

Supplementary Table 3: Pathway analysis of genes harbouring protein truncating mutations in 412 HGSOc cases

Pathway	Num. of Genes	Normalized Enrichment	P	FDR
DNA_REPAIR	42	1.86	1.8E-03	0.26
LIPID_BIOSYNTHETIC_PROCESS	18	1.85	4.2E-03	0.16
FATTY_ACID_METABOLIC_PROCESS	24	1.78	8.3E-03	0.26
POSITIVE_REGULATION_OF_PROTEIN_METABOLIC_PROCESS	15	1.75	1.0E-02	0.27
RESPONSE_TO_ENDOGENOUS_STIMULUS	63	1.75	2.7E-03	0.23
RESPONSE_TO_DNA_DAMAGE_STIMULUS	56	1.73	4.8E-03	0.22
CELLULAR_LIPID_METABOLIC_PROCESS	67	1.72	3.5E-03	0.21
DNA_RECOMBINATION	17	1.70	1.6E-02	0.22
MONOCARBOXYLIC_ACID_METABOLIC_PROCESS	29	1.70	1.4E-02	0.21
NEGATIVE_REGULATION_OF_TRANSCRIPTION	34	1.67	1.5E-02	0.24
DNA_METABOLIC_PROCESS	75	1.67	3.9E-03	0.22
NEGATIVE_REGULATION_OF_NUCLEOBASENUCLEOSIDENUCLEOTIDE_AND_NUCLEIC_ACID_METABOLIC_PROCESS	39	1.61	2.4E-02	0.33
REGULATION_OF_CELL_PROLIFERATION	63	1.58	1.9E-02	0.41
POSITIVE_REGULATION_OF_DEVELOPMENTAL_PROCESS	54	1.56	2.6E-02	0.43
REGULATION_OF_CELLULAR_PROTEIN_METABOLIC_PROCESS	37	1.54	4.5E-02	0.46
NEGATIVE_REGULATION_OF_CELLULAR_METABOLIC_PROCESS	50	1.53	3.7E-02	0.48
CELL_PROLIFERATION_GO_0008283	93	1.53	1.7E-02	0.46
REGULATION_OF_PROGRAMMED_CELL_DEATH	73	1.52	2.6E-02	0.45
REGULATION_OF_APOPTOSIS	73	1.52	3.0E-02	0.43
NEGATIVE_REGULATION_OF_METABOLIC_PROCESS	51	1.52	4.2E-02	0.41
RESPONSE_TO_CHEMICAL_STIMULUS	78	1.50	3.1E-02	0.44
REGULATION_OF_PROTEIN_METABOLIC_PROCESS	39	1.49	6.5E-02	0.46
MONOVALENT_INORGANIC_CATION_TRANSPORT	23	1.48	8.1E-02	0.46
NEGATIVE_REGULATION_OF_CELL_PROLIFERATION	30	1.46	7.6E-02	0.49
PROGRAMMED_CELL_DEATH	90	1.46	3.5E-02	0.48
LIPID_METABOLIC_PROCESS	90	1.46	3.8E-02	0.47
APOPTOSIS_GO	90	1.46	3.8E-02	0.46
REGULATION_OF_DEVELOPMENTAL_PROCESS	98	1.43	4.2E-02	0.50
CELLULAR_BIOSYNTHETIC_PROCESS	67	1.43	6.6E-02	0.51
CELL_CYCLE_PROCESS	54	1.40	9.5E-02	0.58
MITOSIS	21	1.39	1.3E-01	0.60
NEGATIVE_REGULATION_OF_CELLULAR_PROCESS	133	1.38	4.1E-02	0.59
RESPONSE_TO_STRESS	135	1.38	4.0E-02	0.59
ORGANIC_ACID_METABOLIC_PROCESS	52	1.37	1.1E-01	0.59
