

Pathway-based dissection of the genomic heterogeneity of cancer hallmarks' acquisition with SLAPenrich

Francesco Iorio, Luz Garcia-Alonso, Jonathan S. Brummel, Inigo Martincorena, David R. Wille, Ultan McDermott, and Julio Saez-Rodriguez

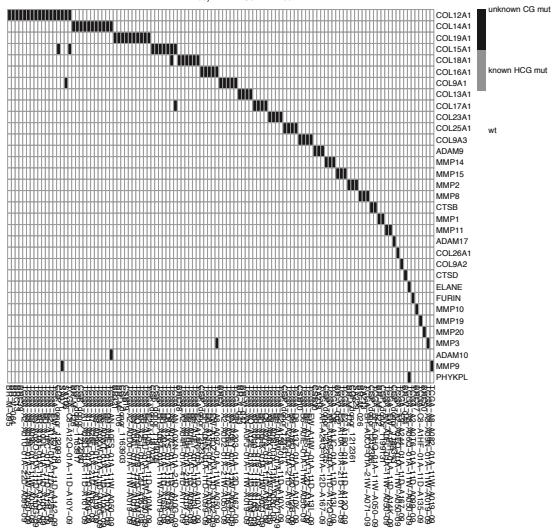
Supplementary Results

Color legend:

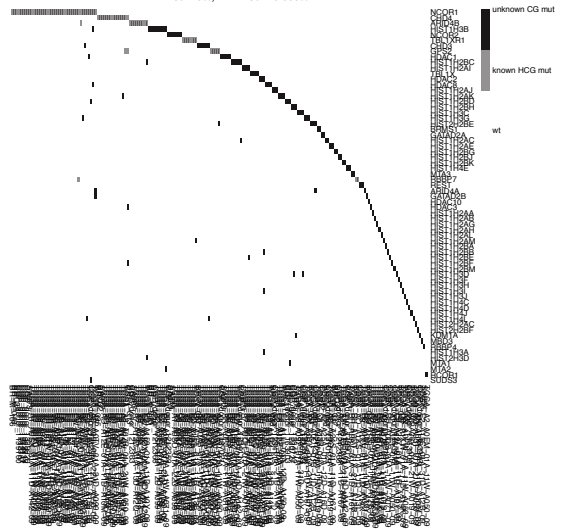
Sustaining Proliferative Signaling
Evading Growth Suppressors
Avoiding Immune Destruction
Enabling Replicative Immortality
Tumour-Promoting Inflammation
Activating Invasion and Metastasis
Inducing Angiogenesis
Genome Instability and Mutation
Resisting Cell Death
Deregulating Cellular Energetics

BRCA

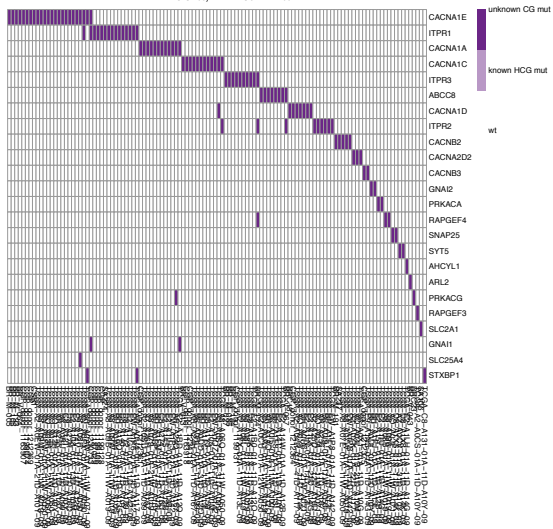
Collagen Degradation
FDR = 1.1%, FDR nod = 2.2%



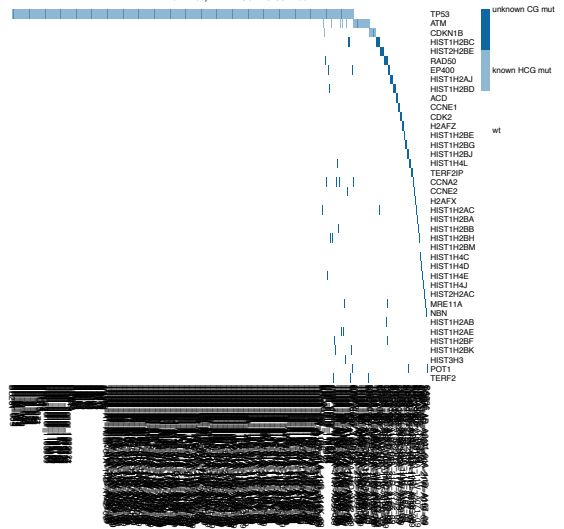
HDACs Deacetylate Histones
FDR = 1.6e-10%, FDR nod = 0.066%



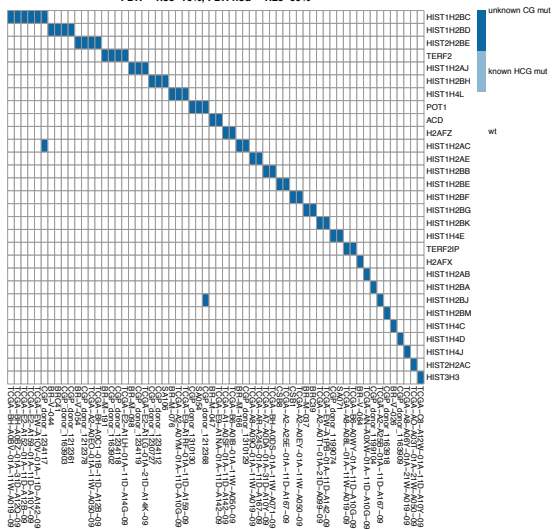
Regulation Of Insulin Secretion
FDR = 0.57%, FDR nod = 1.2%



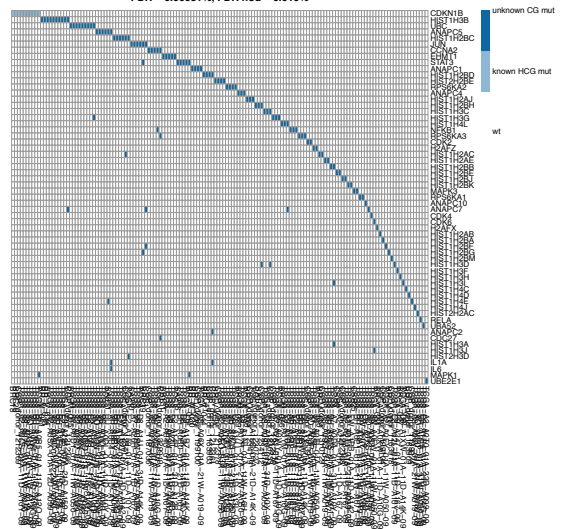
DNA Damage/Telomere Stress Induced Senescence
FDR = 7e-12%, FDR nod = 0.0024%



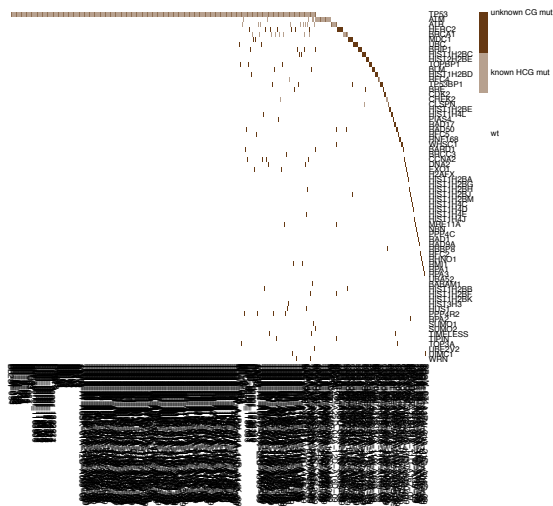
Packaging Of Telomere Ends
FDR = 1.3e-10%, FDR nod = 1.2e-09%



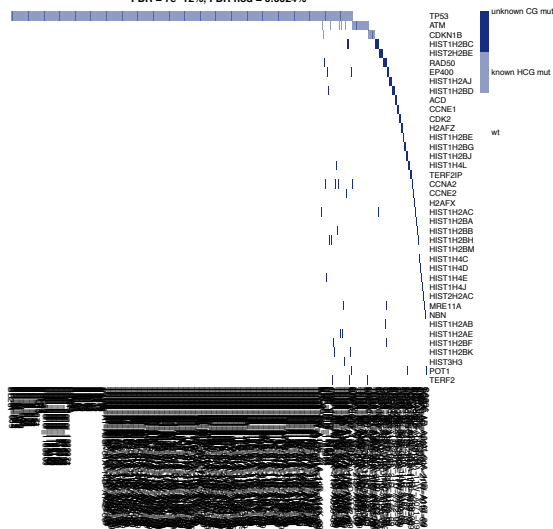
Senescence Associated Secretory Phenotype (SASP)
FDR = 0.00031%, FDR nod = 0.016%



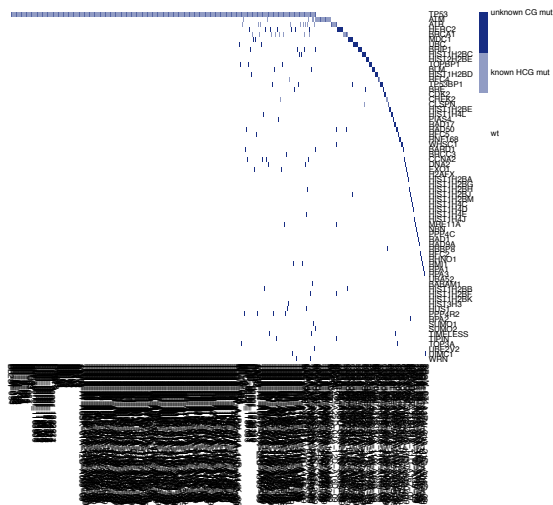
G2/M DNA Damage Checkpoint
Processing Of DNA Double Strand Break Ends
FDR = 7e-12%, FDR nod = 1.1%



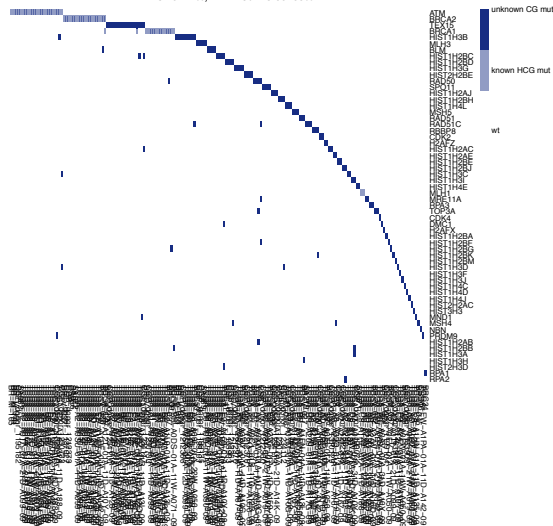
DNA Damage/Telomere Stress Induced Senescence
FDR = 7e-12%, FDR nod = 0.0024%



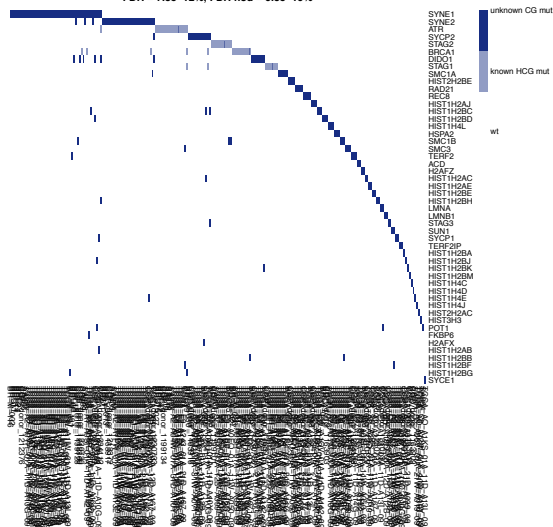
G2/M DNA Damage Checkpoint
Processing Of DNA Double Strand Break Ends
FDR = 7e-12%, FDR nod = 1.1%



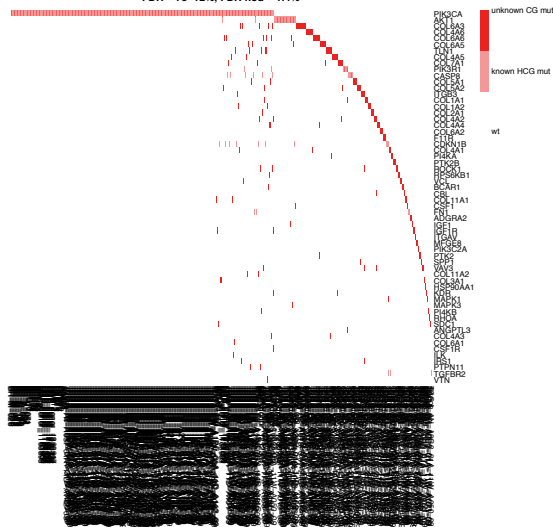
Meiotic Recombination
FDR = 8.1e-12%, FDR nod = 3.6e-06%



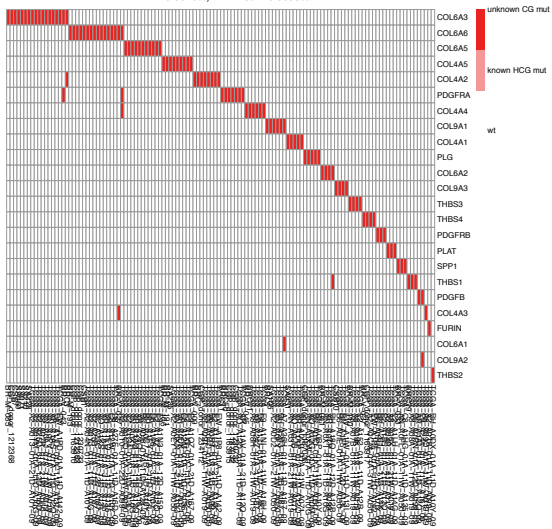
Meiotic Synapsis
FDR = 7.3e-12%, FDR nod = 6.3e-10%



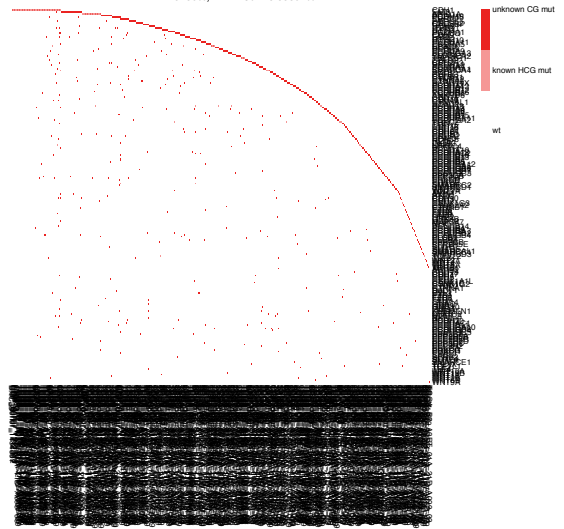
Integrins In Angiogenesis
FDR = 7e-12%, FDR nod = 1.4%



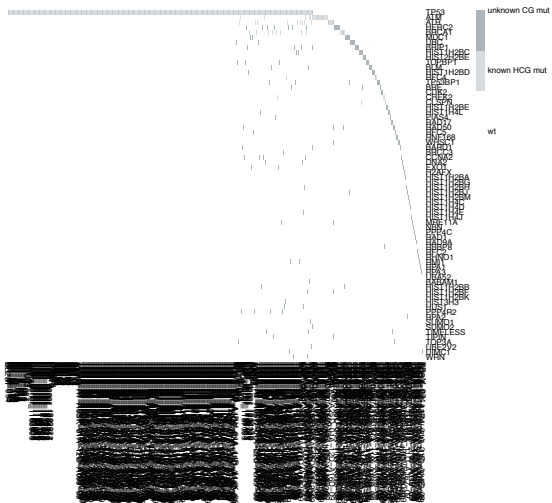
Signaling By PDGF
FDR = 0.0026%, FDR nod = 0.0058%



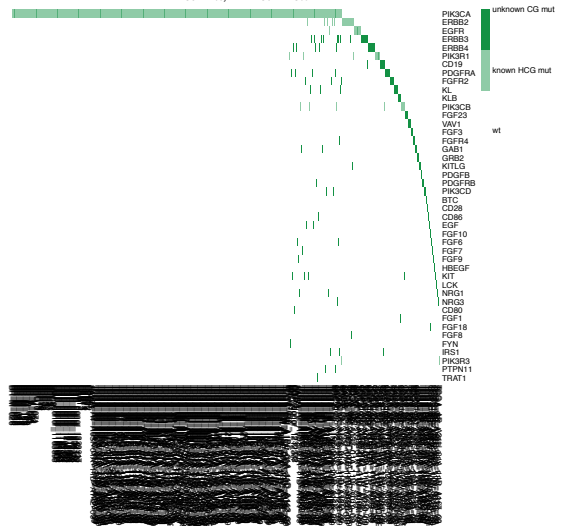
Wnt Signaling Pathway
FDR = 1.4e-09%, FDR nod = 0.00094%



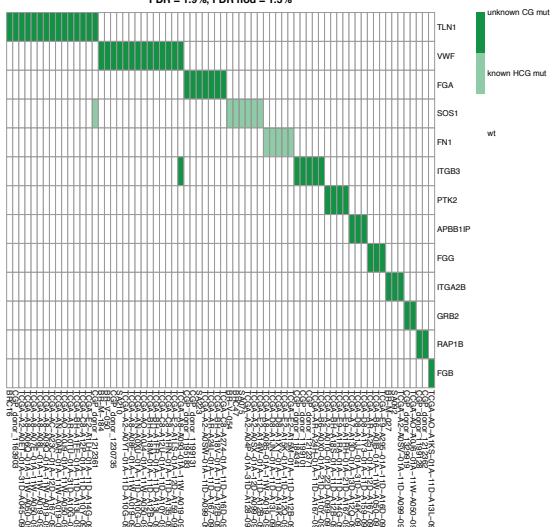
G2/M DNA Damage Checkpoint
Processing Of DNA Double Strand Break Ends
FDR = 7e-12%, FDR nod = 1.1%



