

Supplementary Figures:

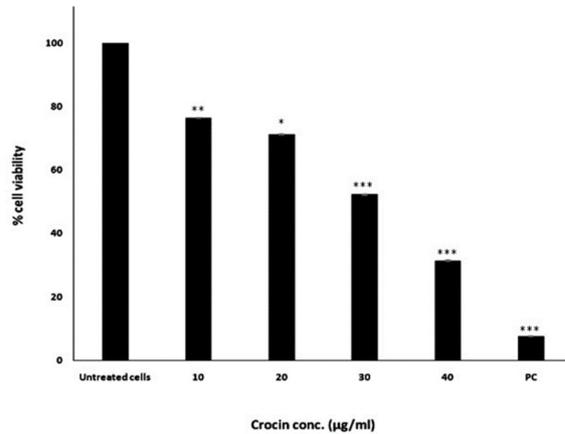


Figure S1. Cytotoxicity of crocin on BXPC3 cells. BXPC3 cells were treated with 10, 20, 30 and 40 µg/mL of crocin. After 24 h treatment, the cell viability was measured by MTT assay. Data presented as mean ± SD of triplicates of three independent experiments. PC: Positive control (doxorubicin).

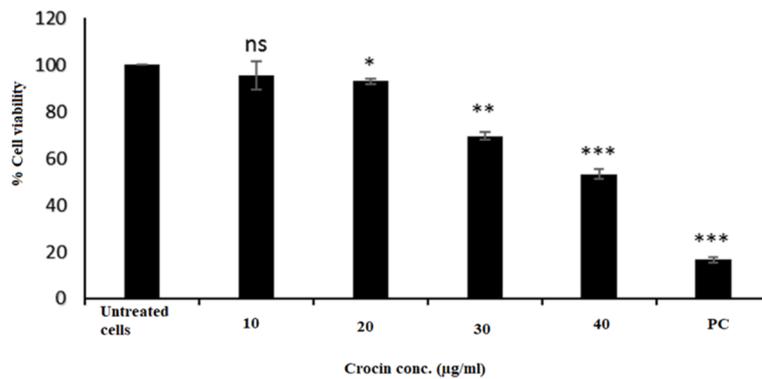


Figure S2. Cytotoxicity of crocin on Capan-2 cells. Capan-2 cells were treated with 10, 20, 30 and 40 µg/mL of crocin. After 24 h treatment, the cell viability was measured by MTT assay. Data presented as mean ± SD of triplicates of three independent experiments. PC: Positive control (doxorubicin).

Tables and Legends

Table S1. Crocin enriched checkpoints and pathways of BXPC3 cells.

Term	Number of Genes	P-Value
Upregulated checkpoints		
Cell cycle checkpoint	7	0.00018
Response to DNA damage stimulus	22	0.000678
DNA integrity check point	5	0.000227
DNA damage checkpoint	5	0.000227
Mitotic Spindle checkpoint	2	0.0056
Spindle checkpoint	2	0.0056
Mitotic checkpoint	3	0.0058
Programed cell death	35	0.0134
DNA modification	5	0.0219
Regulation of cell differentiation	10	0.0227

Cell death	35	0.0316
Death	35	0.0367
Cell adhesion molecule binding	3	0.00377
Upregulated pathways		
Cell cycle	32	1.34E-14
Pyrimidine metabolism	13	0.000262
Purine metabolism	16	0.000438
DNA polymerase	4	0.00144
Glycan structure–biosynthesis-2	9	0.00382
Neurodegenerative disorders	3	0.0119
Folate biosynthesis	6	0.0122
Amyotrophic lateral sclerosis (ALS)	2	0.0128
Methionine metabolism	4	0.0273
Selenoamino acid metabolism	4	0.0334
One carbon pool by folate	3	0.0345
Glucospinolipid biosynthesis lacto series	2	0.0401
Glycosylate and decarboxylate metabolism	2	0.0401

Table S2. Crocin downregulated checkpoints and pathways in BXPC3 cells.

Term	Number of Genes	P-Value
Downregulated checkpoints		
Organismal physiological process	84	5.35E-05
G-protein coupled receptor protein signaling pathway	65	0.000183
Cell surface receptor linked signal transduction	79	0.00203
Signal transduction	102	0.0203
Prostaglandin transport	1	0.0238
G-protein signaling, adenylate cyclase activity pathways	4	0.0252
Positive regulation of signal transduction	3	0.0282
Regulation of epidermal growth factor receptor-signaling pathway	1	0.0471
Prostaglandin metabolism G-protein signaling coupled to cAMP nucleotide second receptor	4	0.0517
Regulation of MAPK activity	4	0.0517
Regulation of cell growth	4	0.0544
G-protein coupled receptor activity	56	0.00119
G-protein coupled receptor binding	5	0.00686
Notch binding	1	0.0241
Interleukin-11 receptor binding	1	0.0241
Prostaglandin transporter activity	1	0.0476
Downregulated pathways		
Arachidonic acid metabolism	6	0.0181
Cytokine–cytokine receptor interaction	13	0.0147
Complement and coagulation cascades	7	0.00229
Glutathione metabolism	4	0.00471
Metabolism of xenobiotic by cytochrome P450	5	0.011
Glycerolipid metabolism	4	0.0262