CARBOXYLIC_ACID_METABOLIC_PROCESS	52	1.37	1.1E-01	0.58
CELL_DEVELOPMENT	116	1.35	6.9E-02	0.64
CHROMOSOME_ORGANIZATION_AND_BIOGENESIS	31	1.35	1.5E-01	0.63
M_PHASE_OF_MITOTIC_CELL_CYCLE	23	1.35	1.5E-01	0.61
ION_TRANSPORT	50	1.32	1.5E-01	0.69
SECRETORY_PATHWAY	17	1.31	1.9E-01	0.69
NEGATIVE_REGULATION_OF_BIOLOGICAL_PROCESS	142	1.31	7.8E-02	0.67
INTRACELLULAR_SIGNALING_CASCADE	170	1.31	6.1E-02	0.66
APOPTOTIC_PROGRAM	16	1.30	1.9E-01	0.68

PROTEIN_AMINO_ACID_AUTOPHOSPHORYLATION	15	1.30	2.0E-01	0.67
PROTEIN_AUTOPROCESSING	15	1.29	2.1E-01	0.68
CATION_TRANSPORT	39	1.29	1.8E-01	0.67
RNA_PROCESSING	32	1.28	2.0E-01	0.69
METAL_ION_TRANSPORT	33	1.28	1.9E-01	0.68
POST_TRANSLATIONAL_PROTEIN_MODIFICATION	118	1.27	1.2E-01	0.69
ORGANELLE_ORGANIZATION_AND_BIOGENESIS	134	1.27	1.2E-01	0.68
REPRODUCTIVE_PROCESS	33	1.27	2.1E-01	0.67
M_PHASE	31	1.26	2.2E-01	0.68
COFACTOR_METABOLIC_PROCESS	17	1.25	2.3E-01	0.69
DEPHOSPHORYLATION	21	1.25	2.3E-01	0.68
MEMBRANE_LIPID_METABOLIC_PROCESS	17	1.24	2.5E-01	0.71
TRANSMEMBRANE_RECEPTOR_PROTEIN_TYROSINE_KINASE_SIGNALING_PATHWAY	20	1.23	2.6E-01	0.74
PROTEIN_PROCESSING	17	1.19	2.9E-01	0.84
SECRETION	39	1.19	2.7E-01	0.83
NEGATIVE_REGULATION_OF_CATALYTIC_ACTIVITY	20	1.18	2.9E-01	0.85
SECRETION_BY_CELL	25	1.16	3.2E-01	0.91
POSITIVE_REGULATION_OF_CELLULAR_METABOLIC_PROCESS	51	1.15	3.1E-01	0.92
BIOSYNTHETIC_PROCESS	104	1.15	2.8E-01	0.91
REGULATION_OF_TRANSCRIPTION	117	1.15	2.7E-01	0.91
CELL_CYCLE_GO_0007049	85	1.15	2.9E-01	0.90
REGULATION_OF_CELLULAR_COMPONENT_ORGANIZATION_AND_BIOGENESIS	32	1.14	3.3E-01	0.91
REGULATION_OF_NUCLEOBASENUCLEOSIDENUCLEOTIDE_AND_NUCLEIC_ACID_METABOLIC_PROCESS	128	1.13	2.9E-01	0.92
PROTEIN_AMINO_ACID_DEPHOSPHORYLATION	18	1.13	3.4E-01	0.91
REGULATION_OF_CATALYTIC_ACTIVITY	68	1.13	3.3E-01	0.90
POSITIVE_REGULATION_OF_METABOLIC_PROCESS	53	1.13	3.3E-01	0.89
VESICLE_MEDIATED_TRANSPORT	54	1.13	3.3E-01	0.88
STEROID_METABOLIC_PROCESS	19	1.12	3.5E-01	0.88
LOCOMOTORY_BEHAVIOR	20	1.12	3.5E-01	0.87
NUCLEOBASENUCLEOSIDENUCLEOTIDE_AND_NUCLEIC_ACID_METABOLIC_PROCESS	272	1.12	2.4E-01	0.86
