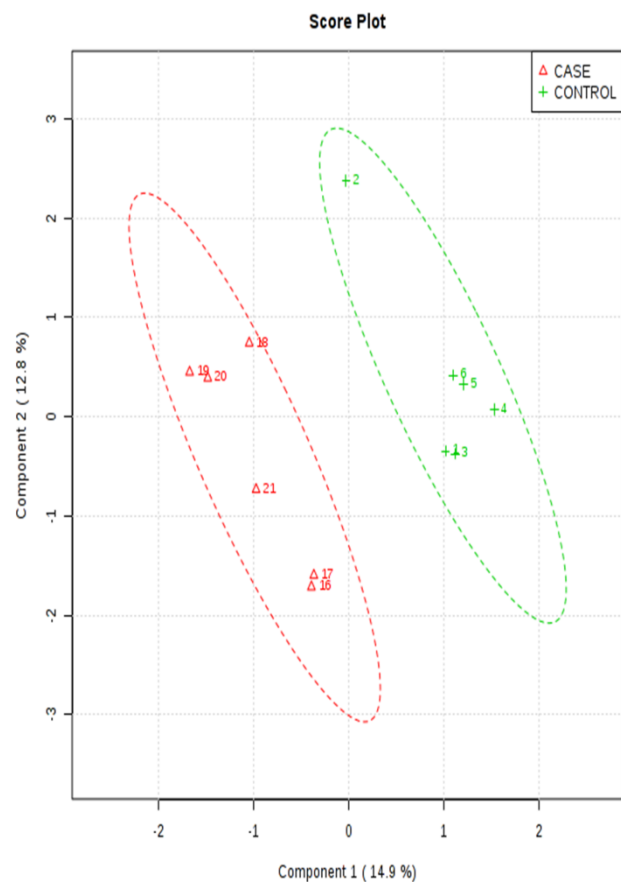


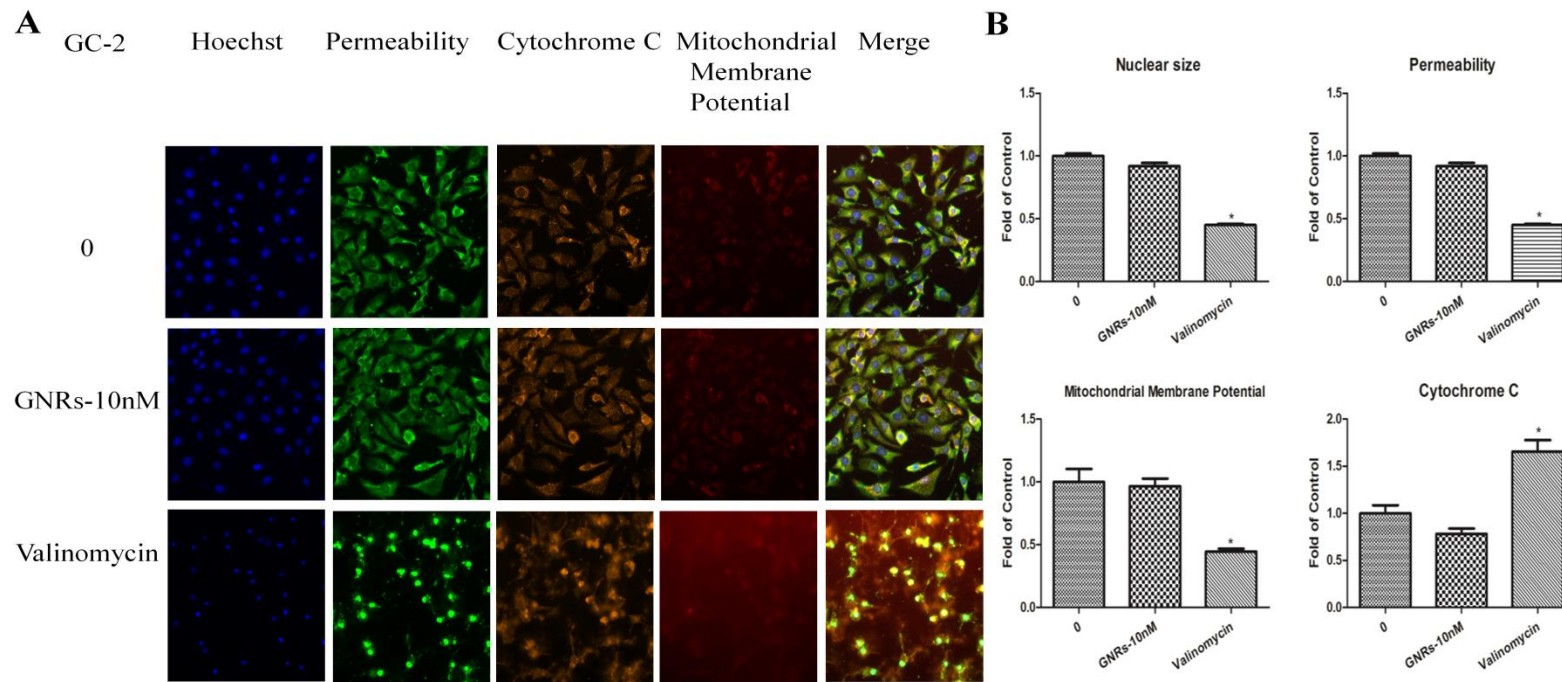
Table S1. Sequences of primers for RT-PCR.