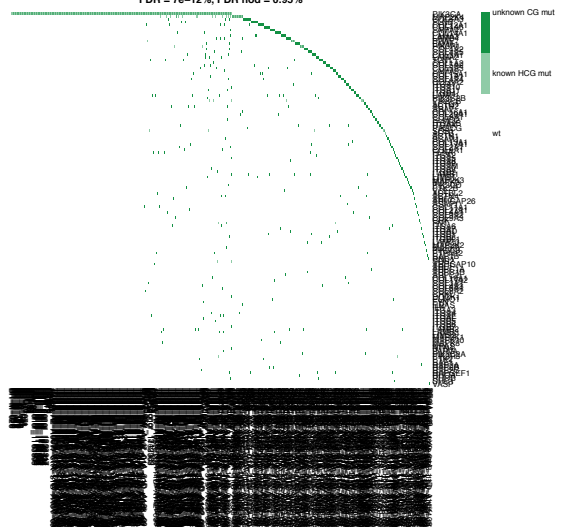
Constitutive Signaling By Aberrant PI3K In Cancer
FDR = 7.3e-12%, FDR nod = 2.8%



GRB2:SOS Provides Linkage To MAPK Signaling For Integrins
FDR = 1.9%, FDR nod = 1.3%

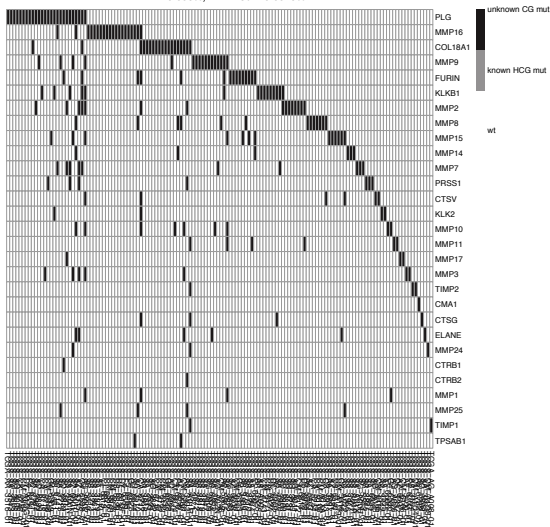


Integrin Signalling Pathway
FDR = 7e-12%, FDR nod = 0.95%

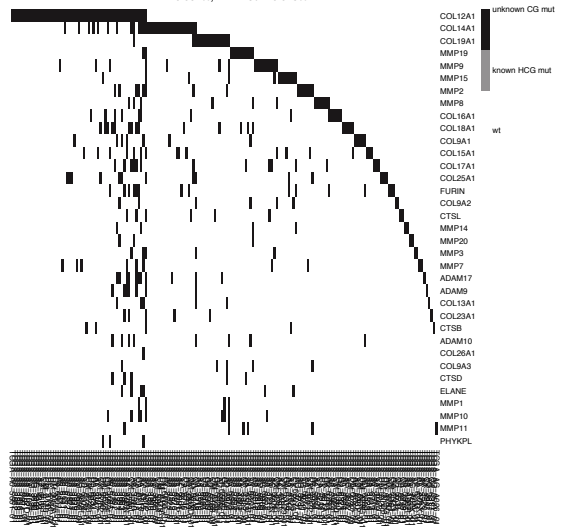


COREAD

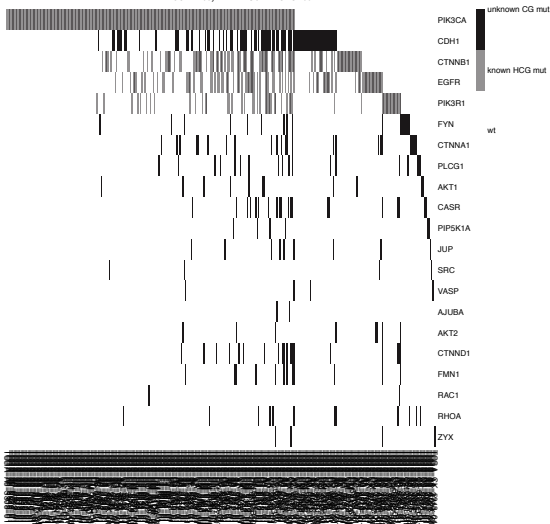
Activation Of Matrix Metalloproteinases
 FDR = 0.003%, FDR nod = 0.0023%



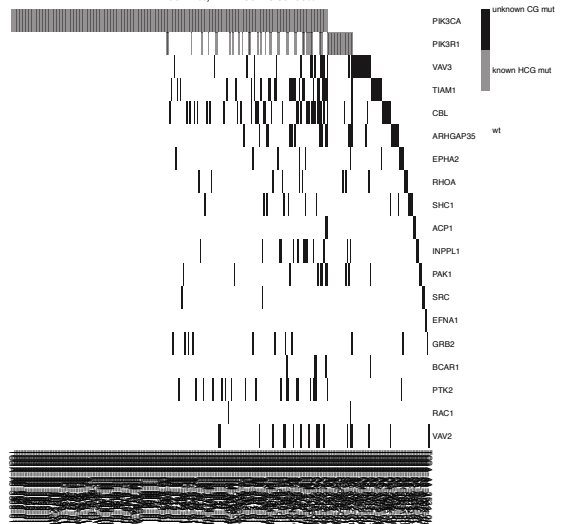
Collagen Degradation
 FDR = 0.054%, FDR nod = 0.028%



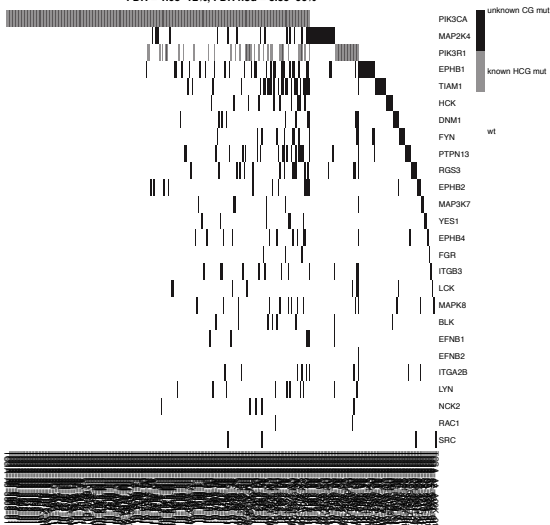
E Cadherin Signaling In Keratinocytes
 FDR = 1.9e-12%, FDR nod = 2e-04%



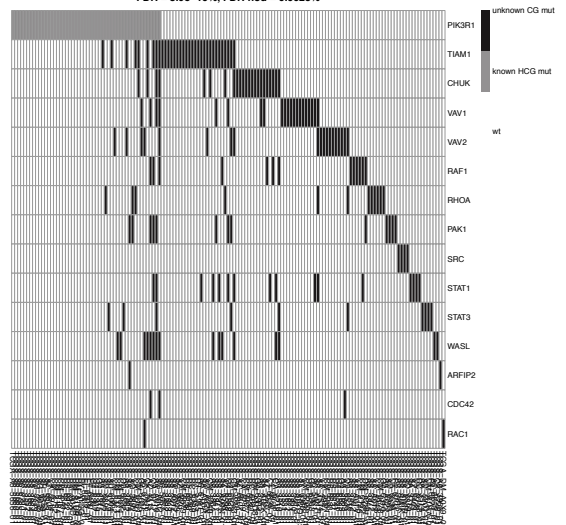
EPHA2 Forward Signaling
 FDR = 1.9e-12%, FDR nod = 5.3e-06%

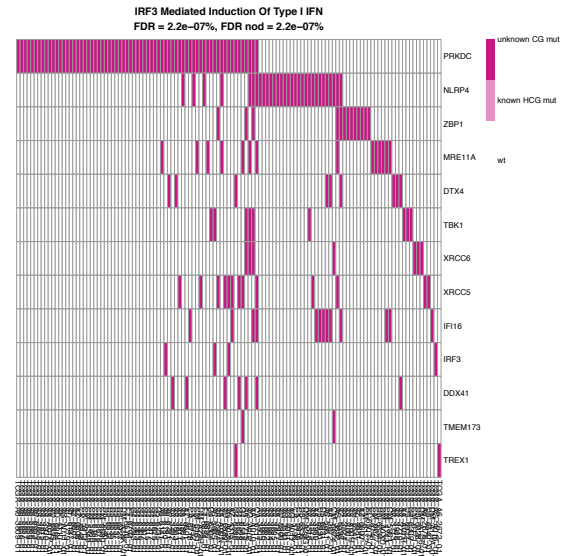
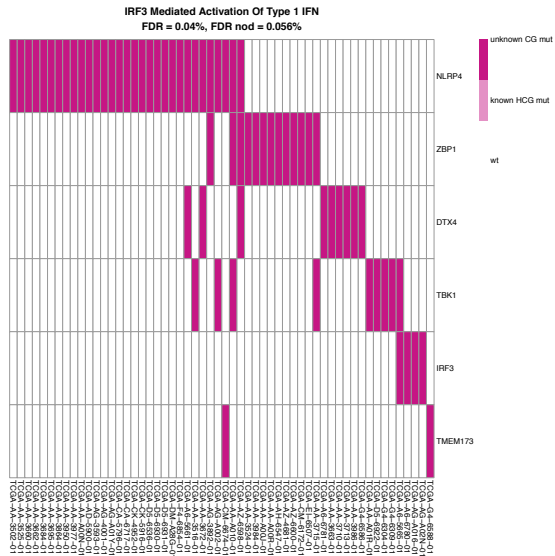
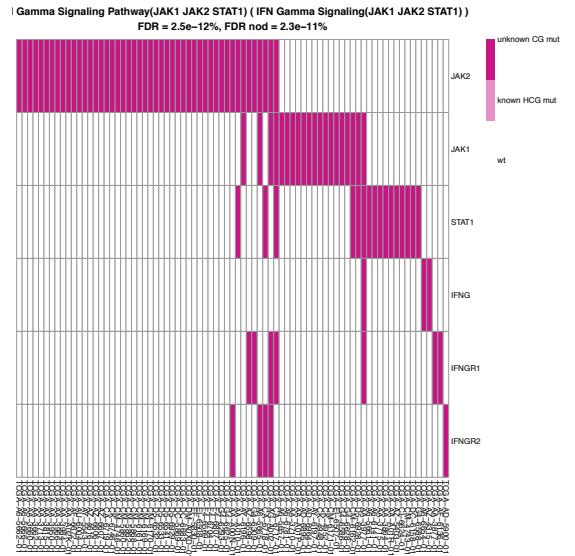
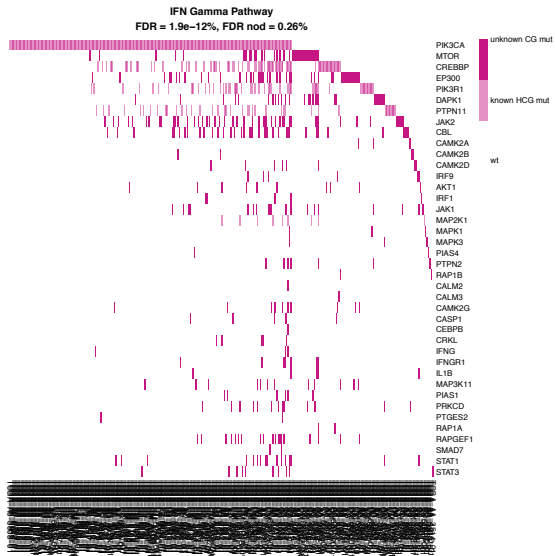
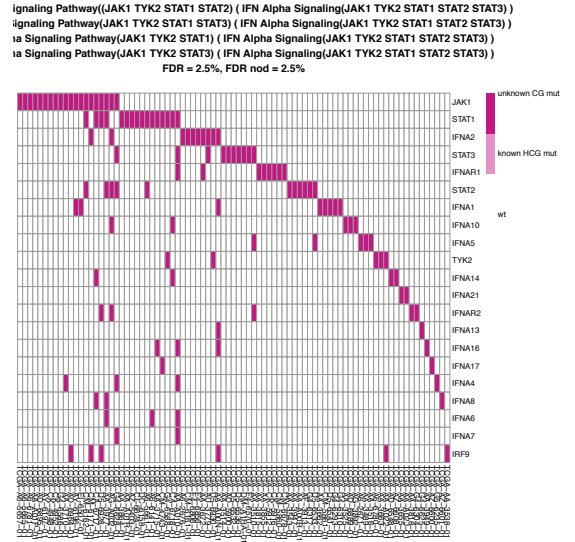
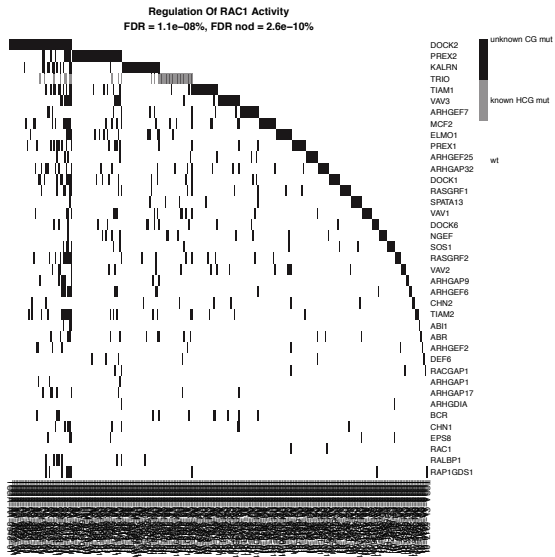


Ephrin B Reverse Signaling
 FDR = 1.9e-12%, FDR nod = 5.3e-06%

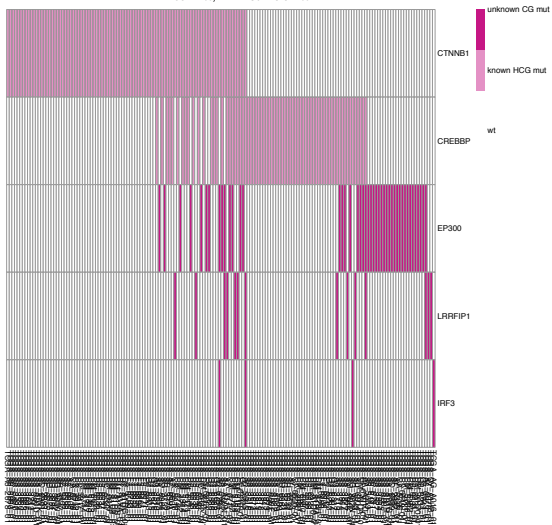


PDGF Pathway
 FDR = 8.9e-10%, FDR nod = 0.0023%

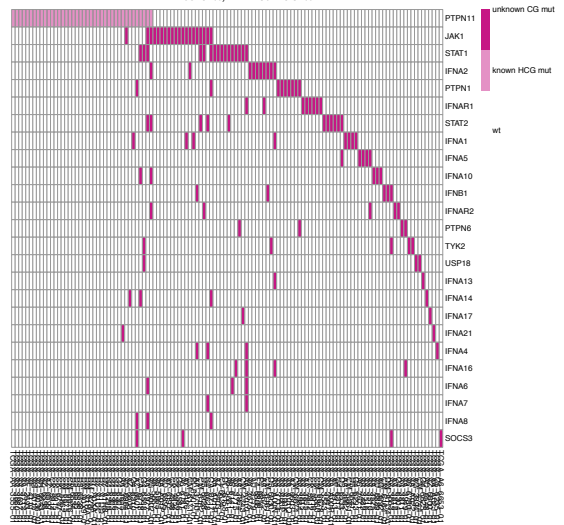




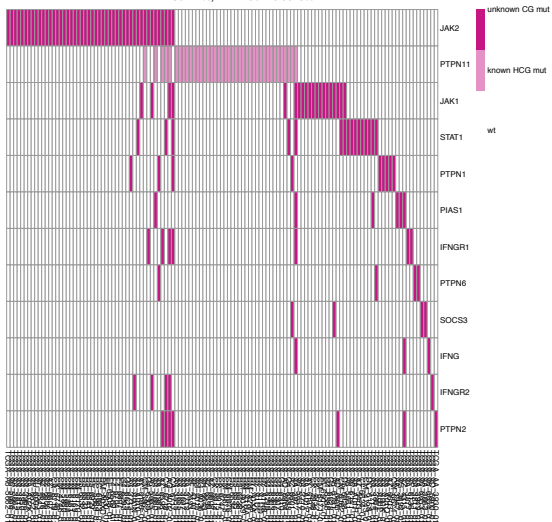
LRR FLII Interacting Protein 1 (LRRFIP1) Activates Type I IFN Production
 FDR = 1.9e-12%, FDR nod = 0.021%



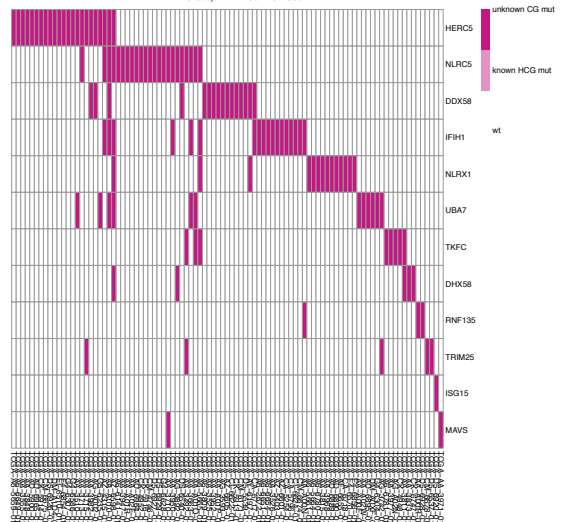
Regulation Of IFNA Signaling
 FDR = 1.9e-07%, FDR nod = 0.54%



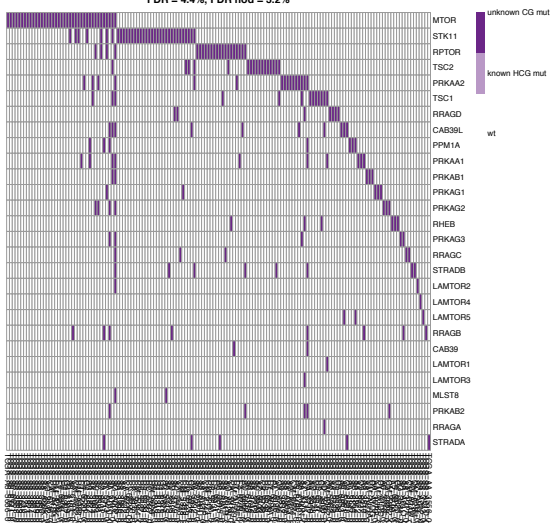
Regulation Of IFNG Signaling
 FDR = 1.5e-11%, FDR nod = 0.0025%



