SUPPLEMENTARY MATERIALS

Integrated transcriptomics and metabolomics explore the effects of infant formula on the growth and development of small intestinal organoids

Tables

Fig.S1 Overall analysis of metabolomics data. (A) PCA analysis of metabolites in SIOs of PMS1-3. The PC1 and PC2 scores of different samples are visualized, and the variance contributed by their corresponding components is presented. (B) Heatmap of the quantity of metabolites of PMS1-3. (C) Volcano plots visualize the differential expressed metabolites of PMS1-3.

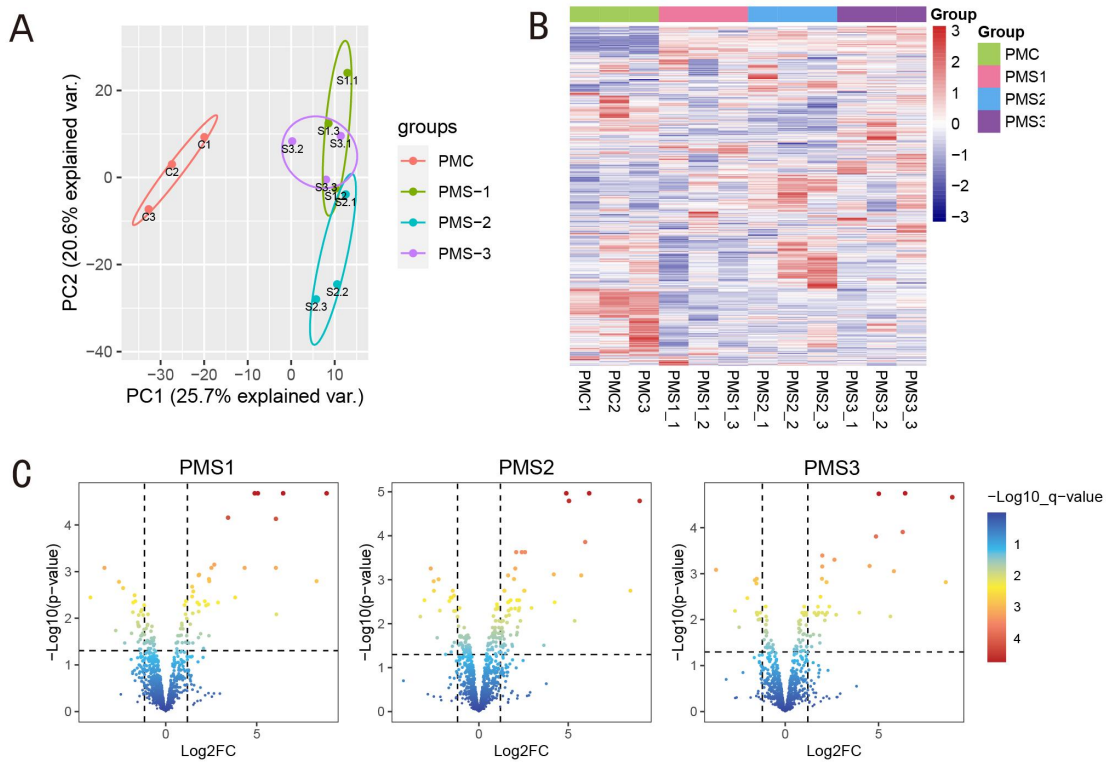
Fig.S2 Bubble diagram illustrating the significant KEGG pathway for common DEGs and common differential expressed metabolites. Color of the dots indicates the level of significance, with red being the most significant and yellow being the least. The pathway impact values from the pathway topology analysis are represented by the size of the dots, and the range of the impact values is 0.00 to 1.00.

Table S1. Ingredients of PMS1-3 formula milk powders.

