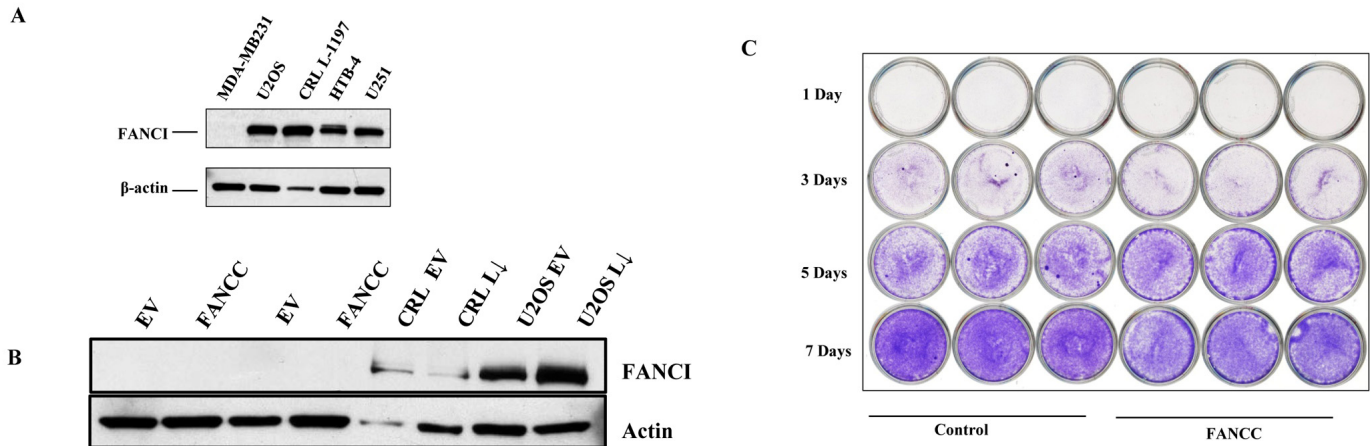
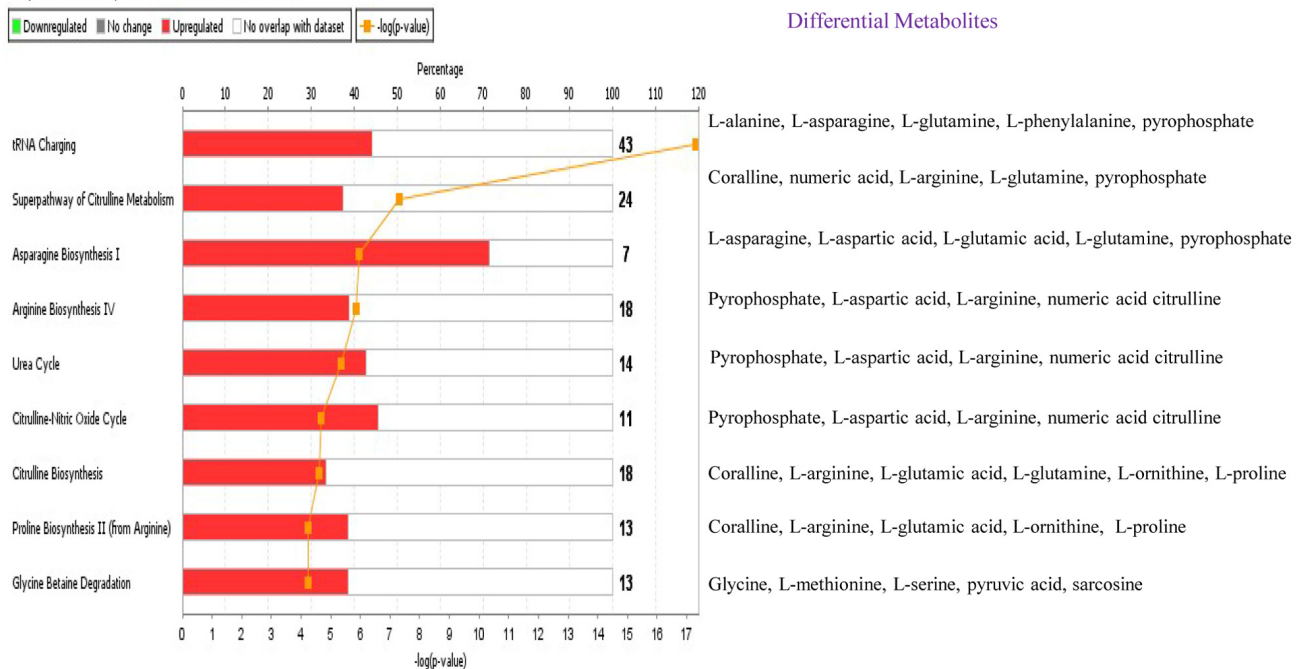