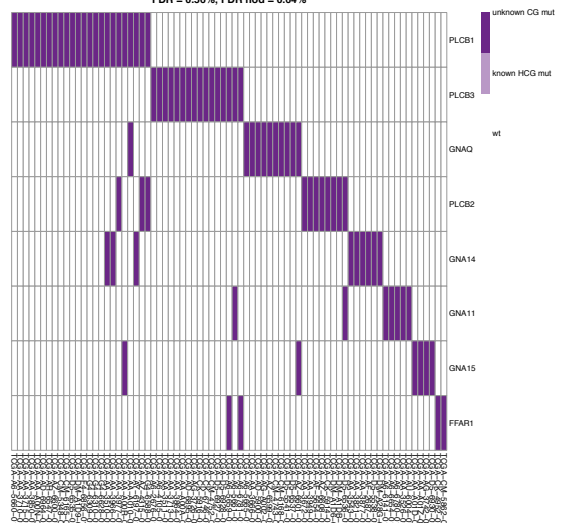
RIG I/MDA5 Mediated Induction Of IFN Alpha/beta Pathways
 FDR = 0.8%, FDR nod = 0.78%

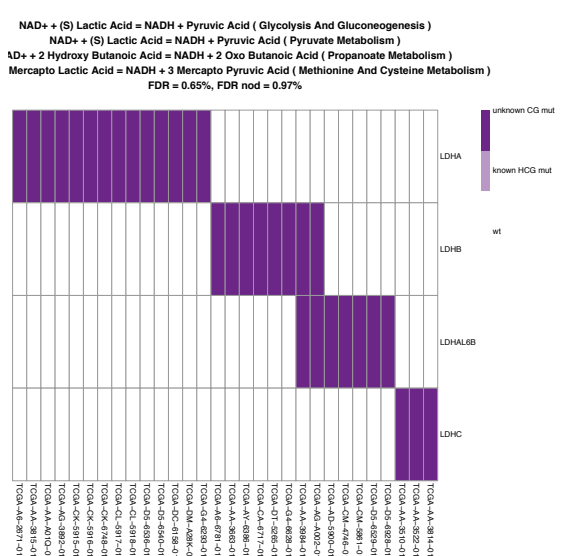
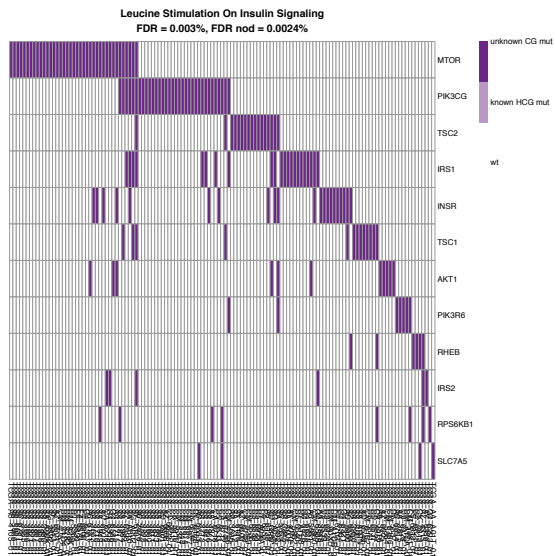
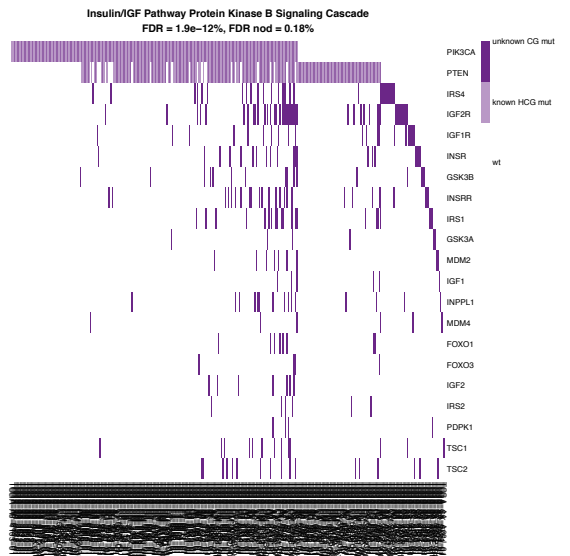
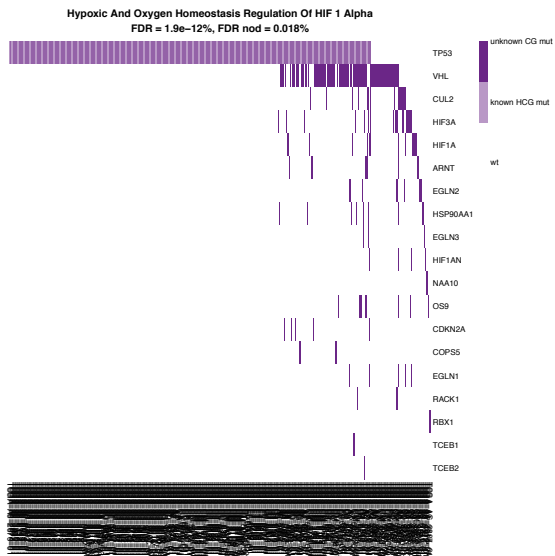
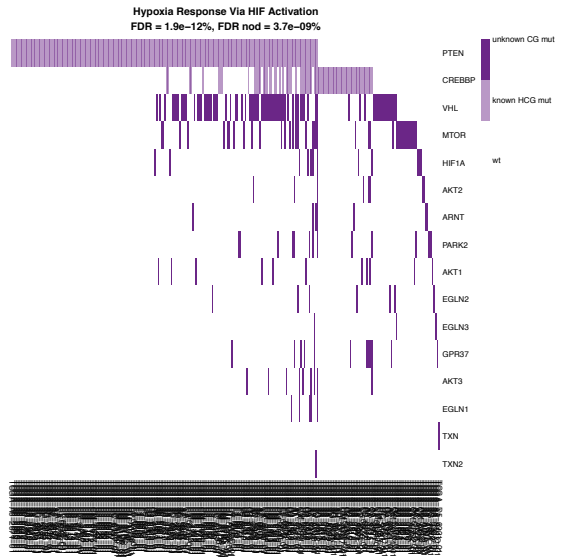
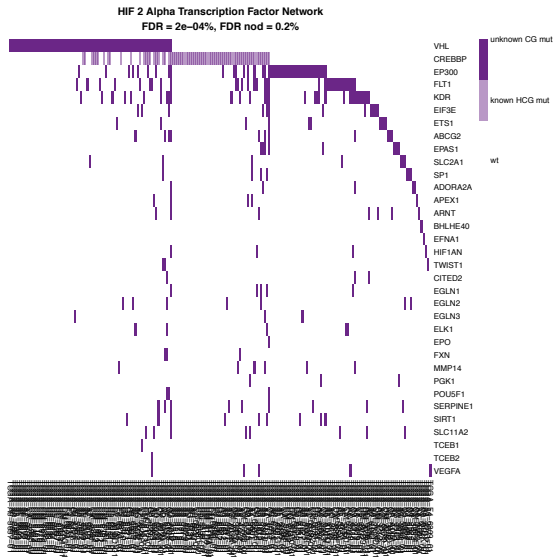


Energy Dependent Regulation Of MTOR By LKB1 AMPK
 FDR = 4.4%, FDR nod = 3.2%

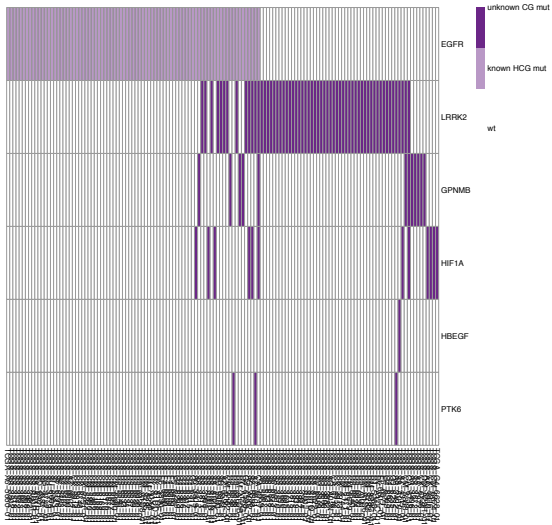


Fatty Acids Bound To GPR40 (FFAR1) Regulate Insulin Secretion
 FDR = 0.56%, FDR nod = 0.64%

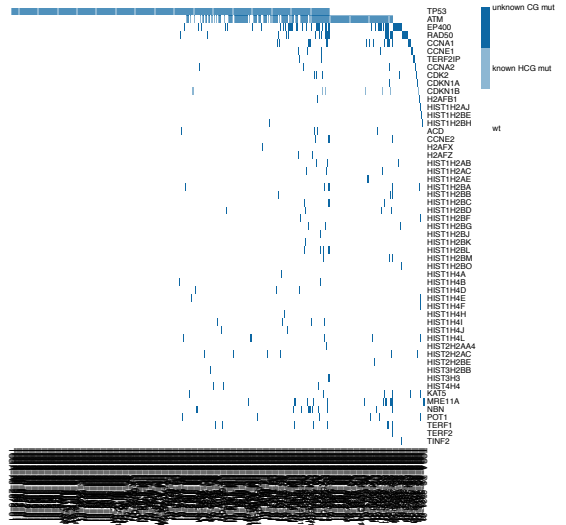




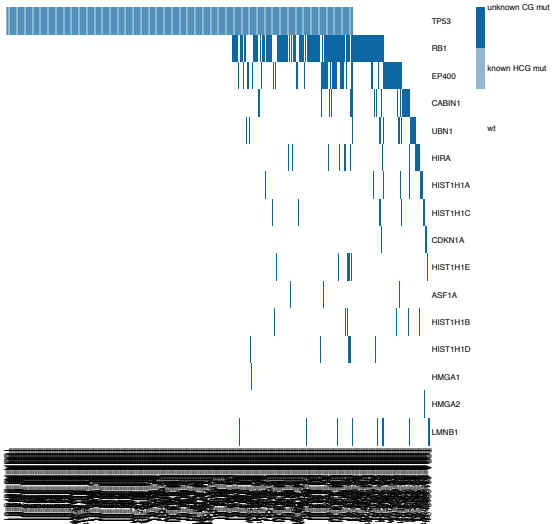
PTK6 Promotes HIF1A Stabilization
 FDR = 2e-12%, FDR nod = 2.6e-08%



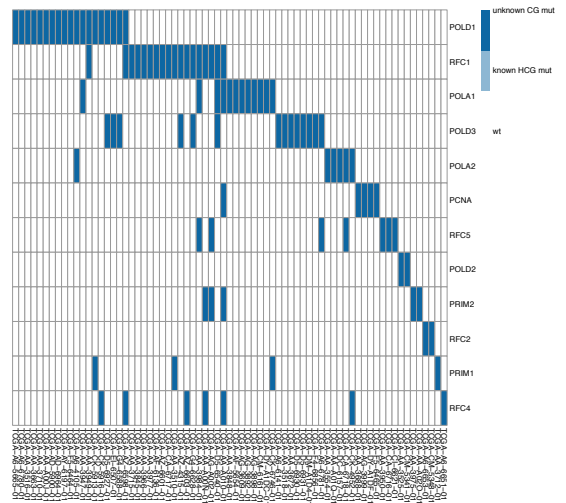
DNA Damage/Telomere Stress Induced Senescence
 FDR = 1.9e-12%, FDR nod = 0.14%



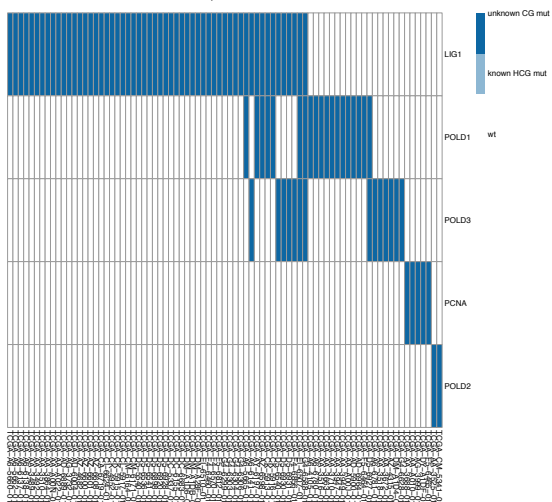
Formation Of Senescence Associated Heterochromatin Foci (SAHF)
 FDR = 1.9e-12%, FDR nod = 2.3e-11%



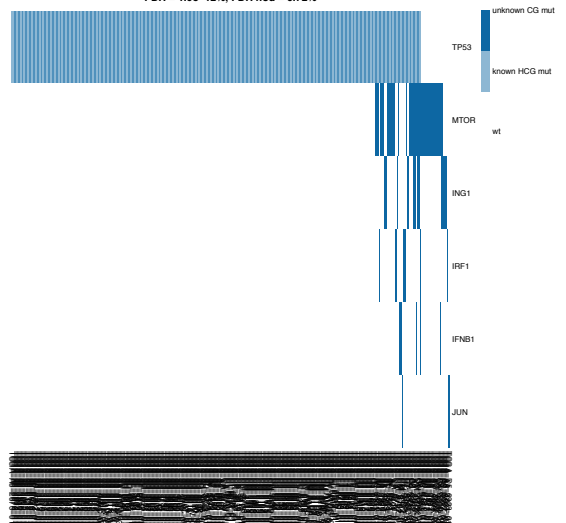
Polymerase Switching
Polymerase Switching On The C Strand Of The Telomere
 FDR = 4.4%, FDR nod = 4.6%



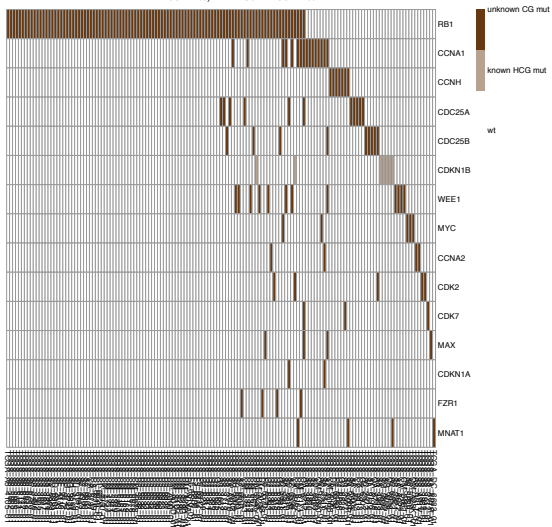
Processive Synthesis On The C Strand Of The Telomere
Telomere C Strand (Lagging Strand) Synthesis
 FDR = 1.9e-12%, FDR nod = 2.3e-11%



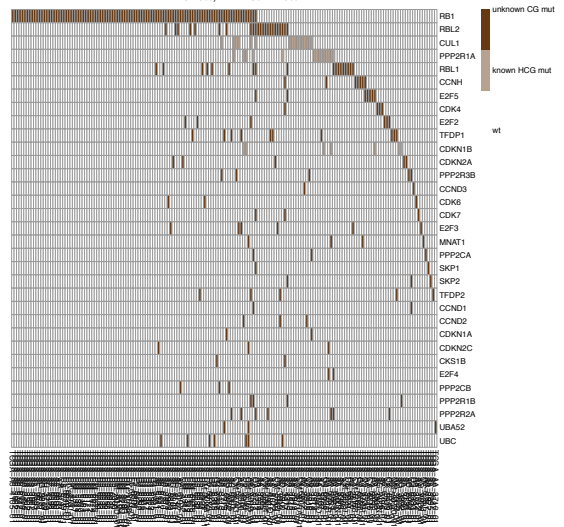
Senescence And Autophagy In Cancer
 FDR = 1.9e-12%, FDR nod = 0.72%



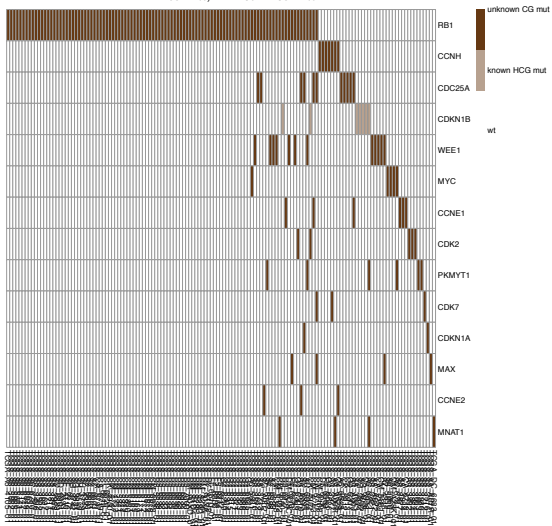
Cyclin A:Cdk2 Associated Events At S Phase Entry
 FDR = 1.9e-12%, FDR nod = 2.3e-11%



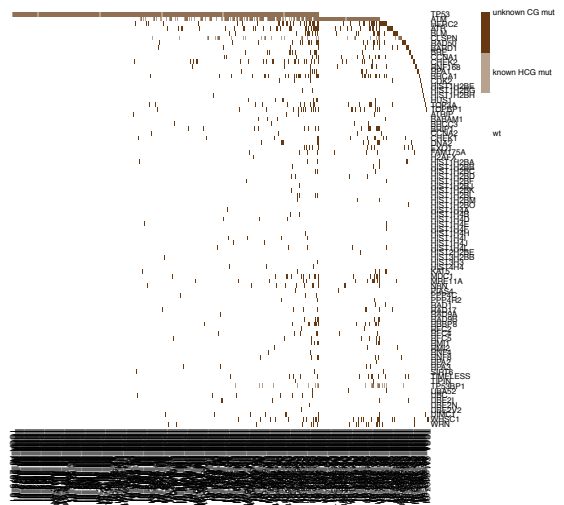
Cyclin D Associated Events In G1
 FDR = 0.79%, FDR nod = 1.9%