Group	Ingredients
PMS1	High oil whey powder [desalinated whey, thin cream, vegetable oil (soybean oil, sunflower seed oil, rapeseed oil, coconut oil), L-ascorbic acid sodium, phospholipids, mixed tocopherol concentrate, ascorbic acid palmitate], whole milk powder, polyfructose, arachidonic acid oil, eicoshexaenoic acid oil, whey protein powder, inositol, nucleotide, choline, L-tryptophan, L-carnitine, lutein, taurine. Minerals: tricalcium phosphate, calcium carbonate, potassium chloride, sodium chloride, magnesium sulfate, ferrous sulfate, zinc lactate, copper sulfate, manganese sulfate, potassium iodate, sodium selenite. Vitamins: Sodium L-ascorbate, dl-α-Acetate tocopherol, niacinamide, D-calcium pantothenate, thiamine hydrochloride, retinol acetate, pyridoxine hydrochloride, folic acid, plant methylphenanthrene, D-biotin, cholecalciferol, cyanocobalamide, ascorbic palmitate, riboflavin.
PMS2	High oil whey powder [desalinated whey, thin cream, vegetable oil (soybean oil, sunflower seed oil, rapeseed oil, coconut oil), L-ascorbic acid sodium, phospholipids, mixed tocopherol concentrate, ascorbic acid palmitate], whey protein concentrate, polyfructose, arachidonic acid oil, eicoshexaenoic acid oil, whey protein powder, inositol, nucleotide, choline, L-tryptophan, L-carnitine, lutein, taurine, Lactobacillus lactis (with an added amount of $1x10^9$ CFU/100 g milk powder) Minerals: tricalcium phosphate, calcium carbonate, potassium chloride, sodium chloride, magnesium sulfate, ferrous sulfate, zinc lactate, copper sulfate, manganese sulfate, potassium iodate, sodium selenite. Vitamins: Sodium L-ascorbate, dl-α-Acetate tocopherol, niacinamide, D-calcium pantothenate, thiamine hydrochloride, retinol acetate, pyridoxine hydrochloride, folic acid, plant methylphenanthrene, D-biotin, cholecalciferol, cyanocobalamide, ascorbic palmitate, riboflavin.
PMS3	High oil whey powder [desalinated whey, thin cream, vegetable oil (soybean oil, sunflower seed oil, rapeseed oil, coconut oil), L-ascorbic acid sodium, phospholipids, mixed tocopherol concentrate, ascorbic acid palmitate], whole milk powder, polyfructose, arachidonic acid oil, eicoshexaenoic acid oil, whey protein powder, inositol, lactoferrin, nucleotide, choline, L-tryptophan, L-carnitine, lutein, taurine, Lactobacillus lactis (with an added amount of $1x10^9$ CFU/100 g milk powder) Minerals: tricalcium phosphate, calcium carbonate, potassium chloride, sodium chloride, magnesium sulfate, ferrous sulfate, zinc lactate, copper sulfate, manganese sulfate, potassium iodate, sodium selenite. Vitamins: Sodium L-ascorbate, dl-α-Acetate tocopherol, niacinamide, D-calcium pantothenate, thiamine hydrochloride, retinol acetate, pyridoxine hydrochloride, folic acid, plant methylphenanthrene, D-biotin, cholecalciferol, cyanocobalamide, ascorbic palmitate, riboflavin.

Table S2. List of primers used in qRT-PCR experiments.

