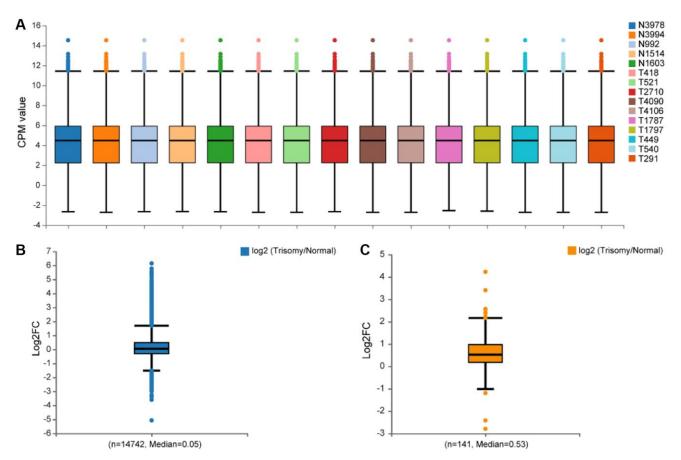
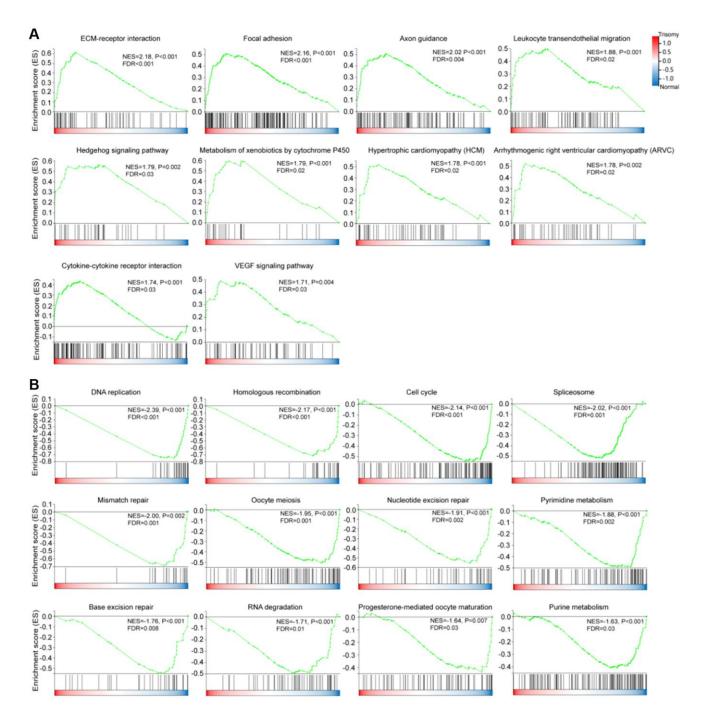
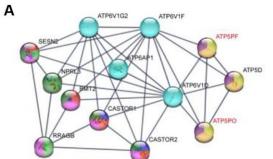
SUPPLEMENTARY FIGURES

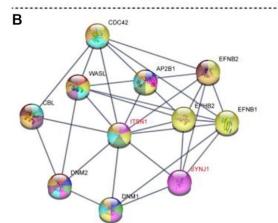


Supplementary Figure 1. Distribution of mRNA expression and fold change in Normal versus Trisomy. (A) Boxplot of mRNA expression in each sample from this study. (B) Boxplot of all the mRNA fold change distribution in Normal versus Trisomy. (C) Boxplot of HSA21 genes' fold change distribution in Normal versus Trisomy.



Supplementary Figure 2. Gene set enrichment analysis (GSEA) of all expressed genes in the "C2: curated gene sets" KEGG gene sets collection of MSigDB (Broad Institute). (A) Enriched GSEA KEGG pathways in Trisomy group. (B) Enriched GSEA KEGG pathways in Normal group.