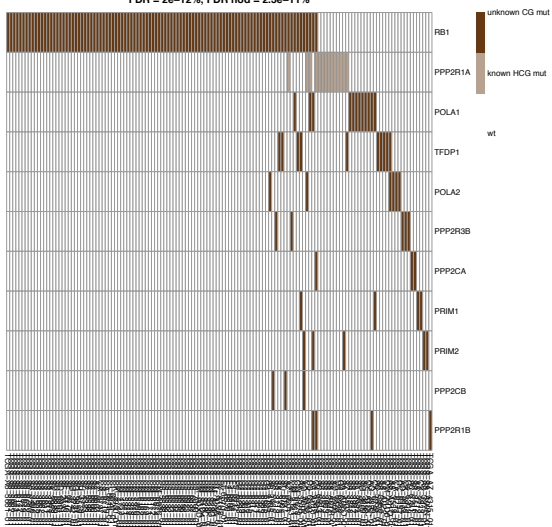
Cyclin E Associated Events During G1/S Transition
 FDR = 1.9e-12%, FDR nod = 2.3e-11%



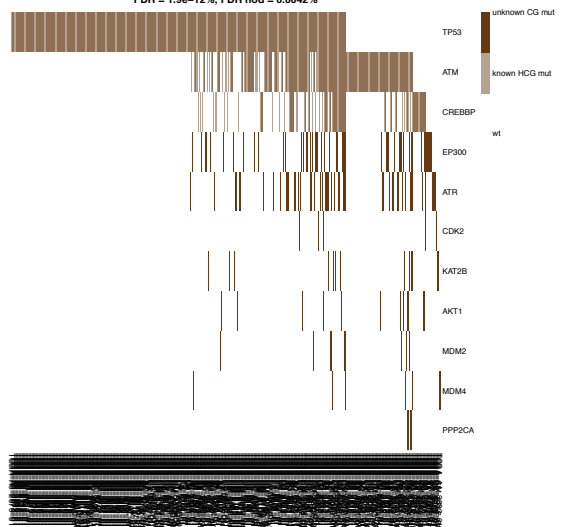
G2/M DNA Damage Checkpoint Processing Of DNA Double Strand Break Ends
 FDR = 1.9e-12%, FDR nod = 4.6%



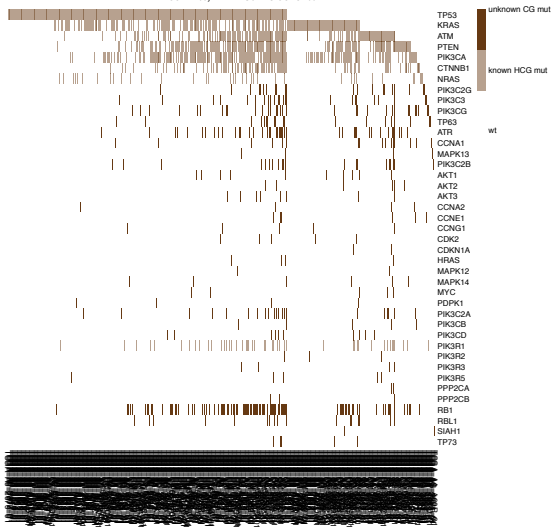
Inhibition Of Replication Initiation Of Damaged DNA By RB1/E2F1
 FDR = 2e-12%, FDR nod = 2.3e-11%



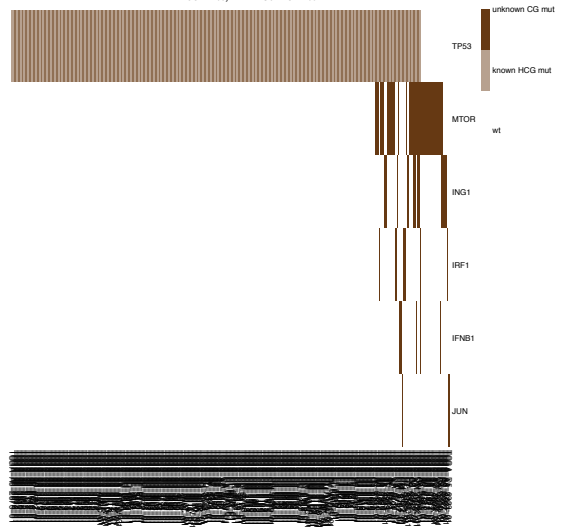
PS3 Pathway
 FDR = 1.9e-12%, FDR nod = 0.0042%



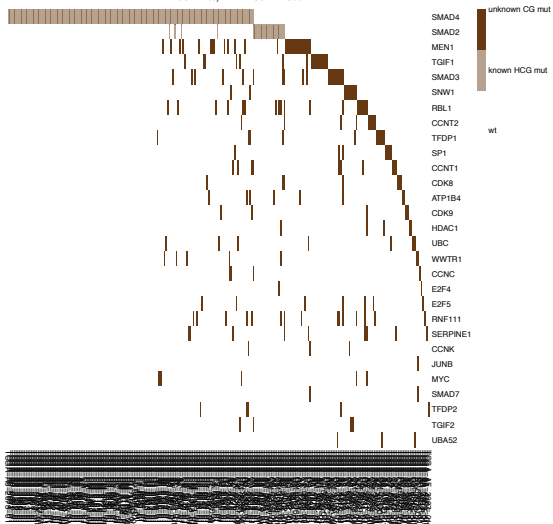
P53 Pathway Feedback Loops 2
 FDR = 1.9e-12%, FDR nod = 6.9e-07%



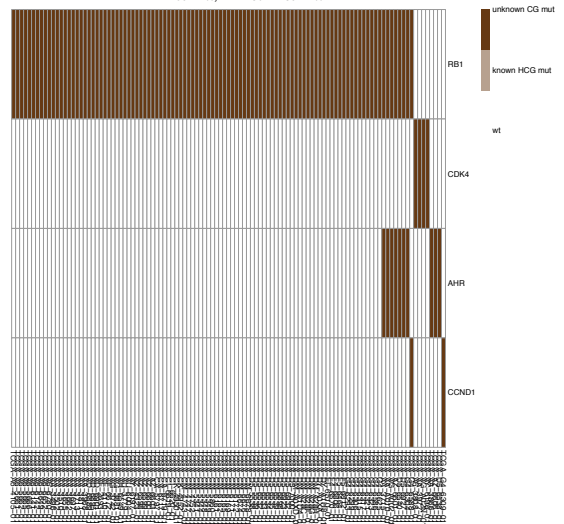
Senescence And Autophagy In Cancer
 FDR = 1.9e-12%, FDR nod = 0.72%



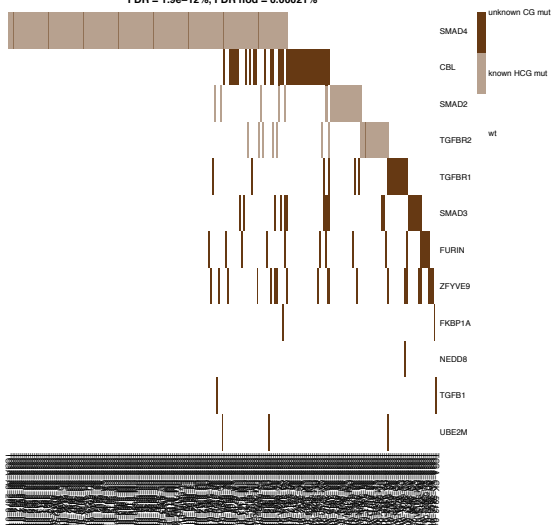
SMAD2/SMAD3:SMAD4 Heterotrimer Regulates Transcription
 FDR = 1.9e-12%, FDR nod = 2.5%



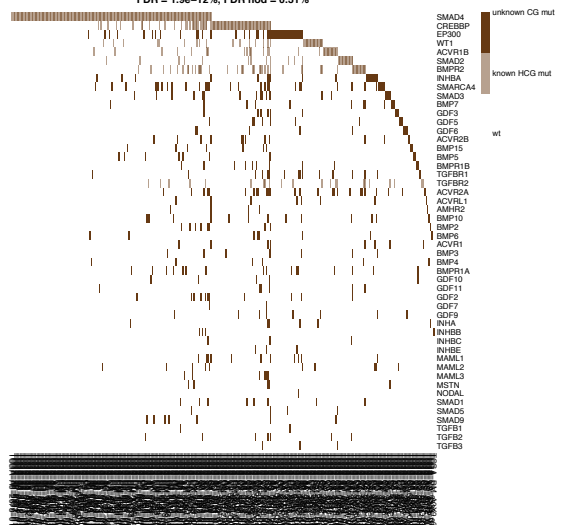
The Reaction [[AHR Protein Binds To CDK4 Protein, CCND1 Protein] Results In Increased Phosphorylation Of RB1
 FDR = 1.9e-12%, FDR nod = 2.3e-11%



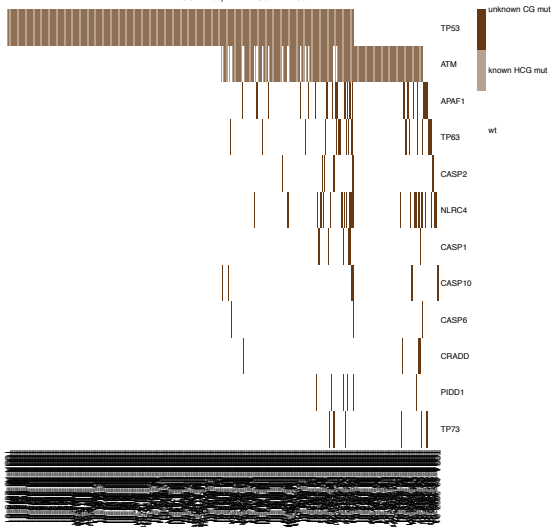
TGF Beta Receptor Signaling Activates SMADs
 FDR = 1.9e-12%, FDR nod = 0.00021%



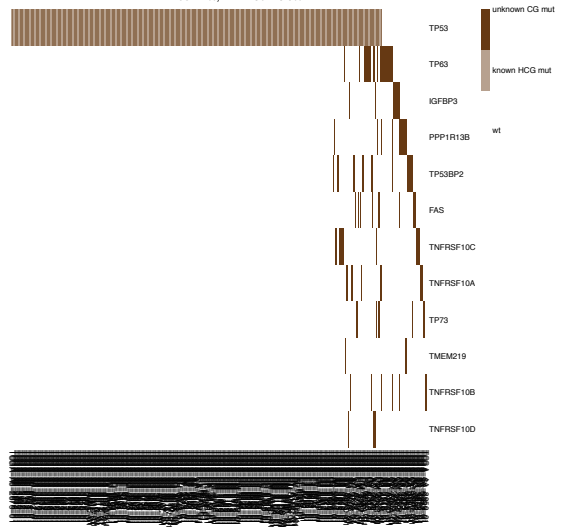
ta Super Family Signaling Pathway(canonical) (TGF Beta BMP Diagram(MolecularVariation))
 FDR = 1.9e-12%, FDR nod = 0.31%



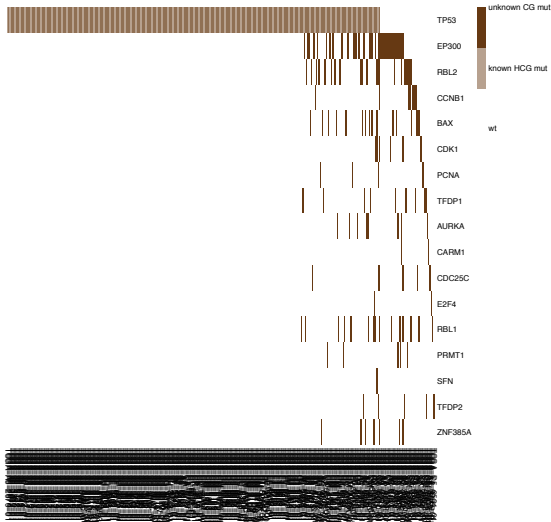
TP53 Regulates Transcription Of Caspase Activators And Caspases
 FDR = 1.9e-12%, FDR nod = 1.1%



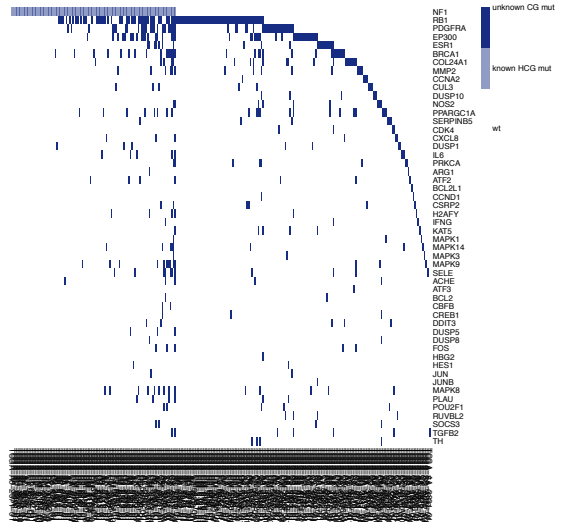
TP53 Regulates Transcription Of Death Receptors And Ligands
 FDR = 1.9e-12%, FDR nod = 3.6%



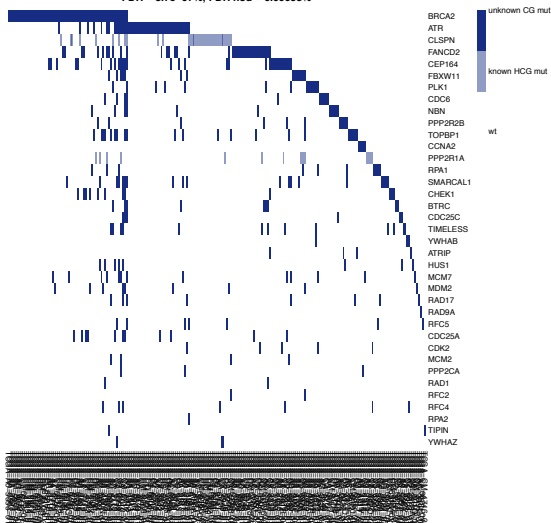
TP53 Regulates Transcription Of Genes Involved In G2 Cell Cycle Arrest
 FDR = 1.9e-12%, FDR nod = 0.011%



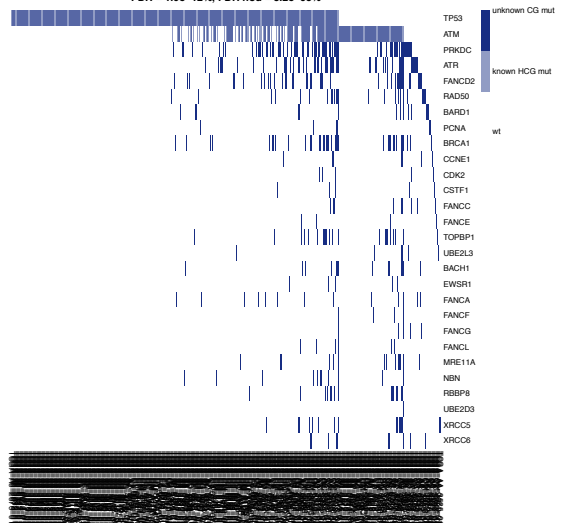
ATF 2 Transcription Factor Network
 FDR = 7e-08%, FDR nod = 0.00047%



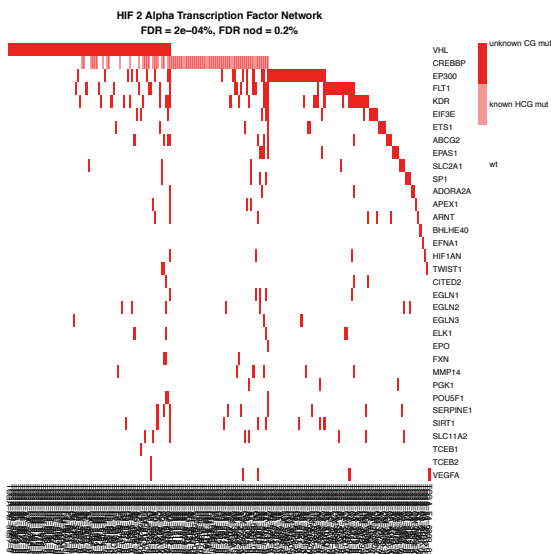
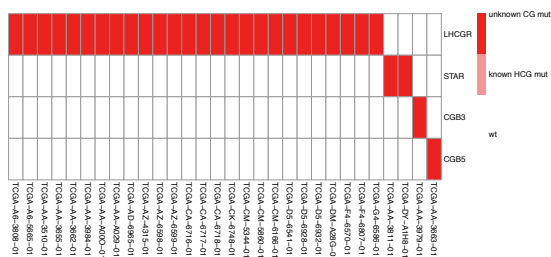
ATR Signaling Pathway
 FDR = 8.7e-07%, FDR nod = 0.00038%



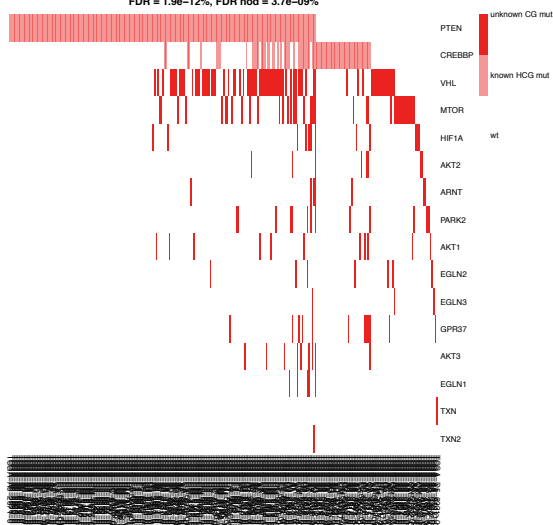
BARD1 Signaling Events
 FDR = 1.9e-12%, FDR nod = 5.2e-05%