<i>gene</i>		Sequences
<i>mmu</i> - SHMT2	Forward Primer	5'- TGGCAAGAGATACTACGGAGG-3'
	Reverse Primer	5'-AGATCCGCTTGACATCAGACA-3'
<i>mmu</i> - MTHFD1L	Forward Primer	5'-GCATGGCCTTACCCTTCAGAT-3'
	Reverse Primer	5'-GTACGAGCTTCCCCAGATTGA-3'
<i>mmu</i> - SHMT1	Forward Primer	5'- CAGGGCTCTGTCTGATGCAC-3'
	Reverse Primer	5'-CGTAACGCGCTCTTGTCAC-3'
<i>mmu</i> - MTHFD1	Forward Primer	5'-GGGAATCCTGAACGGGAAACT-3'
	Reverse Primer	5'-TGAGTGGCTTTGATCCCAATC-3'
<i>mmu</i> - Claudin-5	Forward Primer	5'- GCAAGGTGTATGAATCTGTGCT-3'
	Reverse Primer	5'- GTCAAGGTAACAAAGAGTGCCA-3'
<i>mmu</i> - Occludin	Forward Primer	5'- CCACCCCATCTGACTATGC-3'
	Reverse Primer	5'- TCGCTTGCCATTCACTTTGC-3'
<i>mmu</i> - ZO-1	Forward Primer	5'- CCTGACGGTTGGTCTTTTGC-3'
	Reverse Primer	5'-ACAGTTGGCTCCAACAAGGT-3'
<i>mmu</i> - Connexin-43	Forward Primer	5'- ATCGTGGATCAGCGACCTTC-3'
	Reverse Primer	5'- GTTGAGTACCACCTCCACGG-3'
<i>mmu</i> -GAPDH	Forward Primer	5'-AGGTCGGTGTGAACGGATTTG-3'
	Reverse Primer	5'-GGGGTCGTTGATGGCAACA-3'

**A****B**

Metabolic pathways	Total Cmpd Hits	Raw p	FDR	Impact	
Steroid hormone biosynthesis	72	2	0.03417	0.88754	0.06863
Tyrosine metabolism	44	3	0.058293	0.88754	0.21024
Primary bile acid biosynthesis	46	2	0.12156	0.88754	0.05952
Cyanoamino acid metabolism	6	1	0.19374	0.88754	0
Methane metabolism	9	1	0.19374	0.88754	0
Porphyrin and chlorophyll metabolism	27	1	0.19374	0.88754	0
beta-Alanine metabolism	17	4	0.1989	0.88754	0.44444
Biotin metabolism	5	1	0.23118	0.88754	0
Lysine degradation	23	2	0.24974	0.88754	0.08824
Lysine biosynthesis	4	2	0.24974	0.88754	0
Propanoate metabolism	20	2	0.25307	0.88754	0
Tryptophan metabolism	40	2	0.2601	0.88754	0.00068
Nitrogen metabolism	9	3	0.29901	0.88754	0
Pantothenate and CoA biosynthesis	15	5	0.30306	0.88754	0.02041
Glycine, serine and threonine metabolism	31	6	0.34359	0.89053	0.38693
Arachidonic acid metabolism	36	1	0.34752	0.89053	0.02076
Nicotinate and nicotinamide metabolism	13	2	0.3716	0.8962	0.2381
Arginine and proline metabolism	44	8	0.42354	0.94777	0.2727
Pyrimidine metabolism	41	11	0.45937	0.94777	0.36444
Alanine, aspartate and glutamate metabolism	24	3	0.48513	0.94777	0.26687
Glutathione metabolism	26	5	0.48544	0.94777	0.38169
Purine metabolism	68	6	0.57339	0.96566	0.06357
Taurine and hypotaurine metabolism	8	2	0.58446	0.96566	0.42857
Pentose phosphate pathway	19	1	0.60015	0.96566	0.01952
Fatty acid biosynthesis	43	1	0.648	0.96566	0
Valine, leucine and isoleucine degradation	38	3	0.64942	0.96566	0
Steroid biosynthesis	35	1	0.66957	0.96566	0.00207
Cysteine and methionine metabolism	27	4	0.71156	0.96566	0.3088
D-Glutamine and D-glutamate metabolism	5	1	0.73558	0.96566	0
Sphingolipid metabolism	21	1	0.73975	0.96566	0.01504
Aminoacyl-tRNA biosynthesis	69	8	0.76613	0.96566	0
Citrate cycle (TCA cycle)	20	3	0.78579	0.96566	0.12564
Glycerophospholipid metabolism	30	3	0.80489	0.96566	0.06667
Butanoate metabolism	22	1	0.81367	0.96566	0.02899
Valine, leucine and isoleucine biosynthesis	11	2	0.82434	0.96566	0.66666
Pyruvate metabolism	23	1	0.91019	0.97615	0
Phenylalanine metabolism	11	1	0.9143	0.97615	0.22222
Thiamine metabolism	7	1	0.91602	0.97615	0
Glyoxylate and dicarboxylate metabolism	18	3	0.92853	0.97615	0.32258
Histidine metabolism	15	1	0.9697	0.97995	0.24194
Glycerolipid metabolism	18	3	0.97995	0.97995	0.13031

**Figure S1.** Metabolite profiling analysis in GC-2 cells. (A) PCA plot for GC/MS data. (B) Metabolites pathways changes detected using GC/MS.



**Figure S2.** Representative images from the HCS after GNRs exposure to GC-2 cells. (A) Staining for nuclei (blue), cell membrane permeability (green), cytochrome c (yellow) and mitochondria membrane potential (red). Images were acquired with the ArrayScan HCS Reader with a 20 x objective. (B) The relative expressions of nuclear size, permeability, cytochrome c and mitochondria membrane potential. \* indicates significant difference when the values were compared to that of the control ( $p < 0.05$ ).