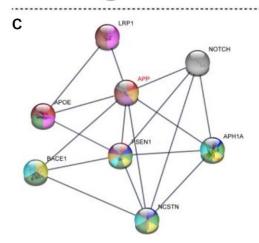




GO-BP term	count in network	strength	FDR	colour
Cellular response to I-arginine	2 of 3	3.0	0.0011	۲
Negative regulation of torc1 signaling	4 of 17	2.55	1.79e-06	
Cellular response to leucine starvation	2 of 10	2.48	0.0051	
Mitochondrial atp synthesis coupled proton transport	3 of 21	2.33	0.00021	
Regulation of torc1 signaling	5 of 39	2.29	2.47e-07	
Negative regulation of tor signaling	5 of 43	2.24	2.91e-07	
Transferrin transport	4 of 36	2.22	1.50e-05	
Cristae formation	3 of 31	2.16	0.00045	
Mitochondrion organization	4 of 452	1.12	0.0262	

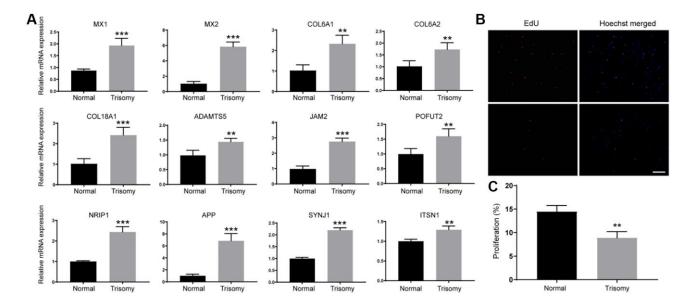
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GO-BP term	count in network	strength	FDR	colour
Positive regulation of clathrin-dependent endocytosi	s 2 of 4	2.95	0.00088	
Postsynaptic neurotransmitter receptor internalization	on 3 of 8	2.82	1.47e-05	
Synaptic vesicle budding from presynaptic endocytic zone membrane	2 of 7	2.71	0.0017	
Synaptic vesicle endocytosis	5 of 48	2.27	1.00e-07	
Ephrin receptor signaling pathway	8 of 86	2.22	4.36e-13	
Clathrin-dependent endocytosis	2 of 29	2.09	0.0135	
Positive regulation of endocytosis	7 of 103	2.08	2.02e-10	
Positive regulation of receptor-mediated endocytosis	s 3 of 53	2.0	0.00078	
Regulation of endocytosis	8 of 205	1.84	1.77e-10	
Regulation of receptor-mediated endocytosis	4 of 102	1.84	0.00011	



GO-BP term	count in network	strength	FDR	colour
Positive regulation of amyloid fibril formation	3 of 4	3.26	2.58e-06	
Notch receptor processing, ligand-dependent	3 of 7	3.02	4.15e-06	
Amyloid-beta formation	3 of 7	3.02	4.15e-06	
Amyloid precursor protein catabolic process	4 of 12	2.91	8.91e-08	
Positive regulation of amyloid-beta clearance	2 of 7	2.84	0.00088	
Amyloid precursor protein metabolic process	5 of 19	2.81	1.27e-09	۲
Amyloid-beta metabolic process	4 of 18	2.74	2.68e-07	
Modulation of age-related behavioral decline	2 of 9	2.74	0.0012	
Neuron projection maintenance	2 of 10	2.69	0.0013	
Regulation of amyloid-beta clearance	3 of 17	2.64	2.34e-05	
Notch signaling pathway	5 of 120	2.01	1.16e-06	

Supplementary Figure 3. HSA21 up-regulated genes involved STRING protein network. (A–C) Secondary 3 networks clustered in the upregulated genes. The HSA21-related genes are marked in red.



Supplementary Figure 4. Gene expression validation and cell proliferation assay. (A) RT-qPCR validation of 12 HSA21 genes (n = 4, **p < 0.01, ***p < 0.001). (B) Microscope images of EdU staining in amniocytes from Normal and Trisomy group (scale bar = 100 μ m). (C) Quantitative results of proliferation ability in each group (n = 3, **p < 0.01).