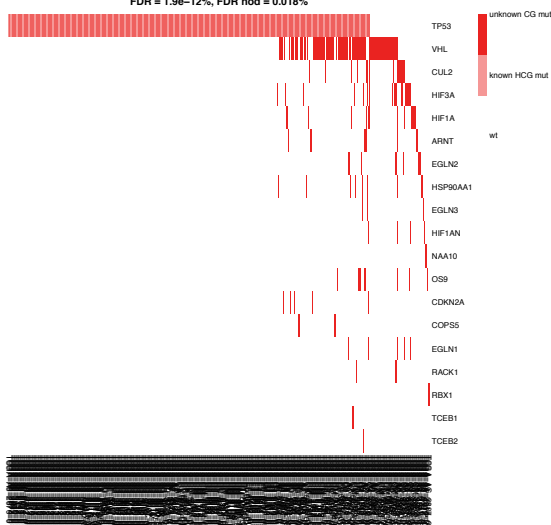
[CGB Protein Results In Increased Activity Of LHCGR Protein]
je Results In Decreased Activity Of PTGS2 Protein] Inhibits The Reaction [CGB Protein Results In Increased Chen
(3, 2 F)quinazoline 1,3 Diamine Binds To F2R Protein] Promotes The Reaction [CGB Protein Results In Increased I
ne Inhibits The Reaction [CGB Protein Results In Increased Chemical Synthesis Of Androgens]
itrazine Inhibits The Reaction [CGB Protein Results In Increased Secretion Of Cyclic AMP]
orsin Promotes The Reaction [CGB Protein Results In Increased Abundance Of Cyclic AMP]
Reaction [[Gonadotropins, Equine Co Treated With CGB Protein] Results In Increased Abundance Of Progesterone
inhibits The Reaction [[CGB Protein Co Treated With Colforsin] Results In Increased Abundance Of Cyclic AMP]
rotein Promotes The Reaction [CGB Protein Results In Increased Abundance Of Progesterone]
se Metabolite Inhibits The Reaction [CGB Protein Results In Increased Abundance Of Testosterone]
se Chloride Inhibits The Reaction [CGB Protein Results In Increased Expression Of STAR Protein]
terone Promotes The Reaction [CGB Protein Results In Increased Expression Of VEGFA MRNA]
one Enanthate Inhibits The Reaction [CGB Protein Results In Increased Abundance Of Androgens]
FDR = 0.0063%, FDR nod = 0.012%



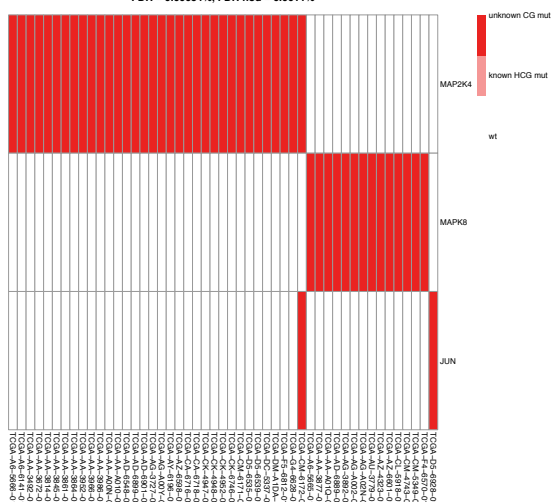
Hypoxia Response Via HIF Activation
FDR = 1.9e-12%, FDR nod = 3.7e-09%



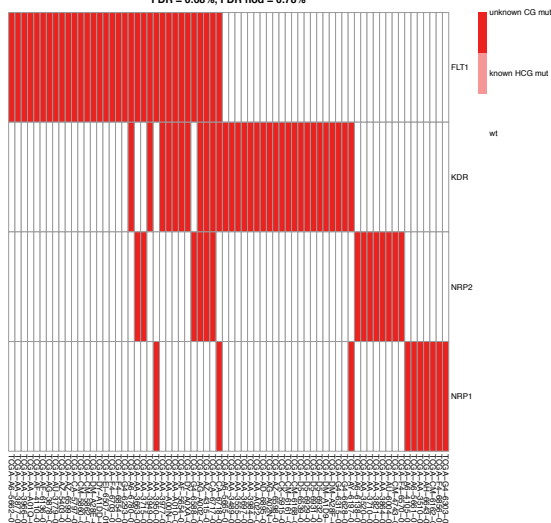
Hypoxic And Oxygen Homeostasis Regulation Of HIF 1 Alpha
FDR = 1.9e-12%, FDR nod = 0.018%



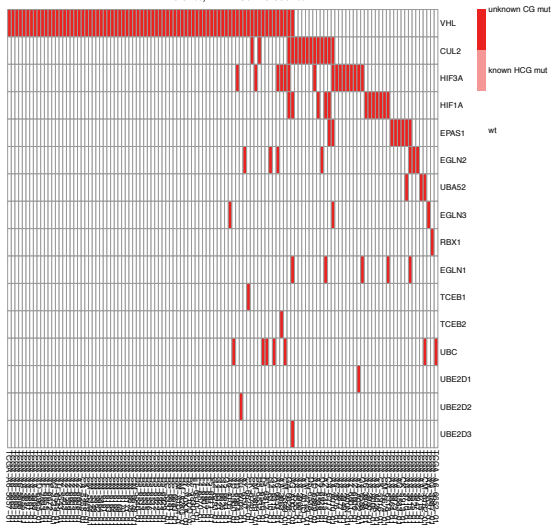
JNK Cascade (EGF Signaling Pathway Diagram)
JNK Cascade (PDGF Signaling Pathway)
FDR = 0.00054%, FDR nod = 0.0011%



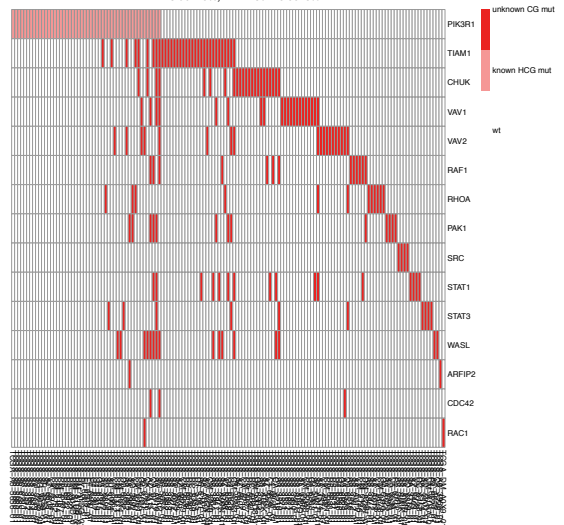
Neurophilin Interactions With VEGF And VEGFR
FDR = 0.68%, FDR nod = 0.78%



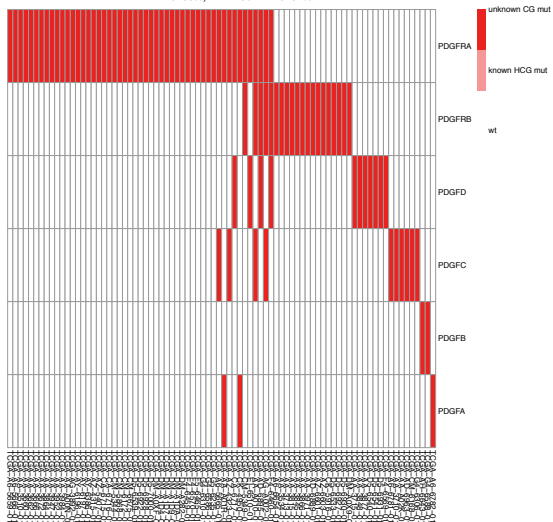
Oxygen Dependent Proline Hydroxylation Of Hypoxia Inducible Factor Alpha
 FDR = 0.01%, FDR nod = 0.0092%



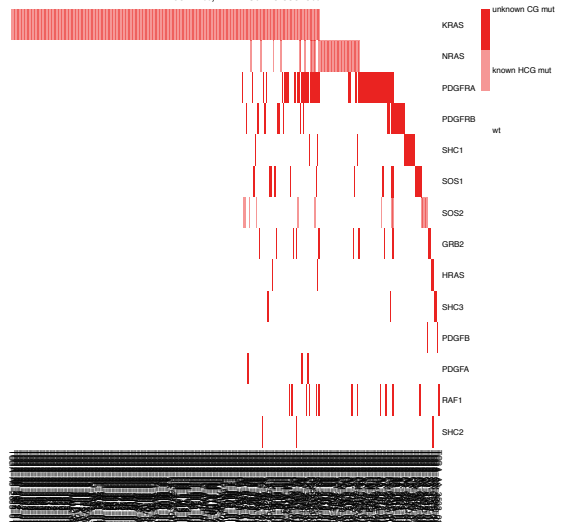
PDGF Pathway
 FDR = 8.9e-10%, FDR nod = 0.0023%



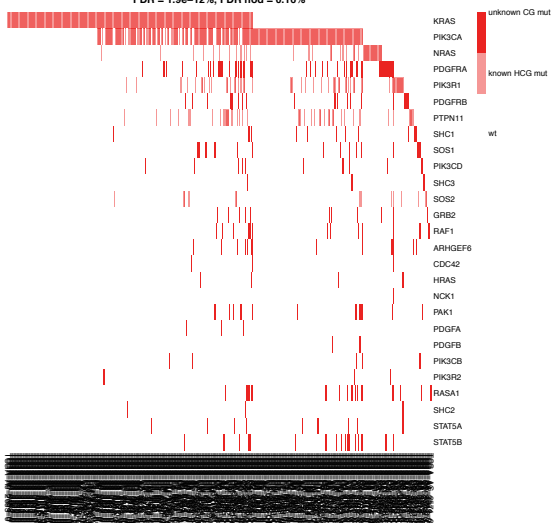
PDGF Receptor Signaling Network
 FDR = 7e-08%, FDR nod = 1.2e-07%



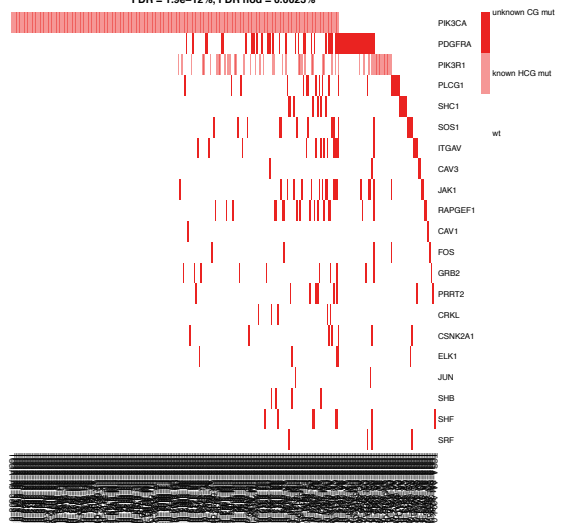
PDGF Signaling Pathway (PDGF Signaling Pathway)
 FDR = 1.9e-12%, FDR nod = 0.00016%



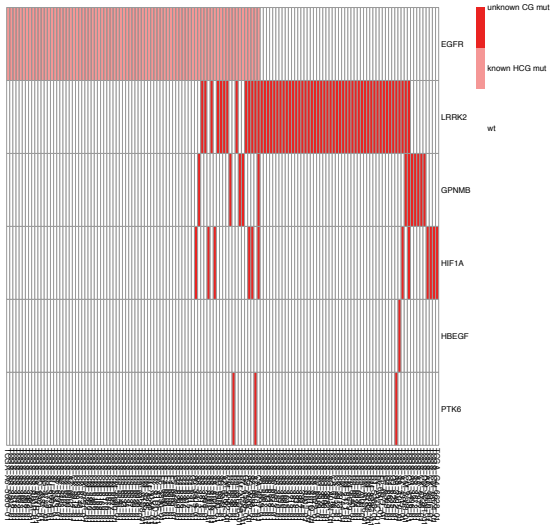
PDGF Signaling Pathway (Mammal) (PDGF Signaling Pathway)
 FDR = 1.9e-12%, FDR nod = 0.16%



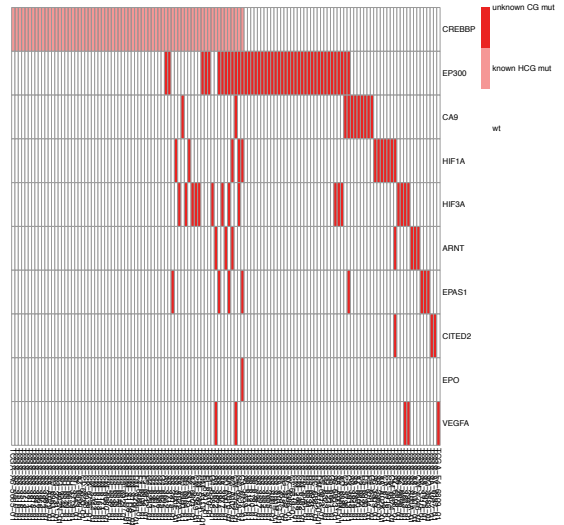
PDGFR Alpha Signaling Pathway
 FDR = 1.9e-12%, FDR nod = 0.0023%



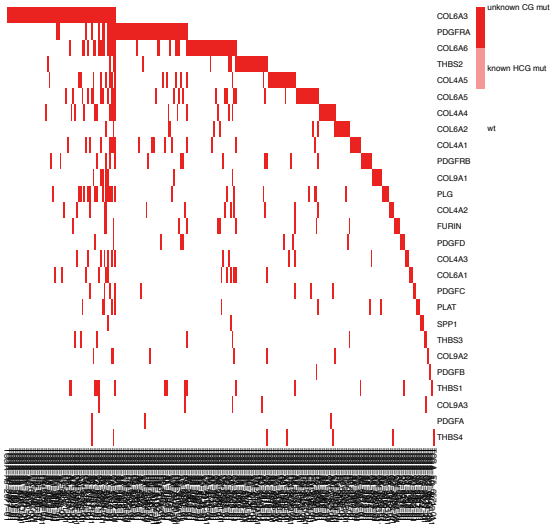
PTK6 Promotes HIF1A Stabilization
 FDR = 2e-12%, FDR nod = 2.6e-08%



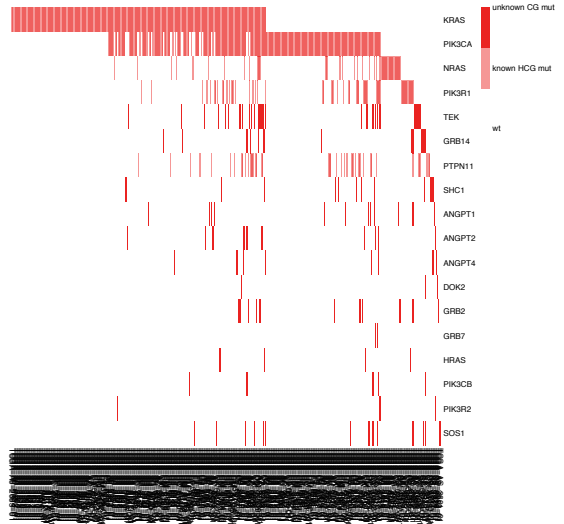
Regulation Of Gene Expression By Hypoxia Inducible Factor
 FDR = 4.9e-09%, FDR nod = 1.8%



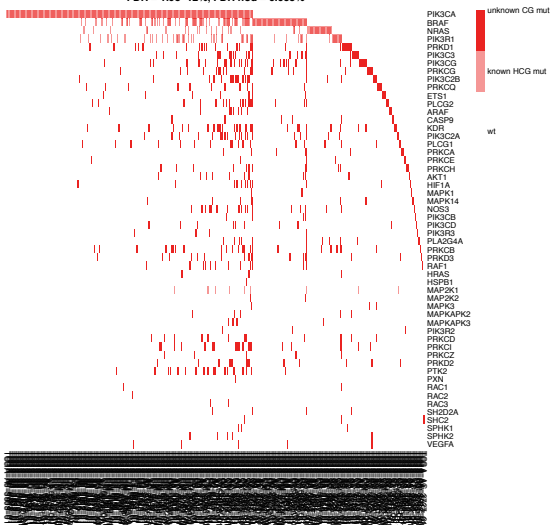
Signaling By PDGF
 FDR = 1.9e-12%, FDR nod = 2.3e-11%



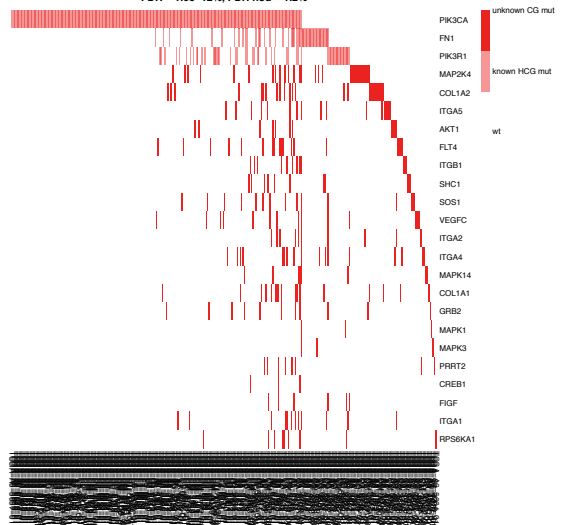
Tie2 Signaling
 FDR = 1.9e-12%, FDR nod = 0.074%



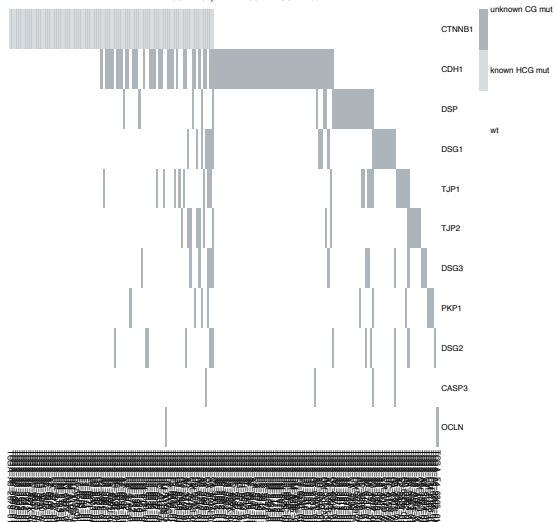
VEGF Signaling Pathway
 FDR = 1.9e-12%, FDR nod = 0.053%



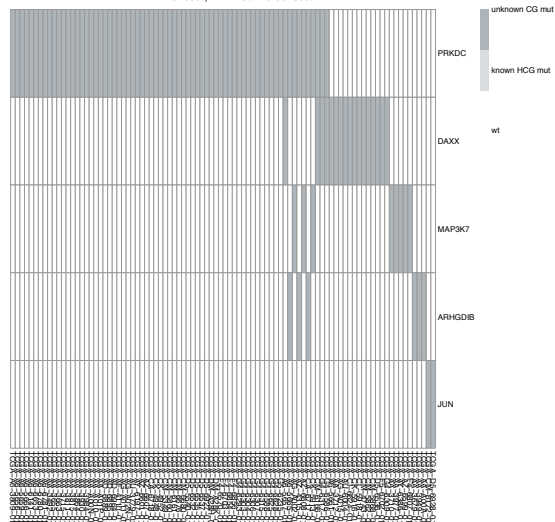
VEGFR3 Signaling In Lymphatic Endothelium
 FDR = 1.9e-12%, FDR nod = 1.2%



