Table SI. Composition analysis of LA20k9 and BMFM.

Metabolite name and group	LA20k9 composition	BMFM composition
Protein, mg/g	418.00	484.90
Monosaccharides and disaccharides, mg/g		
Fructose	21.19	23.58
Glucose	31.19	306.56
Sucrose	19.34	47.78
Maltose		0.29
Organic acids, mg/g		
Tartaric acid	24.47	15.01
Malic acid	26.63	
Lactic acid	96.31	152.07
Pyruvic acid	6.38	5.71
Oxalic acid	1.33	2.67
Acetic acid	92.92	39.74
Citric acid	99.75	144.75
Succinic acid	59.17	
Propionic acid	35.84	30.60
Benzenolactic acid	0.57	1.17
Amino acids, mg/g		
Aspartic acid	26.50	87.20
Threonine	11.80	39.80
Serine	14.50	45.20
Glutamic acid	53.50	175.90
Glycine	40.00	72.60

Alanine	23.80	73.90
Cystine	0.30	7.80
Valine	14.80	50.80
Methionine	5.40	14.70
Isoleucine	12.20	44.90
Leucine	21.90	67.30
Tyrosine	6.90	19.20
Phenylalanine	12.60	11.20
Histidine	17.70	9.30
Lysine	18.30	16.90
Arginine	15.30	14.10
Proline	35.30	33.00

LA20k9, Life Age 20k9; BMFM, blank substrate fermentation metabolite.

Table SII. Differential genes of DOX vs. NC.

Gene name	$\log_2$ (Fold change)	Gene function
TOB1	8.927085672	An anti-proliferative protein that negatively regulates cell cycle progression
UBR4	8.824640823	An E3 ubiquitin-protein ligase involved in protein degradation and cellular stress responses
TM7SF2	8.376097983	A transmembrane protein associated with lipid metabolism and membrane homeostasis
TUBB4B	8.181267611	A tubulin isoform contributing to microtubule cytoskeleton organization
PIDD	8.051143064	A p53-induced death domain protein mediating apoptosis and cell cycle arrest
FOSL1	8.005824614	A Fos-like transcription factor regulating cell proliferation and stress responses
ESYT3	7.913758759	An extended synaptotagmin involved in membrane trafficking and lipid transport
FAAH	7.874893073	A serine hydrolase responsible for the degradation of endocannabinoids and lipid signaling termination
CD70	7.569743062	A transmembrane TNF superfamily ligand mediating T cell co-stimulation and immune regulation
CHRD	7.551288373	A secreted BMP antagonist regulating dorsal-ventral patterning and embryonic development
WDR75	-9.185282148	A ribosome biogenesis factor required for rRNA processing and ribosomal assembly
CFI	-7.697788409	A trypsin-like serine protease involved in complement system regulation
HSPA13	-7.468369209	A heat shock protein 70 family member that mediates protein folding and cellular protection
MSH2	-6.963739916	A core component of the post-replicative DNA mismatch repair system maintaining genomic stability
NOP58	-6.839301172	A ribonucleoprotein essential for ribosome biogenesis and pre-rRNA processing
CCDC112	-6.628058119	A coiled-coil domain-containing protein implicated in cytoskeletal organization
SNX2	-6.396921493	A sorting nexin involved in intracellular vesicle trafficking and protein sorting

ZNF25	-6.3741846	A KRAB-containing C2H2 zinc finger transcription factor regulating RNA polymerase II transcription and osteoblast differentiation
ETAA1	-6.20422276	An ATR kinase activator mediating replication stress response and genome stability maintenance
NUDT12	-6.095673342	A pyrophosphohydrolase involved in dinucleotide metabolism and redox homeostasis

DOX, doxorubicin, NC, negative control; rRNA, ribosomal RNA.

Table SIII. Differential genes of DOX vs. LA20k9.

Gene name	$\log_2$ (Fold change)	Gene function
EIF3E	9.106190487	A core subunit of eukaryotic translation initiation factor 3 mediating protein synthesis initiation
CFI	7.501459692	Complement factor I regulating immune and inflammatory responses
SULT1C4	7.420665137	A sulfotransferase involved in metabolism and detoxification
IMPACT	7.179603818	A GCN2 inhibitor regulating amino acid sensing and translational control
PPP4R2	7.027404486	A regulatory subunit of protein phosphatase 4 mediating NF-κB signaling and DNA repair
SERINC1	6.869860505	A membrane protein modulating virus restriction and lipid homeostasis
SLC38A2	6.707449805	A solute carrier responsible for amino acid transport and nutrient sensing
YME1L1	6.439208777	A mitochondrial AAA zinc metalloprotease regulating OPA1 processing, cristae structure and respiratory chain quality control
SCFD1	6.429832626	A Sec1/Munc18 family protein controlling ER-Golgi SNARE assembly, retrograde transport and Golgi integrity
ZC3H15	6.404424701	A zinc-finger protein involved in mRNA processing and cellular homeostasis
MKI67	-6.721087417	Ki-67, a canonical marker of cell proliferation and active cell cycle progression
INPP5J	-6.535465501	An inositol 5-phosphatase regulating phosphoinositide signaling
PLA2G3	-6.521121991	A secretory phospholipase A2 associated with lipid metabolism and inflammation
CYR61	-6.473492476	A cellular communication network factor involved in cell adhesion, migration and stress responses
UBR4	-6.465897198	An E3 ligase associated with protein ubiquitination and stress signaling
TM7SF2	-6.204851059	A transmembrane protein associated with lipid metabolism and membrane homeostasis
MVD	-5.963348698	A mevalonate diphosphate decarboxylase responsible for isoprenoid biosynthesis and cholesterol metabolism
DHCR7	-5.931949328	A 7-dehydrocholesterol reductase mediating cholesterol biosynthesis and Sonic Hedgehog signaling
FADS2	-5.928799293	A fatty acid desaturase regulating polyunsaturated fatty acid biosynthesis and lipid homeostasis
FASN	-5.888018459	A fatty acid synthase catalyzing *de novo* lipogenesis and lipid synthesis

DOX, doxorubicin; LA20k9, Life Age 20k9.