

Common processes enriched in fulvestrant-resistant CAMA-1, MCF7 and T47D identified by DAVID bioinformatics tool.

<b>Enriched gene ontology function for correlated genes</b>					
<b>Annotation cluster 1**</b>	<b>Enrichment score: 22.9</b>				
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
UP_KEYWORDS	Cell cycle	47	33.6	1.8E-34	3.0E-32
UP_KEYWORDS	Cell division	32	22.9	1.4E-24	7.5E-23
GOTERM_BP_DIRECT	cell division	31	22.1	2.5E-23	7.0E-21
UP_KEYWORDS	Mitosis	25	17.9	1.6E-20	4.3E-19
GOTERM_BP_DIRECT	mitotic nuclear division	21	15.0	3.3E-15	3.7E-13
<b>Annotation Cluster 2**</b>	<b>Enrichment Score: 10.69</b>				
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
GOTERM_BP_DIRECT	DNA repair	19	13.6	2.1E-13	2.0E-11
UP_KEYWORDS	DNA damage	19	13.6	2.9E-11	4.3E-10
UP_KEYWORDS	DNA repair	16	11.4	1.4E-9	1.7E-8
<b>Annotation Cluster 3**</b>	<b>Enrichment Score: 9.58</b>				
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
UP_KEYWORDS	Chromosome	24	17.1	3.3E-15	7.6E-14
UP_KEYWORDS	Centromere	14	10.0	9.0E-12	1.5E-10
GOTERM_BP_DIRECT	sister chromatid cohesion	13	9.3	1.9E-11	1.6E-9
GOTERM_CC_DIRECT	condensed chromosome kinetochore	10	7.1	1.3E-8	3.8E-7
UP_KEYWORDS	Kinetochore	10	7.1	2.3E-8	2.6E-7
GOTERM_CC_DIRECT	kinetochore	8	5.7	2.0E-6	4.3E-5
<b>Enriched KEGG pathways for correlated genes***</b>					
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
KEGG_PATHWAY	DNA replication	15	10.7	1.3E-21	8.7E-20
KEGG_PATHWAY	Cell cycle	18	12.9	1.2E-17	4.3E-16
KEGG_PATHWAY	Mismatch repair	6	4.3	6.6E-7	1.5E-5
KEGG_PATHWAY	Base excision repair	6	4.3	4.4E-6	7.6E-5
KEGG_PATHWAY	Pyrimidine metabolism	8	5.7	1.2E-5	1.7E-4
KEGG_PATHWAY	Nucleotide excision repair	6	4.3	2.6E-5	3.0E-4
KEGG_PATHWAY	p53 signaling pathway	6	4.3	1.5E-4	1.5E-3
KEGG_PATHWAY	Fanconi anemia pathway	5	3.6	6.8E-4	5.9E-3
KEGG_PATHWAY	Purine metabolism	7	5.0	2.1E-3	1.6E-2
KEGG_PATHWAY	Small cell lung cancer	5	3.6	3.9E-3	2.7E-2
<b>Enriched BIOCARTA pathways for correlated genes****</b>					
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
BIOCARTA	CDK Regulation of DNA Replication	9	6.4	7.4E-11	2.8E-9
BIOCARTA	Cyclins and Cell Cycle Regulation	5	3.6	6.0E-4	1.1E-2

\* Gene list of regulated genes that follow the analysed pattern contains 160 significant genes, out of which 140 genes were recognised by DAVID and used in the % calculation.

\*\* 24 annotation clusters were identified using standard settings, the three most enriched annotation clusters are included.

\*\*\* KEGG pathway analysis yielded 19 chart records, entries with Benjamini  $\leq 0.05$  are included.

\*\*\*\* BIOCARTA analysis yielded seven chart entries, entries with Benjamini  $\leq 0.05$  are included.

DAVID functional categories and gene ontology (GO) functions as well as KEGG and Biocarta pathways for genes commonly downregulated upon fulvestrant treatment in parental cells and then upregulated again upon development of resistance.