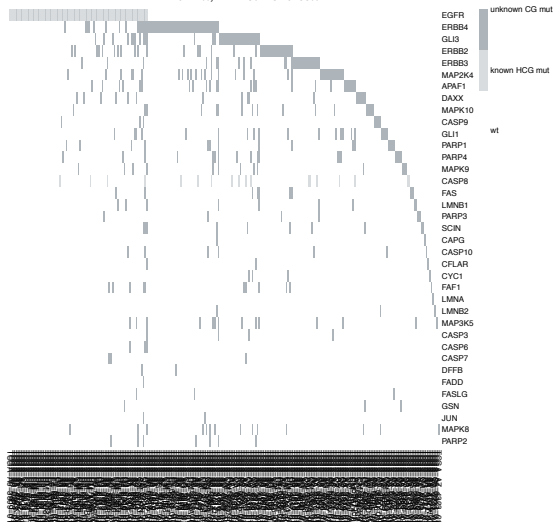
Apoptotic Cleavage Of Cell Adhesion Proteins
FDR = 1.9e-12%, FDR nod = 2.3e-11%



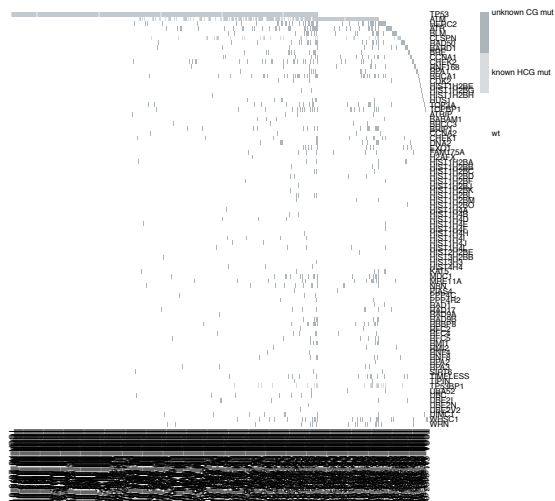
FAS Pathway And Stress Induction Of HSP Regulation
FDR = 4e-06%, FDR nod = 5.5e-06%



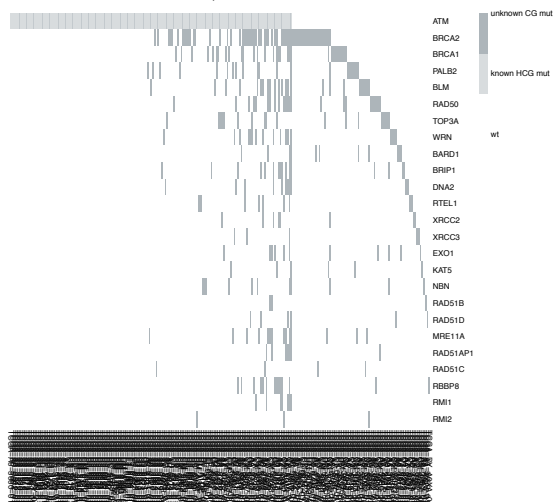
FAS Signaling Pathway
FDR = 2.4e-12%, FDR nod = 3.7e-06%



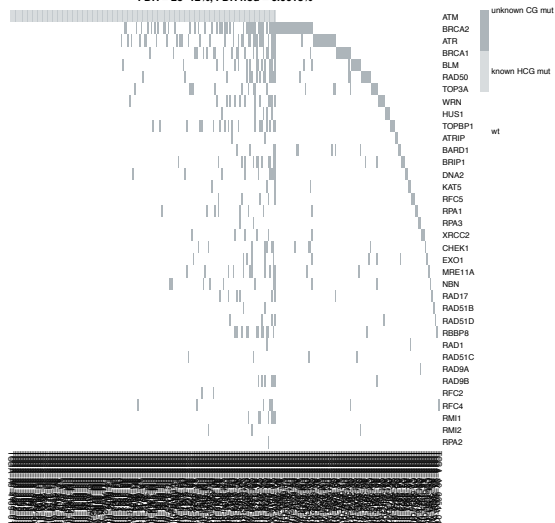
G2/M DNA Damage Checkpoint
Processing Of DNA Double Strand Break Ends
FDR = 1.9e-12%, FDR nod = 4.6%



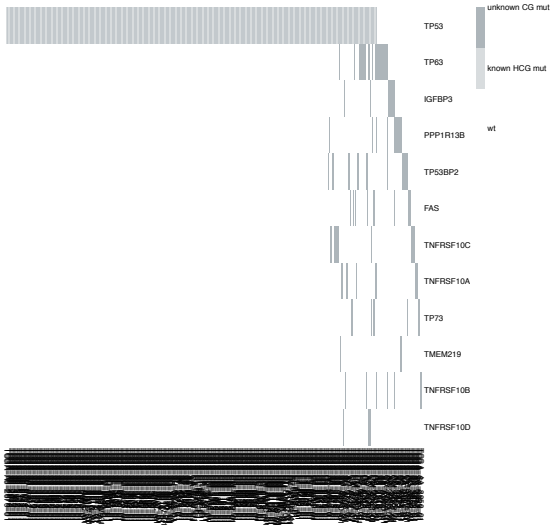
Homologous DNA Pairing And Strand Exchange
Resolution Of D Loop Structures Through Synthesis Dependent Strand Annealing (SDSA)
FDR = 1.9e-12%, FDR nod = 0.014%



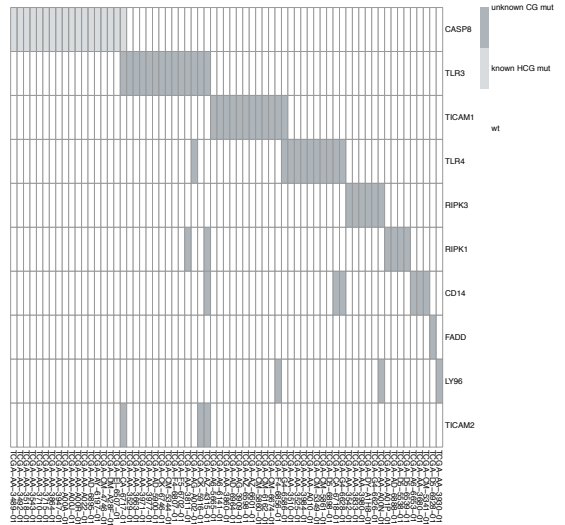
Presynaptic Phase Of Homologous DNA Pairing And Strand Exchange
FDR = 2e-12%, FDR nod = 0.0018%



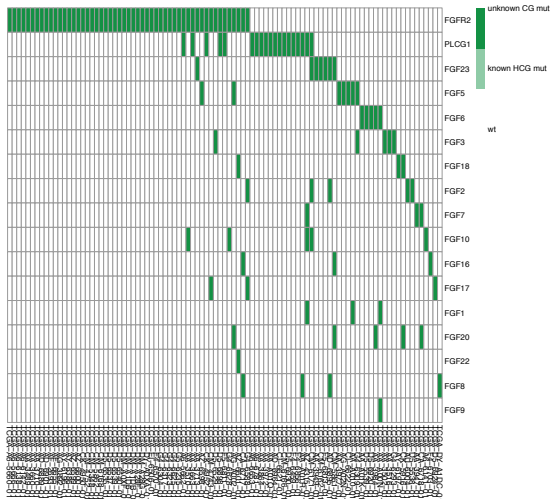
TP53 Regulates Transcription Of Death Receptors And Ligands
 FDR = 1.9e-12%, FDR nod = 3.6%



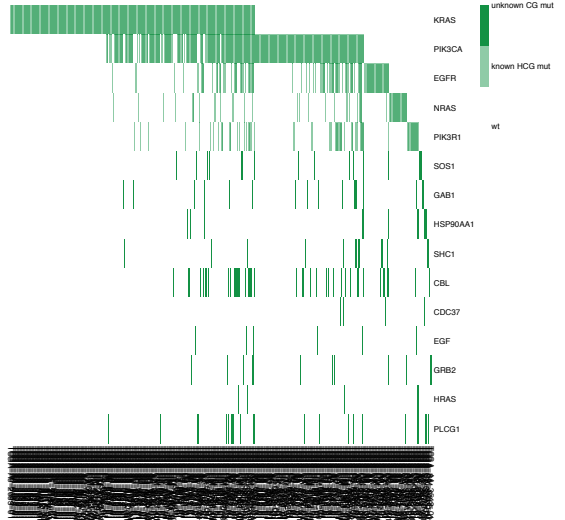
TRIF Mediated Programmed Cell Death
 FDR = 0.052%, FDR nod = 3.8%



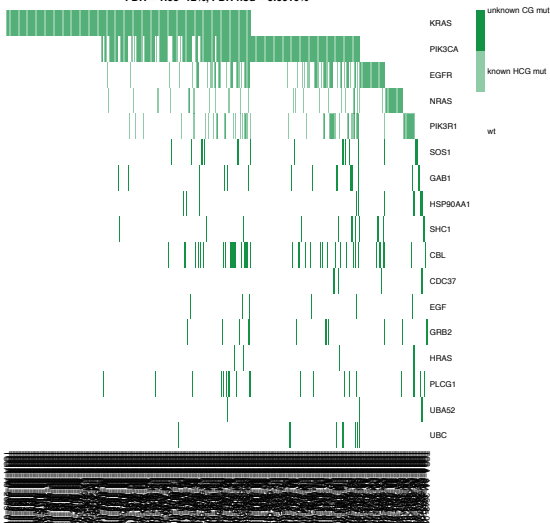
Activated Point Mutants Of FGFR2
 Phospholipase C Mediated Cascade; FGFR2
 FDR = 0.22%, FDR nod = 0.22%



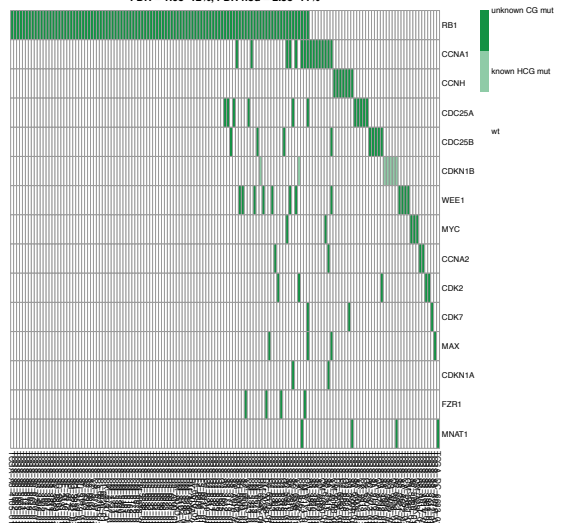
Constitutive Signaling By EGFR/III
 FDR = 1.9e-12%, FDR nod = 0.00014%



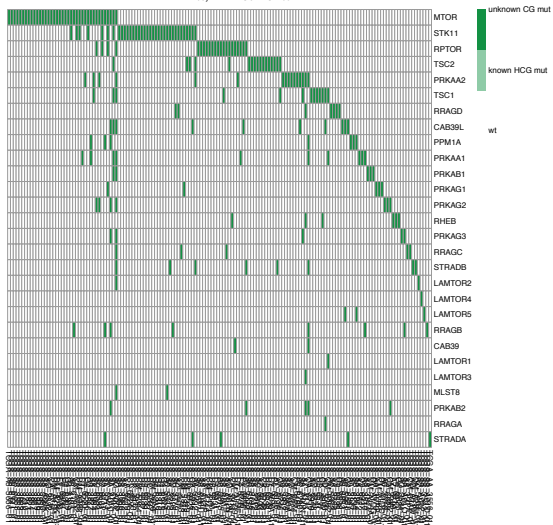
Constitutive Signaling By Ligand Responsive EGFR Cancer Variants
 FDR = 1.9e-12%, FDR nod = 0.0019%



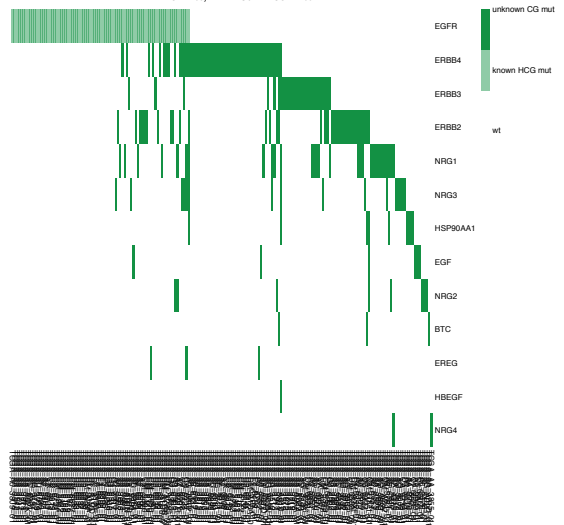
Cyclin A:Cdk2 Associated Events At S Phase Entry
 FDR = 1.9e-12%, FDR nod = 2.3e-11%



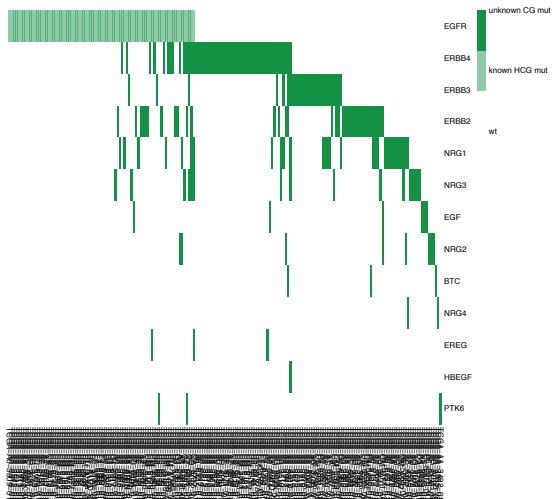
Energy Dependent Regulation Of MTOR By LKB1 AMPK
FDR = 4.4%, FDR nod = 3.2%



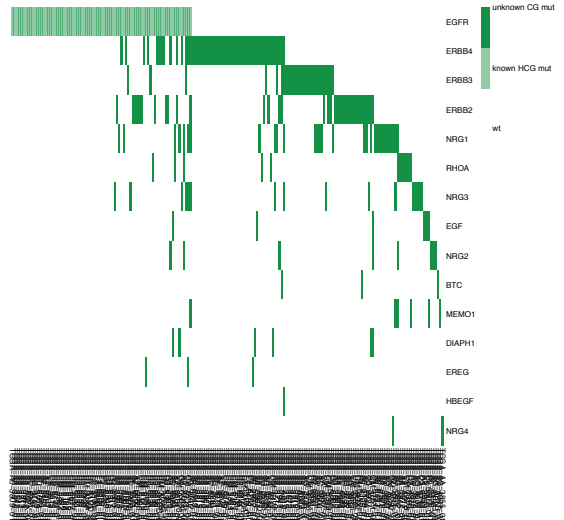
ErbB Receptor Signaling Network
FDR = 2e-12%, FDR nod = 2.3e-11%



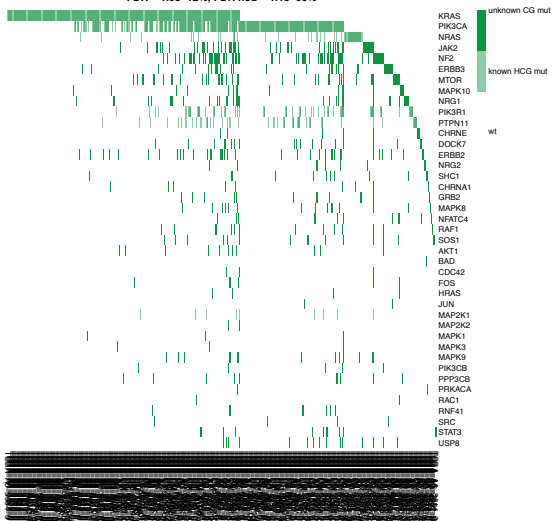
ERBB2 Activates PTK6 Signaling By ERBB4
FDR = 1.9e-12%, FDR nod = 2.3e-11%



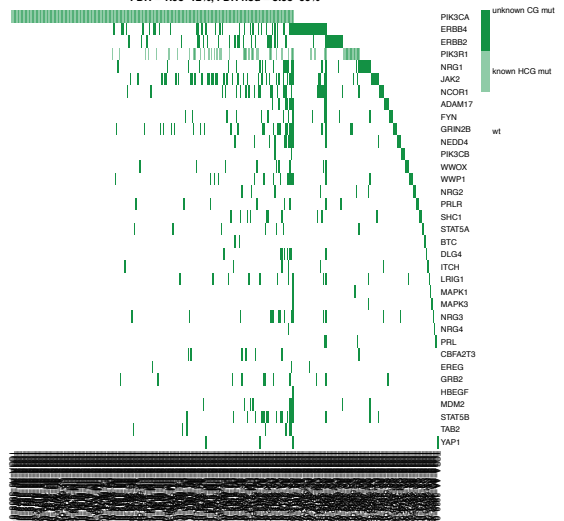
ERBB2 Regulates Cell Motility
FDR = 1.9e-12%, FDR nod = 5.5e-11%