REGULATION_OF_MOLECULAR_FUNCTION	81	1.12	3.3E-01	0.87
SIGNAL_TRANSDUCTION	393	1.11	2.3E-01	0.88
TRANSPORT	209	1.11	2.9E-01	0.87
ACTIN_CYTOSKELETON_ORGANIZATION_AND_BIOGENESIS	28	1.10	3.6E-01	0.87
POSITIVE_REGULATION_OF_SIGNAL_TRANSDUCTION	27	1.10	3.8E-01	0.88
RAS_PROTEIN_SIGNAL_TRANSDUCTION	22	1.10	3.7E-01	0.87
CELL_CYCLE_PHASE	43	1.09	3.8E-01	0.87
MITOTIC_CELL_CYCLE	37	1.08	3.9E-01	0.88
ESTABLISHMENT_OF_LOCALIZATION	227	1.08	3.4E-01	0.89
REGULATION_OF_PROTEIN_KINASE_ACTIVITY	36	1.07	4.0E-01	0.89
REGULATION_OF_SIGNAL_TRANSDUCTION	50	1.07	4.0E-01	0.89
REGULATION_OF_KINASE_ACTIVITY	37	1.07	4.0E-01	0.88
IMMUNE_RESPONSE	43	1.07	4.0E-01	0.88
REGULATION_OF_TRANSFERASE_ACTIVITY	37	1.07	4.0E-01	0.87
REGULATION_OF_GENE_EXPRESSION	144	1.06	3.9E-01	0.87
MUSCLE_DEVELOPMENT	21	1.06	4.2E-01	0.88

REGULATION_OF_TRANSCRIPTION_FROM_RNA_POLYMERASE_II_PROMOTER	55	1.05	4.2E-01	0.88
BIOPOLYMER_MODIFICATION	172	1.05	4.1E-01	0.87
REPRODUCTION	54	1.05	4.3E-01	0.87
POSITIVE_REGULATION_OF_HYDROLASE_ACTIVITY	16	1.05	4.2E-01	0.86
REGULATION_OF_RNA_METABOLIC_PROCESS	97	1.05	4.3E-01	0.86
PROTEIN_MODIFICATION_PROCESS	167	1.05	4.2E-01	0.85
REGULATION_OF_CELLULAR_METABOLIC_PROCESS	168	1.04	4.2E-01	0.85
REGULATION_OF_METABOLIC_PROCESS	170	1.03	4.3E-01	0.86
SMALL_GTPASE_MEDIATED_SIGNAL_TRANSDUCTION	26	1.02	4.6E-01	0.89
POSITIVE_REGULATION_OF_CELLULAR_PROCESS	152	1.02	4.7E-01	0.89
ACTIN_FILAMENT_BASED_PROCESS	33	1.01	4.8E-01	0.90
G_PROTEIN_COUPLED_RECEPTOR_PROTEIN_SIGNALING_PATHWAY	74	1.00	5.0E-01	0.92
REGULATION_OF_HYDROLASE_ACTIVITY	25	0.99	4.9E-01	0.92
MAPKKK_CASCADE_GO_0000165	25	0.99	4.9E-01	0.91
ENZYME_LINKED_RECEPTOR_PROTEIN_SIGNALING_PATHWAY	36	0.99	4.9E-01	0.91
TRANSCRIPTION	155	0.99	5.3E-01	0.91
REGULATION_OF_TRANSCRIPTIONDNA_DEPENDENT	94	0.98	5.3E-01	0.91
IMMUNE_SYSTEM_PROCESS	67	0.98	5.2E-01	0.92
POSITIVE_REGULATION_OF_BIOLOGICAL_PROCESS	160	0.97	5.5E-01	0.92
POSITIVE_REGULATION_OF_CATALYTIC_ACTIVITY	41	0.97	5.2E-01	0.91
CHROMATIN_MODIFICATION	16	0.96	5.2E-01	0.92