Common processes enriched in fulvestrant-resistant HCC1428 identified by DAVID bioinformatics tool.

<b>Enriched gene ontology function for correlated genes</b>					
<b>Annotation cluster 1**</b>		<b>Enrichment score: 19.6</b>			
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
UP_KEYWORDS	DNA replication	38	7.7	6.6E-37	2.1E-34
GOTERM_BP_DIRECT	DNA replication	42	8.6	5.6E-31	8.6E-28
GOTERM_BP_DIRECT	DNA replication initiation	17	3.5	5.3E-18	4.1E-15
GOTERM_BP_DIRECT	G1/S transition of mitotic cell cycle	25	5.1	2.6E-17	1.3E-14
<b>Annotation Cluster 2**</b>		<b>Enrichment Score: 10.73</b>			
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
UP_KEYWORDS	DNA damage	36	7.3	1.0E-13	6.6E-12
UP_KEYWORDS	DNA repair	30	6.1	1.6E-11	8.5E-10
GOTERM_BP_DIRECT	DNA repair	25	5.1	3.9E-9	7.5E-7
<b>Annotation Cluster 3**</b>		<b>Enrichment Score: 8.86</b>			
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
GOTERM_BP_DIRECT	DNA synthesis involved in DNA repair	14	2.9	8.8E-13	2.3E-10
GOTERM_BP_DIRECT	strand displacement	11	2.2	2.7E-10	5.9E-8
GOTERM_BP_DIRECT	regulation of signal transduction by p53 class mediator	14	2.9	1.1E-5	1.5E-3
<b>Enriched KEGG pathways for correlated genes***</b>					
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
KEGG_PATHWAY	DNA replication	19	3.9	2.6E-20	5.1E-18
KEGG_PATHWAY	Purine metabolism	23	4.7	2.2E-10	2.2E-8
KEGG_PATHWAY	Cell cycle	19	3.9	9.3E-10	6.1E-8
KEGG_PATHWAY	Fanconi anemia pathway	13	2.6	3.6E-9	1.8E-7
KEGG_PATHWAY	Pyrimidine metabolism	16	3.3	1.8E-8	7.2E-7
KEGG_PATHWAY	Homologous recombination	8	1.6	4.7E-6	1.5E-4
KEGG_PATHWAY	Base excision repair	8	1.6	1.2E-5	3.3E-4
KEGG_PATHWAY	Mismatch repair	7	1.4	1.4E-5	3.5E-4
KEGG_PATHWAY	Nucleotide excision repair	8	1.6	1.3E-4	2.8E-3
<b>Enriched BIOCARTA pathways for correlated genes****</b>					
<b>Category</b>	<b>Term</b>	<b>Count</b>	<b>% *</b>	<b>p-value</b>	<b>Benjamini</b>
BIOCARTA	CDK Regulation of DNA Replication	9	1.8	5.4E-9	4.8E-7
BIOCARTA	Role of BRCA1, BRCA2 and ATR in Cancer Susceptibility	7	1.4	1.5E-5	6.7E-4
BIOCARTA	BRCA1-dependent Ub-ligase activity	4	0.8	9.4E-4	2.8E-2

\* Gene list of regulated genes that follow the analysed pattern contains 533 significant genes, out of which 491 genes were recognised by DAVID and used in the % calculation.

\*\* 75 annotation clusters were identified using standard settings, the three most enriched annotation clusters are included.

\*\*\* KEGG pathway analysis yielded 14 chart records, entries with Benjamini  $\leq 0.05$  are included.

\*\*\*\* BIOCARTA analysis yielded five chart entries, entries with Benjamini  $\leq 0.05$  are included.

DAVID functional categories and gene ontology (GO) functions as well as KEGG and Biocarta pathways for genes commonly downregulated upon fulvestrant treatment in parental cells and then upregulated again upon development of resistance.