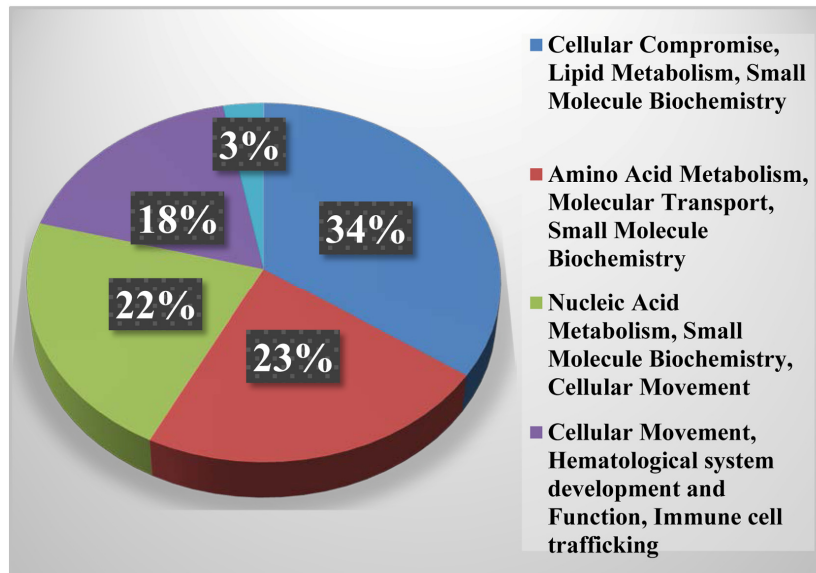
SUPPLEMENTARY MATERIAL



Supplementary Figure 1. (A,B) The FANCI expression is undetectable in MDA-MB231 cells. Additional western blotting showed that FANCI is not detectable in the parental cells (A) as well in derivatives (transfected with empty Vectors for control or FANCC cDNA containing plasmids) (B). (C) Cells containing FANCC cDNA grow slowly. Determination of the cell proliferation of FANCC-high versus low cells. A total of 2000 cells of FANCC-high or low cells were plated in triplicates and stained with crystal violet at the day 1, 3, 5 or 7. FANCC-high cells clearly have a lower density compared to the corresponding FANCC-low cells.



Supplementary Figure 2. Altered basic cellular processes in FANCC-high cells compared to FANCC-low cells. Analysis of molecular processes on the basis of metabolites present in FANCC-high or Low cells. Most significantly altered basic molecular processes and their metabolites revealed by IPA displayed. A total number of signature metabolites for each process were listed at the side.



Supplementary Figure 3. Categories of altered 205 metabolites.

Supplementary Table 1. Summary of metabolomics analysis.

Canonical Pathway	p-Value	Overlap
tRNA Charging	5.1×10^{-18}	44.2% (19/43)
Superpathway of Citrulline Metabolism	4.9×10^{-08}	37.5% (9/24)
Arginine Biosynthesis IV	1.3×10^{-6}	71.4% (5/7)
Asparagine Biosynthesis	1.8×10^{-6}	38.9% (7/18)
Urea Cycle	4.33×10^{-6}	42.9% (6/14)
Diseases and Bio Functions	p-Value	Metabolites
Cancer	$4.39 \times 10^{-02} - 5.93 \times 10^{-14}$	30
Connective tissue Disorders	$3.67 \times 10^{-02} - 3.39 \times 10^{-07}$	15
Gastrointestinal Disease	$4.93 \times 10^{-02} - 5.93 \times 10^{-14}$	28
Inflammatory Disease	$3.67 \times 10^{-02} - 3.39 \times 10^{-07}$	7
Organismal injury and Abnormalities	$4.42 \times 10^{-02} - 5.9 \times 10^{-07}$	36
Molecular and Cellular Functions	p-Value	Metabolites
Cellular growth and Proliferation	$4.93 \times 10^{-02} - 5.93 \times 10^{-14}$	30
Amino Acid metabolism	$3.89 \times 10^{-02} - 2.43 \times 10^{-10}$	21
Molecular Transport	$4.93 \times 10^{-02} - 2.43 \times 10^{-10}$	33
Small Molecule Biochemistry	$4.93 \times 10^{-02} - 2.43 \times 10^{-10}$	36
Cell Cycle	$4.93 \times 10^{-02} - 2.43 \times 10^{-10}$	13
Physiological System Development and Functions	p-Value	Metabolites
Organism Development	$3.36 \times 10^{-02} - 8.20 \times 10^{-10}$	22
Hepatic system Development and Function	$3.67 \times 10^{-02} - 5.85 \times 10^{-11}$	11
Nervous System Development and Function	$4.93 \times 10^{-02} - 2.13 \times 10^{-05}$	15
Organismal Survival	$8.14 \times 10^{-04} - 8.14 \times 10^{-04}$	13
Tissue Morphology	$4.04 \times 10^{-02} - 7.57 \times 10^{-03}$	8