Gene	Forward Primer (5'-3')	Reverse Primer (5'-3')
ASPM	GGCCCTAGACAACCCTAACGA	AGCTTGGTGTTTCAGAACATCA
BCL2L1	TTGCCAGCCGGAACCTATG	CGAAGGCGACCAGCAATGATA
BIRC5	AGGACCACCGCATCTCTACAT	AAGTCTGGCTCGTTCTCAGTG
CASP3	CATGGAAGCGAATCAATGGACT	CTGTACCAGACCGAGATGTCA
CCNB2	CCGACGGTGTCCAGTGATTT	TGTTGTTTTGGTGGGTTGAACT
CCND1	GCTGCGAAGTGGAAACCATC	CCTCCTTCTGCACACATTTGAA
CENPF	CTCTCCCGTCAACAGCGTTC	GTTGTGCATATTCTTGGCTTGC
CXCR4	ACTACACCGAGGAAATGGGCT	CCCACAATGCCAGTTAAGAAGA
ESR1	CCCACTCAACAGCGTGTCTC	CGTCGATTATCTGAATTTGGCCT
FOXO1	TCGTCATAATCTGTCCCTACACA	CGGCTTCGGCTCTTAGCAAA
HNF1A	AACACCTCAACAAGGGCACTC	CCCCACTTGAAACGGTTCCT
HNF1B	ACCAAGCCGGTCTTCCATACT	GGTGTGTCATAGTCGTCGCC
HNF4G	ATGGACATGGCAAATTACAGTGA	TTGACACCGTTGTCTGTGGTA
HSP90AA1	AGGAGGTTGAGACGTTCGC	AGAGTTCGATCTTGTTTGTTCGG
ICAM1	ATGCCCAGACATCTGTGTCC	GGGGTCTCTATGCCCAACAA
IL18	ATGCTCTGTTTGGGCTGGATA	GTGAGAGTCGATTTCTGTGGC
IL1B	ATGATGGCTTATTACAGTGGCAA	GTCGGAGATTCGTAGCTGGA
IRF1	ATGCCCATCACTCGGATGC	CCCTGCTTTGTATCGGCCTG
KIF11	TCCCTTGGCTGGTATAATTCCA	GTTACGGGGATCATCAAACATCT
KIF23	AGTCAGCGAGAGCTAAGACAC	GGTTGAGTCTGTAGCCCTCAG
KIF2C	CTGTTTCCCGGTCTCGCTATC	AGAAGCTGTAAGAGTTCTGGGT
MAPK8	GCGCATGATCTCGTCCATCTC	CCGACTCGTACTCGCTGTTG
MYC	GGATTCCCGCCTCAGAATAAC	GTGGGTGTGGGTTGTTCAGG
NEUROD1	ATGACCAAATCGTACAGCGAG	GTTCATGGCTTCGAGGTCGT
NEUROG3	CTAAGAGCGAGTTGGCACTGA	GAGGTTGTGCATTCGATTGCG
NFKBIA	CTCCGAGACTTTCGAGGAAATAC	GCCATTGTAGTTGGTAGCCTTCA
NKX2-2	CCGGGCCGAGAAAGGTATG	GTTTGCCGTCCCTGACCAA
NKX6-1	GGACTGCCACGCTTTAGCA	TGGGTCTCGTGTGTTTTCTCT
PAX4	ATACCCGGCAGCAGATTGTG	AAGACACCTGTGCGGTAGTAA
RFX6	AAGCAGCGGATCAATACCTGT	ACCGTGGTAAGCAAACTCCTT
RRM2	TGGTGAAGCGGCCTAATCC	GCAACATGAGTCGAAAGGTCG
SIRT1	TAGCCTTGTCAGATAAGGAAGGA	ACAGCTTCACAGTCAACTTTGT
SOCS3	CCTGCGCCTCAAGACCTTC	GTCACTGCGCTCCAGTAGAA



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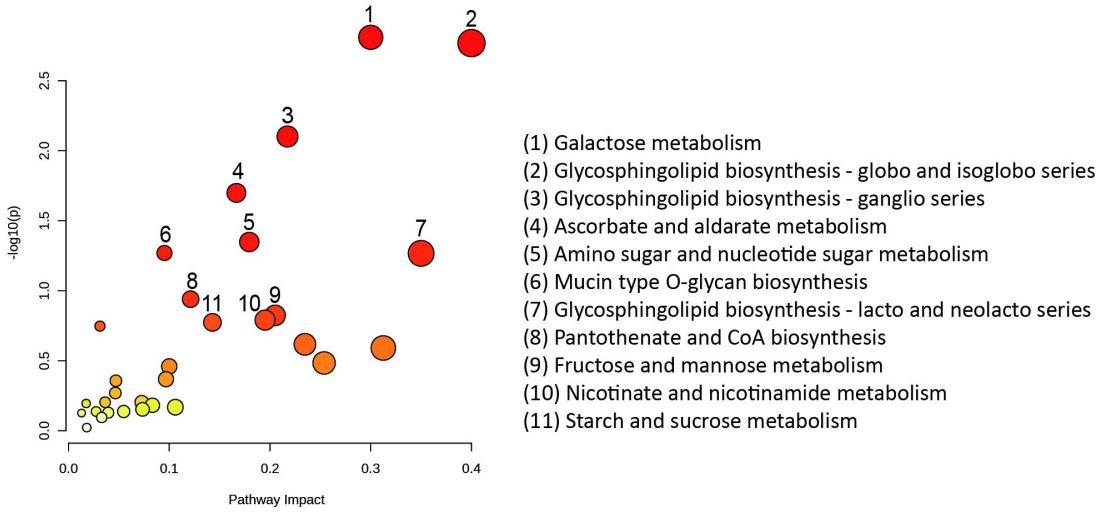

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