ESTABLISHMENT_AND_OR_MAINTENANCE_OF_CHROMATIN_ARCHITECTURE	19	0.96	5.2E-01	0.91
CAMP_MEDIATED_SIGNALING	15	0.96	5.2E-01	0.91
SYSTEM_PROCESS	156	0.96	5.9E-01	0.91
G_PROTEIN_SIGNALING_COUPLED_TO_CAMP_NUCLEOTIDE_SECOND_MESSENGER	15	0.96	5.3E-01	0.91
BIOPOLYMER_METABOLIC_PROCESS	401	0.95	6.4E-01	0.91
I_KAPPAB_KINASE_NF_KAPPAB_CASCADE	26	0.95	5.4E-01	0.90
BEHAVIOR	32	0.93	5.6E-01	0.93
PROTEIN_AMINO_ACID_PHOSPHORYLATION	74	0.93	5.9E-01	0.93
CYTOSKELETON_ORGANIZATION_AND_BIOGENESIS	70	0.92	6.0E-01	0.93
RNA_METABOLIC_PROCESS	174	0.91	6.7E-01	0.95
PHOSPHORYLATION	81	0.91	6.2E-01	0.95
RIBONUCLEOPROTEIN_COMPLEX_BIOGENESIS_AND_ASSEMBLY	15	0.87	6.1E-01	1.00
SENSORY_PERCEPTION	61	0.86	6.7E-01	1.00
CELL_SURFACE_RECEPTOR_LINKED_SIGNAL_TRANSDUCTION_GO_0007166	143	0.85	7.5E-01	1.00
CELLULAR_DEFENSE_RESPONSE	20	0.85	6.4E-01	1.00
POSITIVE_REGULATION_OF_TRANSFERASE_ACTIVITY	20	0.85	6.5E-01	1.00
REGULATION_OF_RESPONSE_TO_STIMULUS	16	0.84	6.4E-01	1.00
CELLULAR_LOCALIZATION	96	0.84	7.2E-01	1.00
CHEMICAL_HOMEOSTASIS	32	0.84	6.6E-01	1.00
SECOND_MESSENGER_MEDIATED_SIGNALING	39	0.84	6.7E-01	1.00
PROTEIN_KINASE_CASCADE	66	0.84	7.1E-01	1.00
ESTABLISHMENT_OF_CELLULAR_LOCALIZATION	87	0.83	7.3E-01	1.00
MEMBRANE_ORGANIZATION_AND_BIOGENESIS	43	0.83	6.9E-01	1.00
TRANSCRIPTION_DNA_DEPENDENT	130	0.83	7.7E-01	1.00

RNA_BIOSYNTHETIC_PROCESS	131	0.82	7.8E-01	1.00
CELLULAR_PROTEIN_METABOLIC_PROCESS	267	0.82	8.5E-01	0.99
ANTI_APOPTOSIS	22	0.82	6.7E-01	0.98
CELLULAR_MACROMOLECULE_METABOLIC_PROCESS	272	0.80	8.9E-01	1.00
EXTRACELLULAR_STRUCTURE_ORGANIZATION_AND_BIOGENESIS	15	0.80	7.0E-01	1.00
REGULATION_OF_BIOLOGICAL_QUALITY	96	0.80	7.8E-01	1.00
SEXUAL_REPRODUCTION	29	0.79	7.1E-01	1.00
CELL_CELL_SIGNALING	77	0.79	7.7E-01	1.00
CYCLIC_NUCLEOTIDE_MEDIATED_SIGNALING	22	0.79	7.1E-01	0.99
RESPONSE_TO_EXTERNAL_STIMULUS	72	0.78	7.7E-01	0.99
G_PROTEIN_SIGNALING_COUPLED_TO_CYCLIC_NUCLEOTIDE_SECOND_MESSENGER	22	0.78	7.1E-01	0.99
TRANSCRIPTION_FROM_RNA_POLYMERASE_II_PROMOTER	89	0.78	8.0E-01	0.98
DNA_DEPENDENT_DNA_REPLICATION	17	0.78	7.2E-01	0.98