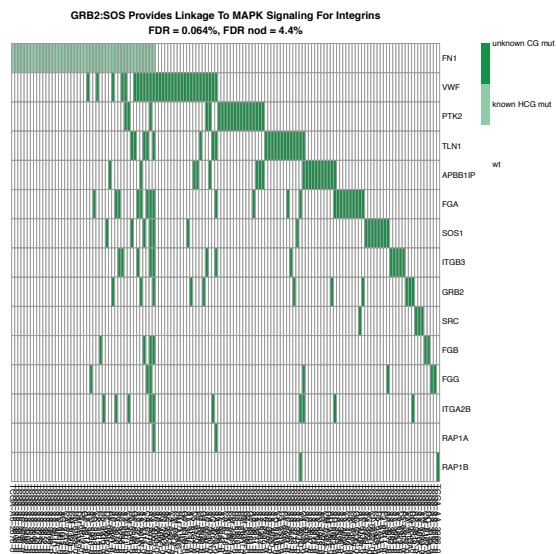
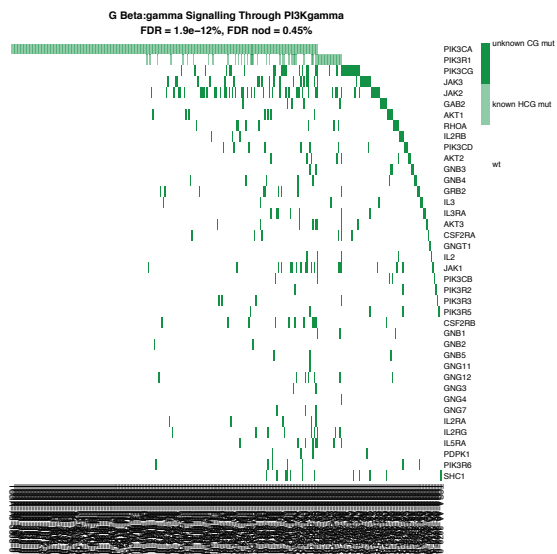
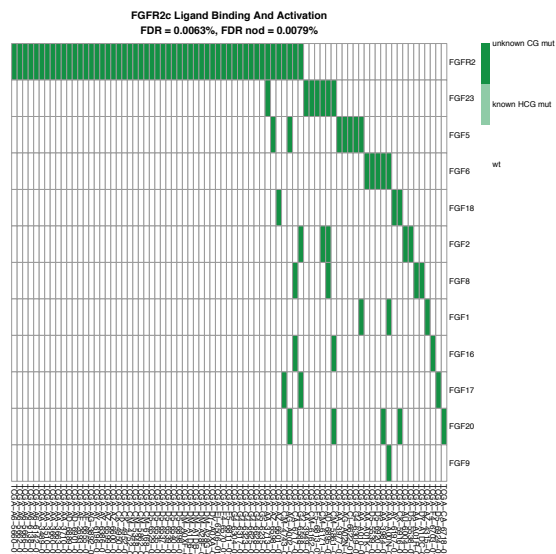
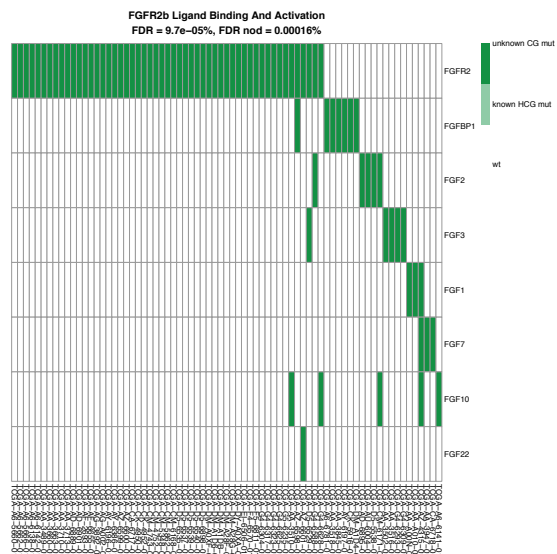
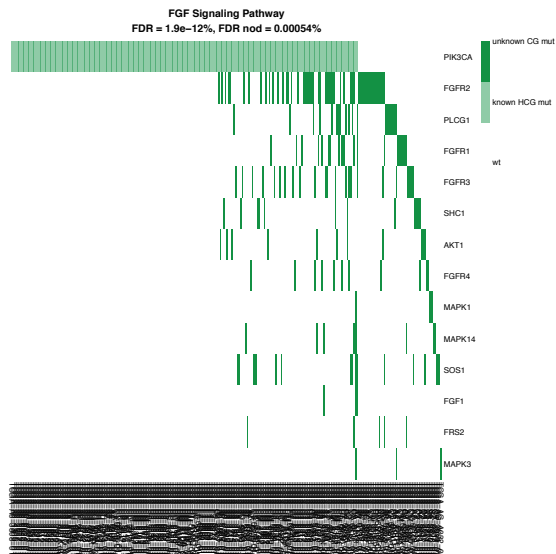
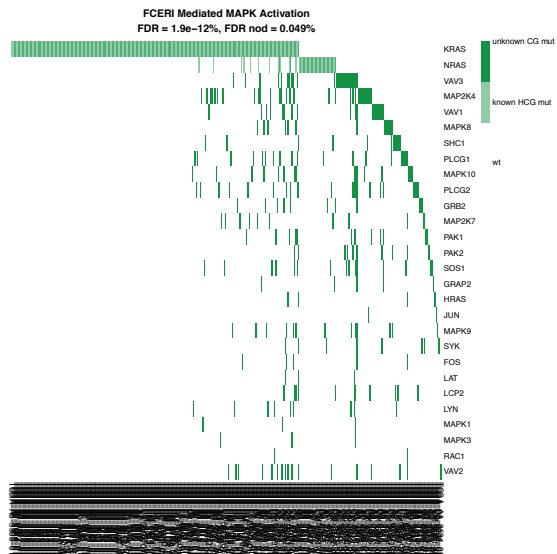


ErbB2/ErbB3 Signaling Events
FDR = 1.9e-12%, FDR nod = 1.1e-09%

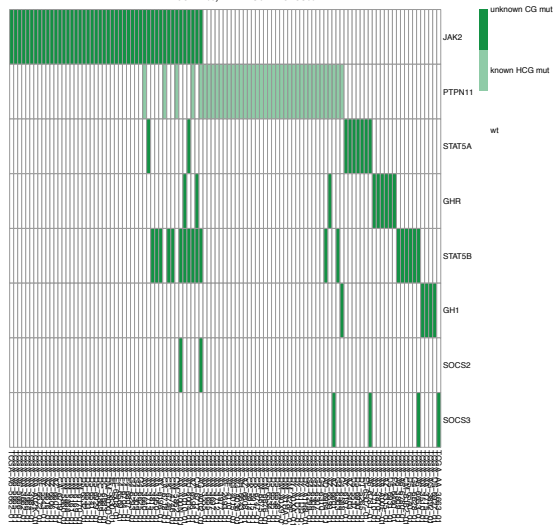


ErbB4 Signaling Events
FDR = 1.9e-12%, FDR nod = 3.6e-06%

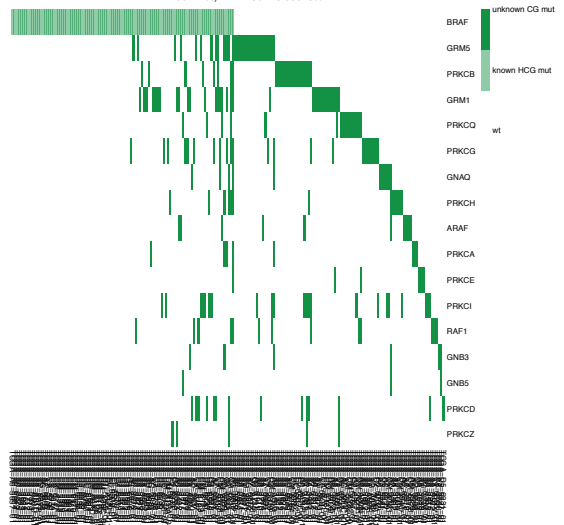




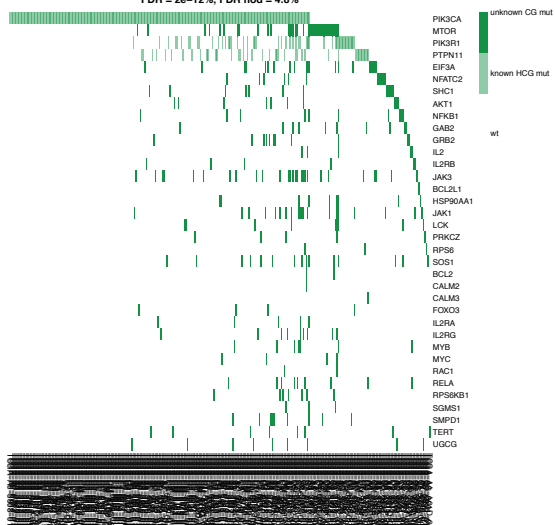
rowth Hormone Signaling Pathway(JAK2 STATS) (Growth Hormone Signaling(JAK2 STATS))
FDR = 1.9e-12%, FDR nod = 2e-05%



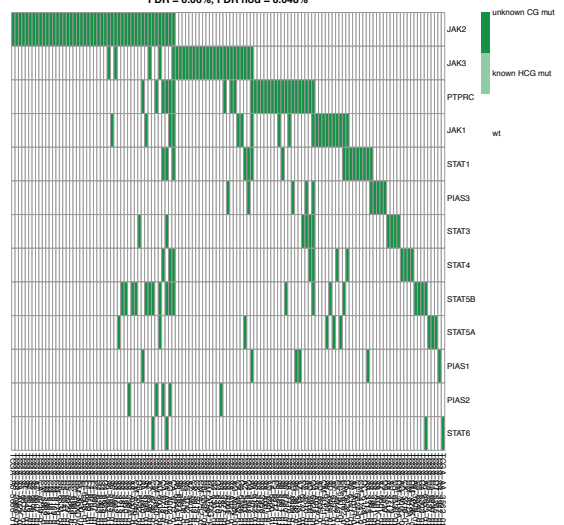
thway (through Glutamate, G Alpha Q And PLC Beta) (GPCR GroupI Metabotropic Glutamate Receptor Signaling I
FDR = 1.9e-12%, FDR nod = 0.00018%



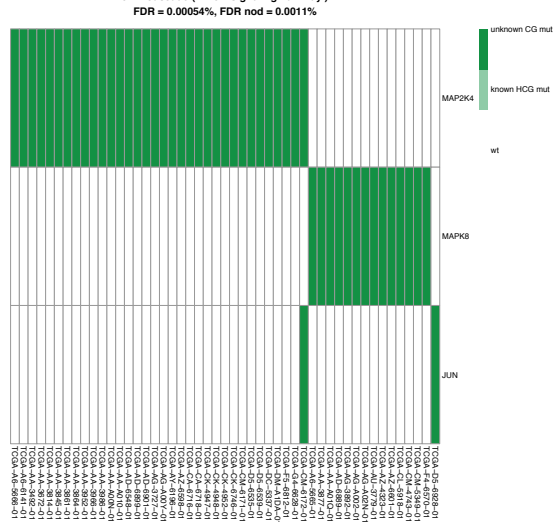
IL2 Signaling Events Mediated By PI3K
FDR = 2e-12%, FDR nod = 4.8%



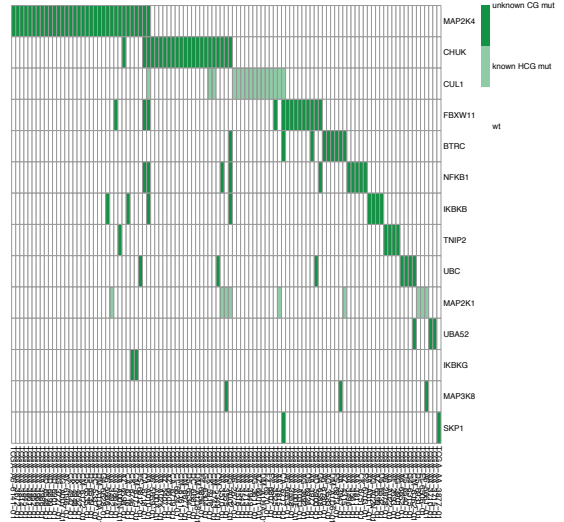
JAK/STAT Signaling Pathway
FDR = 0.06%, FDR nod = 0.048%



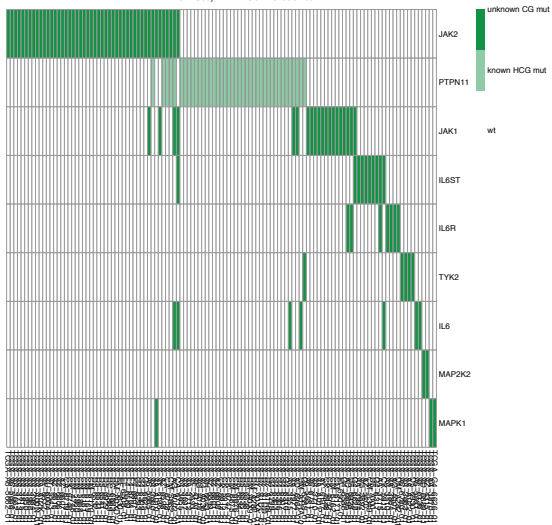
JNK Cascade (EGF Signaling Pathway Diagram)
JNK Cascade (PDGF Signaling Pathway)
FDR = 0.00054%, FDR nod = 0.0011%



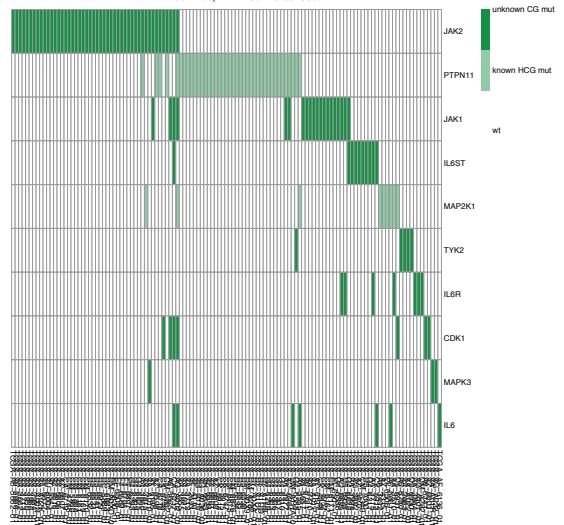
MAP3K8 (TPL2) Dependent MAPK1/3 Activation
FDR = 0.25%, FDR nod = 3.3%



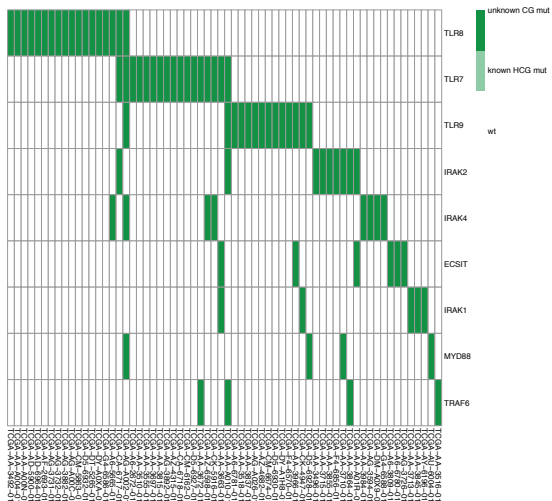
MAPK1 (ERK2) Activation
FDR = 1.2e-10%, FDR nod = 0.0054%



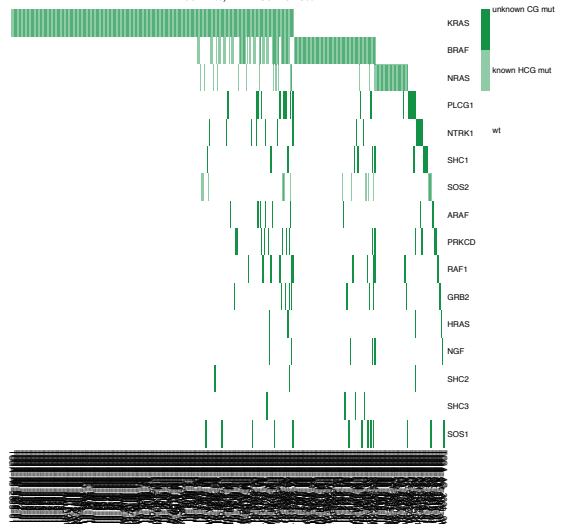
MAPK3 (ERK1) Activation
FDR = 1.9e-12%, FDR nod = 3.6e-06%



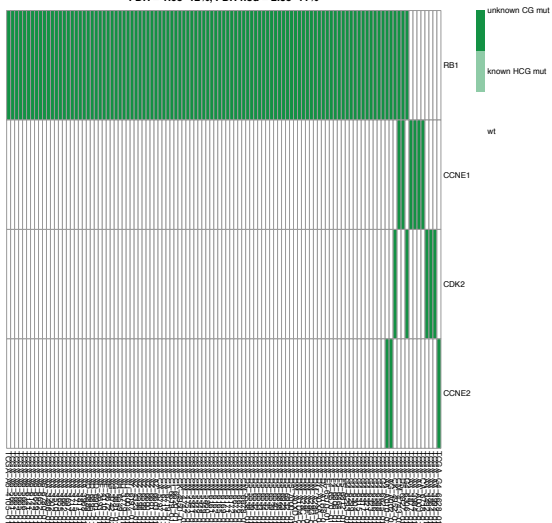
MyD88 Dependent Cascade Initiated On Endosome
TRAF6 Mediated Induction Of NFkB And MAP Kinases Upon TLR7/8 Or 9 Activation
FDR = 0.41%, FDR nod = 0.51%



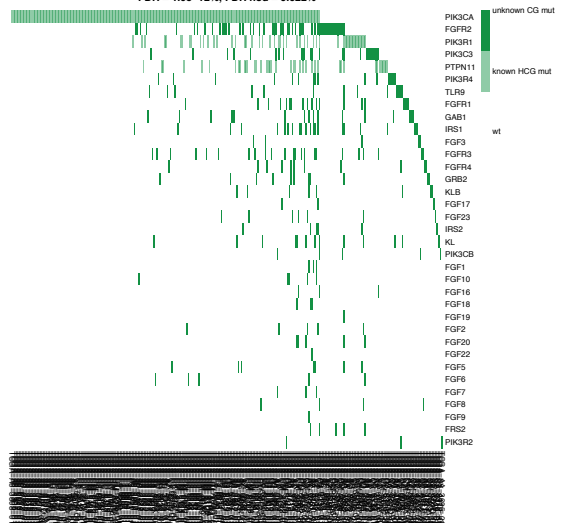
NGF Signaling Pathway (NGF Signaling Pathway)
FDR = 1.9e-12%, FDR nod = 0.23%



