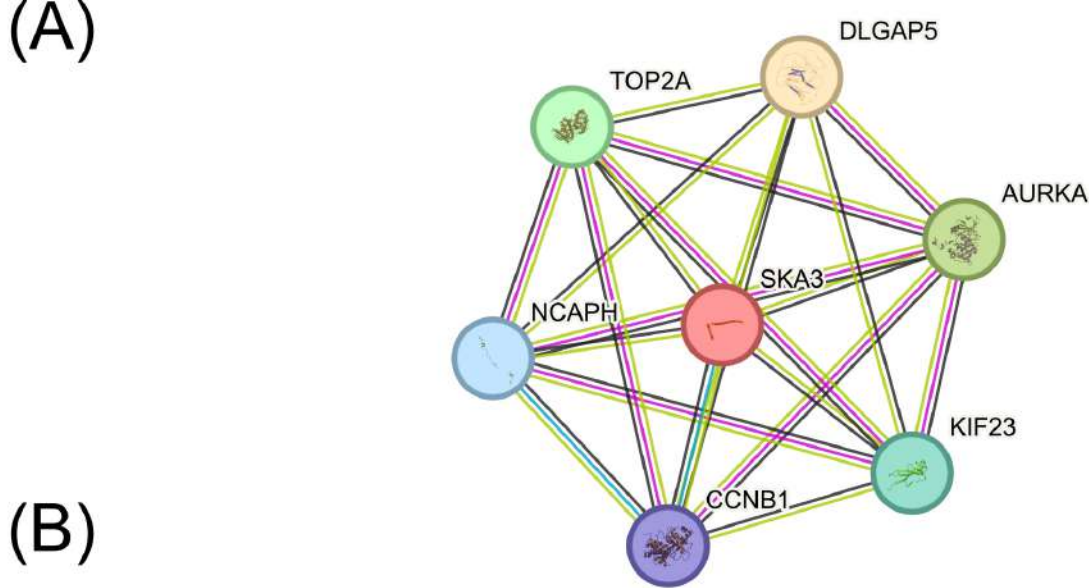
(B)



Supplementary Figure 3. STRING network analysis of significantly upregulated genes in tissues before and after Dupilumab treatment. (A) STRING network of genes upregulated in pre-Dupilumab samples. (B) STRING network of genes upregulated in post-Dupilumab. Networks were clustered using the MCL algorithm with an inflation parameter of 3, and edges connecting different clusters are shown as dotted lines.



Supplementary Figure 4. Functional enrichment of transcriptomic changes in NS skin before and after Dupilumab treatment. (A) CNETplot showing the top 10 enriched Gene Ontology (GO) Biological Process (BP) pathways in genes upregulated before Dupilumab treatment (B) Top 10 enriched GO Cellular Component (CC) and Molecular Function (MF) terms in genes upregulated before Dupilumab treatment; (C) CNETplot showing the top 10 enriched GO BP pathways after Dupilumab treatment; (D) Top 10 enriched GO CC and MF terms in genes upregulated after Dupilumab treatment. (E) Reactome pathway analysis highlighting the most significantly enriched pathways identified after Dupilumab treatment.



Supplementary Figure 5. Enrichment analysis of seven upregulated genes (SKA3, DLGAP5, AURKA, TOP2A, KIF23, NCAPH, and CCNB1) that are common between BPostDup and tissue TNS. (A) STRING network of the candidate genes; (B) Bar plot showing Gene Ontology Biological Process (GO BP) enrichment analysis; (C) Bar plot showing Reactome pathway enrichment analysis.