CELLULAR_COMPONENT_ASSEMBLY	63	0.77	7.7E-01	0.98
PROTEIN_METABOLIC_PROCESS	295	0.75	9.4E-01	1.00
DNA_REPLICATION	31	0.75	7.6E-01	1.00
CELLULAR_CATION_HOMEOSTASIS	23	0.75	7.5E-01	0.99
CELL_MIGRATION	26	0.74	7.6E-01	0.99
CATION_HOMEOSTASIS	24	0.74	7.6E-01	0.99
DEFENSE_RESPONSE	72	0.74	8.2E-01	0.98
POSITIVE_REGULATION_OF_I_KAPPAB_KINASE_NF_KAPPAB_CASCADE	18	0.74	7.5E-01	0.98
RESPONSE_TO_WOUNDING	45	0.73	8.0E-01	0.98
MACROMOLECULE_LOCALIZATION	68	0.72	8.3E-01	0.98
TISSUE_DEVELOPMENT	44	0.72	8.1E-01	0.98
HOMEOSTATIC_PROCESS	47	0.72	8.1E-01	0.97
PROTEIN_TARGETING	30	0.71	8.0E-01	0.98
NEGATIVE_REGULATION_OF_APOPTOSIS	28	0.70	8.1E-01	0.98
NEGATIVE_REGULATION_OF_PROGRAMMED_CELL_DEATH	28	0.70	8.0E-01	0.97
RESPONSE_TO_ABIOTIC_STIMULUS	32	0.70	8.1E-01	0.97
PROTEIN_LOCALIZATION	61	0.69	8.5E-01	0.98
NEUROLOGICAL_SYSTEM_PROCESS	109	0.68	9.0E-01	0.98
PROTEOLYSIS	41	0.68	8.5E-01	0.98
REGULATION_OF_I_KAPPAB_KINASE_NF_KAPPAB_CASCADE	20	0.66	8.4E-01	0.99
INFLAMMATORY_RESPONSE	31	0.66	8.5E-01	0.98
GENERATION_OF_PRECURSOR_METABOLITES_AND_ENERGY	34	0.65	8.7E-01	0.99
CELLULAR_CATABOLIC_PROCESS	48	0.64	8.9E-01	0.99
SKELETAL_DEVELOPMENT	20	0.63	8.6E-01	0.99
MICROTUBULE_BASED_PROCESS	33	0.61	9.0E-01	1.00
REGULATION_OF_TRANSLATION	22	0.60	9.0E-01	1.00
ION_HOMEOSTASIS	28	0.59	9.0E-01	1.00
NEGATIVE_REGULATION_OF_DEVELOPMENTAL_PROCESS	41	0.59	9.2E-01	1.00
CATABOLIC_PROCESS	53	0.58	9.3E-01	1.00
ORGAN_DEVELOPMENT	144	0.58	9.8E-01	1.00
ANATOMICAL_STRUCTURE_DEVELOPMENT	245	0.55	9.9E-01	1.00

INTRACELLULAR_TRANSPORT	68	0.54	9.6E-01	1.00
INTRACELLULAR_PROTEIN_TRANSPORT	38	0.54	9.5E-01	1.00
ANATOMICAL_STRUCTURE_MORPHOGENESIS	93	0.54	9.7E-01	0.99
CELLULAR_CARBOHYDRATE_METABOLIC_PROCESS	30	0.53	9.5E-01	0.99
CELLULAR_HOMEOSTASIS	39	0.53	9.5E-01	0.99
ANATOMICAL_STRUCTURE_FORMATION	17	0.49	9.6E-01	1.00
SYNAPTIC_TRANSMISSION	47	0.49	9.7E-01	0.99
ANGIOGENESIS	16	0.49	9.6E-01	0.99
FEMALE_PREGNANCY	15	0.44	9.8E-01	1.00
TRANSMISSION_OF_NERVE_IMPULSE	49	0.44	9.9E-01	0.99
TRANSLATION	36	0.40	9.9E-01	0.99