Toxicology Functions		
Clinical Chemistry and Hematology	p-Value	Metabolites
Increased Levels of albumin	$8.20 \times 10^{-10} - 2.80 \times 10^{-10}$	8
Increase Levels of LDH	$1.92 \times 10^{-01} - 1.39 \times 10^{-01}$	3
Increase Levels of Alkaline Phosphatase	$1.32 \times 10^{-03} - 1.32 \times 10^{-03}$	2
Increase Levels of Creatinine	$1.32 \times 10^{-03} - 1.32 \times 10^{-03}$	2
Cardiotoxicity	p-Value	Metabolites
Cardiac Damage	$1.06 \times 10^{-01} - 1.06 \times 10^{-01}$	1
Cardiac Degeneration	$1.06 \times 10^{-01} - 1.06 \times 10^{-01}$	1
Bradycardia	$1.71 \times 10^{-01} - 1.71 \times 10^{-01}$	1
Congenital Heart Anomaly	$1.39 \times 10^{-01} - 1.39 \times 10^{-01}$	1
Cardiac Necrosis/Cell Death	$1.39 \times 10^{-01} - 1.39 \times 10^{-01}$	2
Hepatotoxicity	p-Value	Metabolites
Liver Necrosis/Cell Death	$7.34 \times 10^{-01} - 4.38 \times 10^{-03}$	6
Liver Steatosis	$2.31 \times 10^{-01} - 2.96 \times 10^{-04}$	7
Hepatocellular Carcinoma	$3.29 \times 10^{-06} - 3.29 \times 10^{-06}$	8
Liver Hyperplasia/Hyperproliferation	$3.29 \times 10^{-06} - 3.29 \times 10^{-06}$	8
Liver Inflammation/Hepatitis	$3.03 \times 10^{-01} - 3.67 \times 10^{-02}$	3
Nephrotoxicity	p-Value	Metabolites
Kidney Failure	$2.33 \times 10^{-01} - 3.67 \times 10^{-02}$	2
Renal Necrosis/Cell Death	$1.06 \times 10^{-01} - 3.67 \times 10^{-02}$	5
Glomerular Injury	$1.06 \times 10^{-01} - 1.06 \times 10^{-01}$	1
Nephrosis	$1.06 \times 10^{-01} - 1.06 \times 10^{-01}$	1
Renal Fibrosis	$1.06 \times 10^{-01} - 1.06 \times 10^{-01}$	1

Supplementary Table 2. Top analysis-ready molecules.

Experimental Fold Change up-regulated / down-regulated Molecules	
Metabolites	Fold Change
Inosine	↑ 20.990
Hypoxanthine	↑ 12.640
Pyrophosphate	↑ 8.310
L-asparagine	↑ 7.240
L-phenylalanine	↑ 7.130
Acetyl-L-carnitine	↑ 6.550
Beta-alanine	↑ 6.300
Glutaryl-carnitine	↑ 6.110
Niacinamide	↑ 6.030
Creatinine	↑ 5.910
14:0/22:0 phosphatidylcholine	↓ -8.400
22:1(13Z)/20:3(5Z,8Z,11Z) phosphatidylcholine	↓ -5.880
18:0/24:1(15Z) phosphatidylcholine	↓ -5.610
20:0/22:2(13Z,16Z) phosphatidylcholine	↓ -5.590
20:0/20:2(11Z,14Z) phosphatidylcholine	↓ -5.530
20:0/22:5(7Z,10Z,13Z,16Z,19Z) phosphatidylcholine	↓ -5.380
16:0/24:1(15Z) phosphatidylcholine	↓ -5.320
20:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z) phosphatidylcholine	↓ -4.910
18:3(9Z,12Z,15Z)/22:0 phosphatidylcholine	↓ -4.700
dm18:0/18:1(9Z) phosphatidylcholine	↓ -4.680

Supplementary Table 3. Top networks of the metabolites.

ID	Associated Network Functions	Score
1	Cellular Compromise, Lipid Metabolism, Small Molecule Biochemistry	35
2	Amino Acid Metabolism, Molecular Transport, Small Molecule Biochemistry	23
3	Nucleic Acid Metabolism, Small Molecule Biochemistry, Cellular Movement	22
4	Cellular Movement, Hematological system development and Function, Immune cell trafficking	18
5	Cellular Growth and Proliferation, Organism Development, Organismal Injury and Abnormalities	3