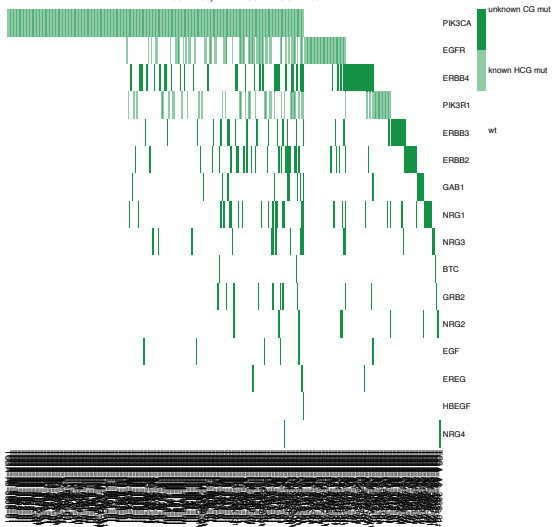
Phosphorylation Of Proteins Involved In G1/S Transition By Active Cyclin E:Cdk2 Complexes
FDR = 1.9e-12%, FDR nod = 2.3e-11%



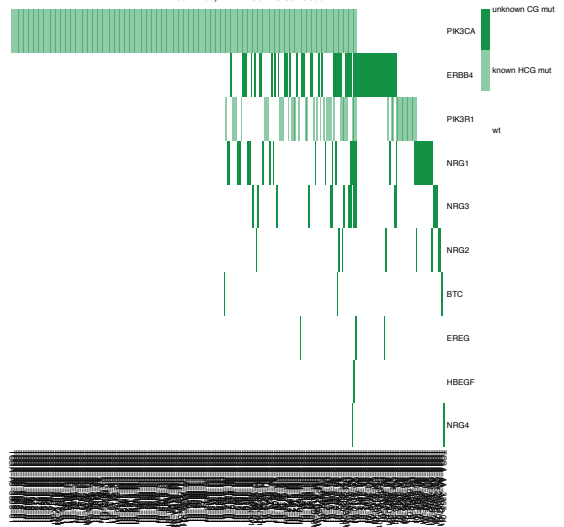
PI3K Cascade
FDR = 1.9e-12%, FDR nod = 0.022%



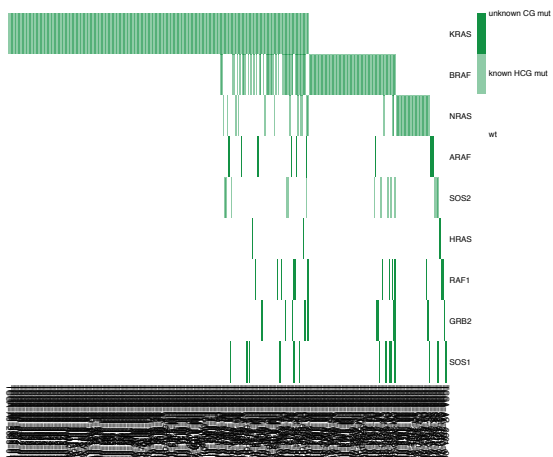
PI3K Events In ERBB2 Signaling
 FDR = 1.9e-12%, FDR nod = 2.3e-11%



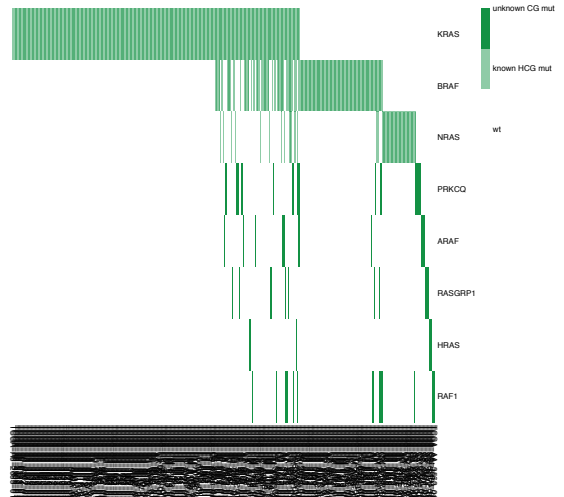
PI3K Events In ERBB4 Signaling
 FDR = 1.9e-12%, FDR nod = 3.5e-06%



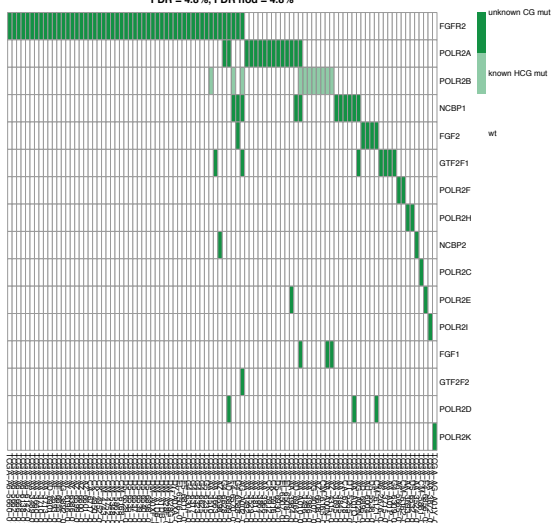
Raf Activation Signaling (through Grb2 And Sos) (B Cell Receptor Signaling)
Activation Signaling (through Grb2 And Sos) (CD4 T Cell Receptor Signaling (ERK Cascade))
Raf Activation Signaling (through Grb2 And Sos) (CD4 T Cell Receptor Signaling)
Activation Signaling (through Grb2 And Sos) (JAK STAT Pathway And Regulation Pathway Diagram)
 FDR = 1.9e-12%, FDR nod = 2.5%



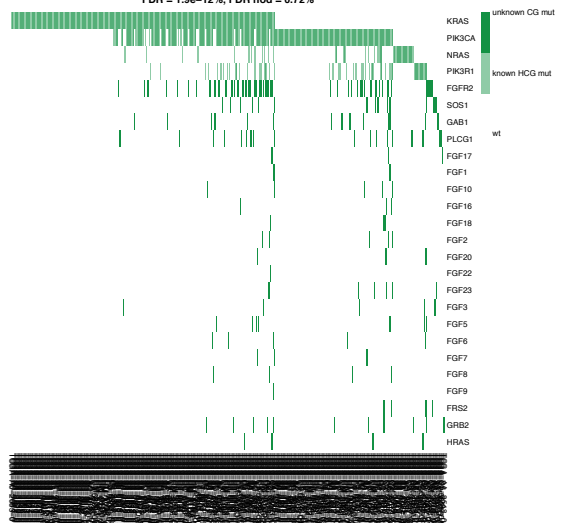
f Activation Signaling (through RasGRP) (CD4 T Cell Receptor Signaling (ERK Cascade))
Raf Activation Signaling (through RasGRP) (CD4 T Cell Receptor Signaling)
 FDR = 1.9e-12%, FDR nod = 0.2%



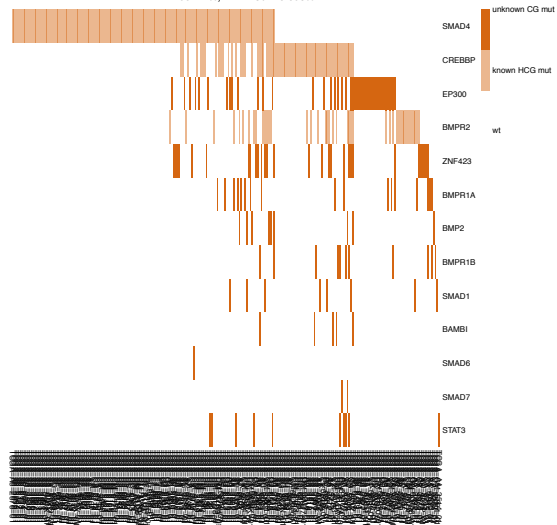
Signaling By FGFR2 IIs TM
 FDR = 4.8%, FDR nod = 4.8%



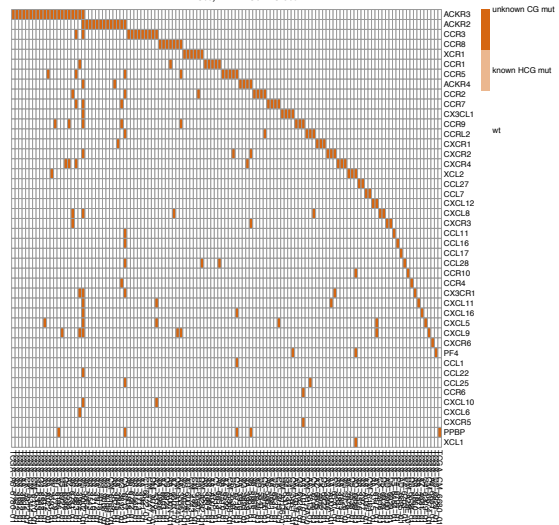
Signaling By FGFR2 In Disease
 FDR = 1.9e-12%, FDR nod = 0.72%



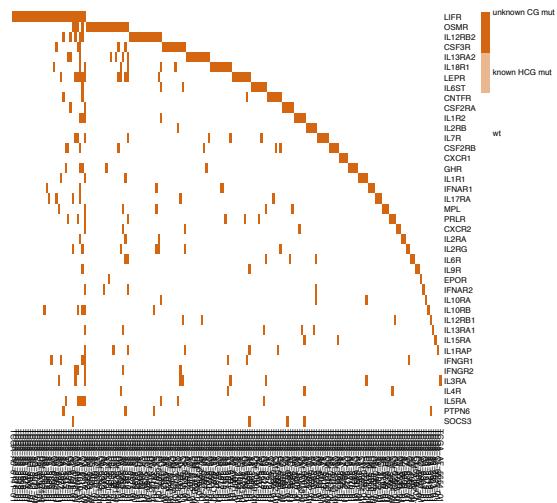
BMP2 Signaling Pathway(through Smad) (TGF Beta BMP Diagram(MolecularVariation))
FDR = 1.9e-12%, FDR nod = 0.095%



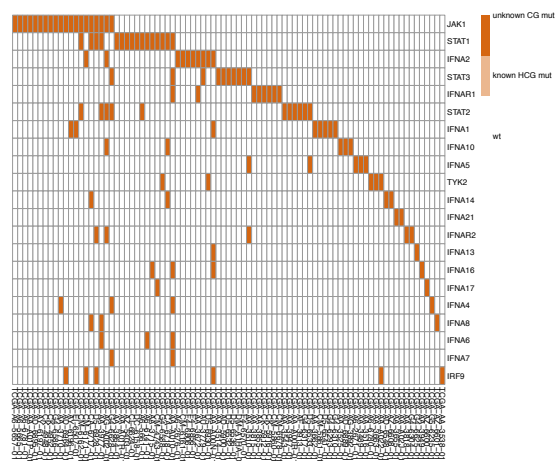
Chemokine Receptors Bind Chemokines
FDR = 4.8%, FDR nod = 3.9%



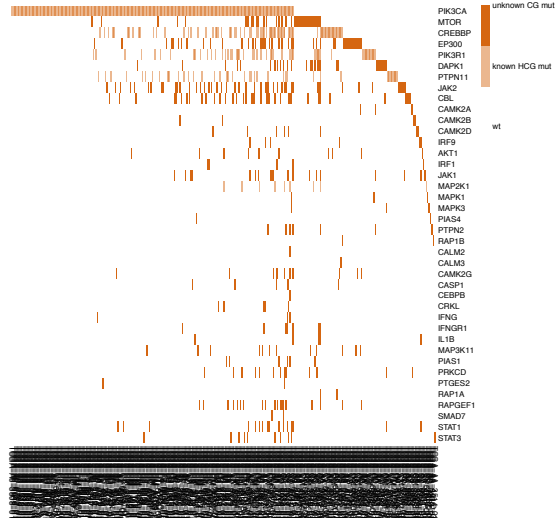
Cytokine Receptor Degradation Signaling (JAK STAT Pathway And Regulation Pathway Diagram)
osphorylation Of Cytokine Receptor) in JAK STAT Pathway (JAK STAT Pathway And Regulation Pathway Diagram)
FDR = 2.3%, FDR nod = 1.3%



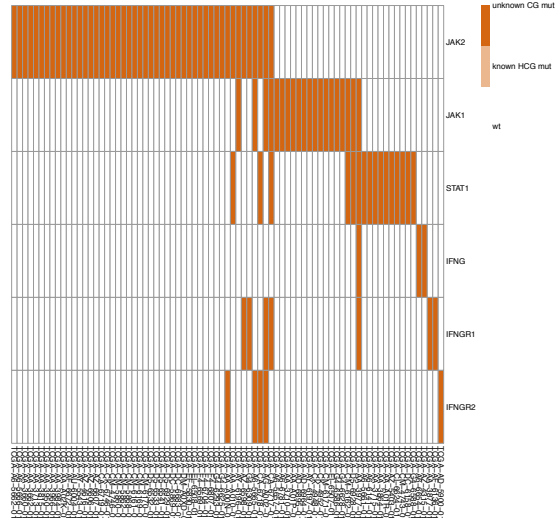
Signaling Pathway(JAK1 TYK2 STAT1 STAT2) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
Signaling Pathway(JAK1 TYK2 STAT3) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
Signaling Pathway(JAK1 TYK2 STAT1) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
FDR = 2.5%, FDR nod = 2.5%



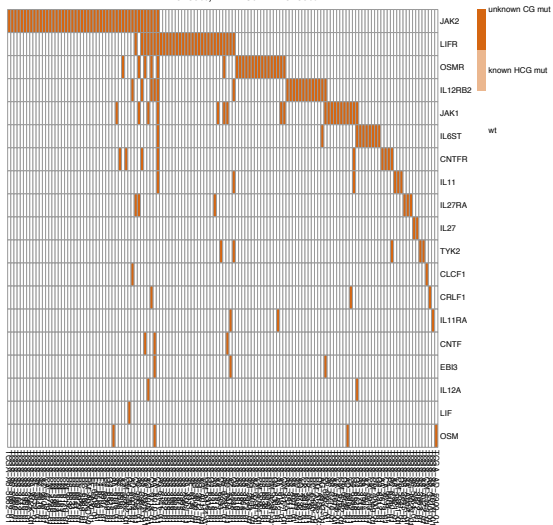
IFN Gamma Pathway
FDR = 1.9e-12%, FDR nod = 0.26%



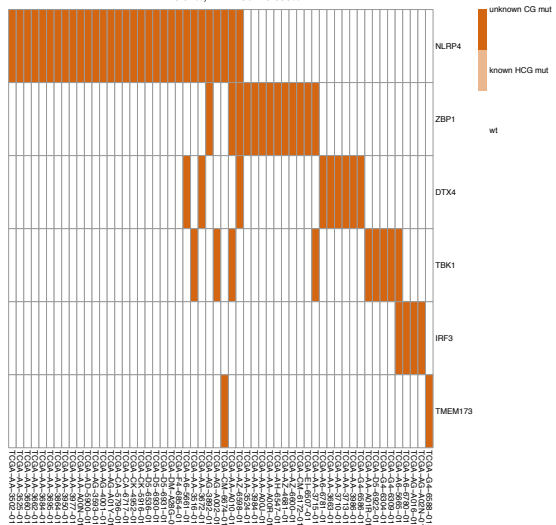
IFN Gamma Signaling Pathway(JAK1 JAK2 STAT1) (IFN Gamma Signaling(JAK1 JAK2 STAT1))
FDR = 2.5e-12%, FDR nod = 2.3e-11%



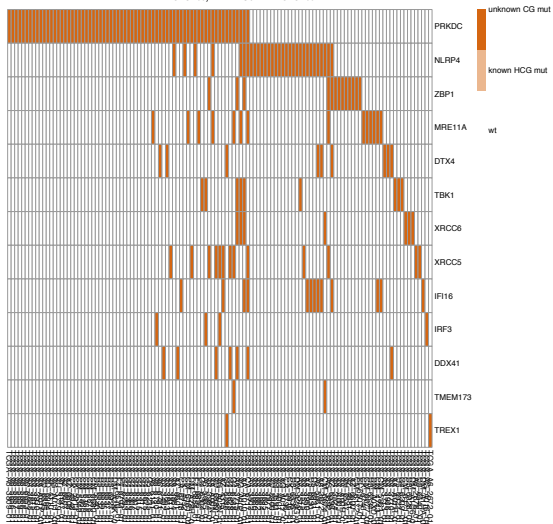
IL 6 Type Cytokine Receptor Ligand Interactions
 FDR = 1.4e-09%, FDR nod = 1.2e-09%



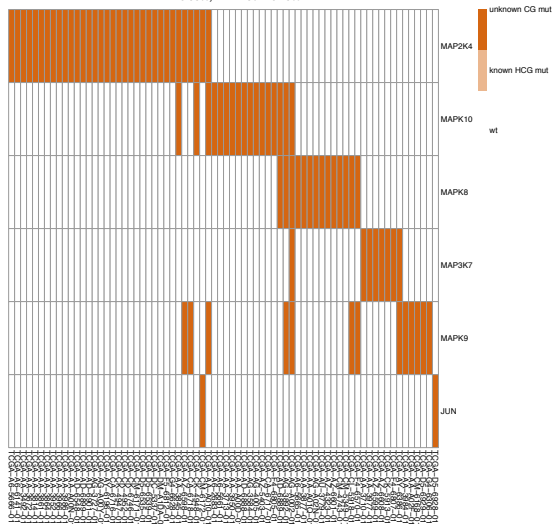
IRF3 Mediated Activation Of Type 1 IFN
 FDR = 0.04%, FDR nod = 0.056%



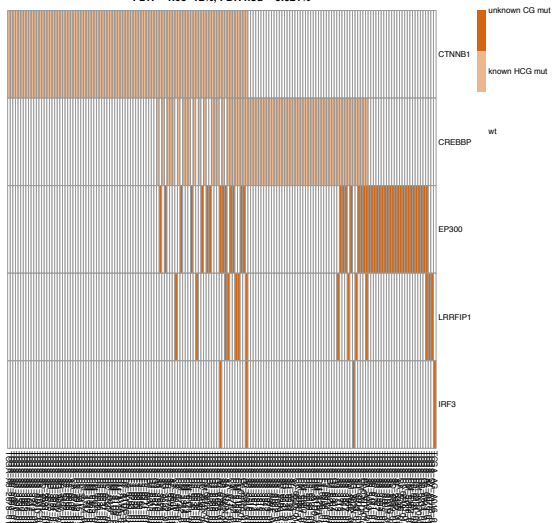
IRF3 Mediated Induction Of Type I IFN
 FDR = 2.2e-07%, FDR nod = 2.2e-07%



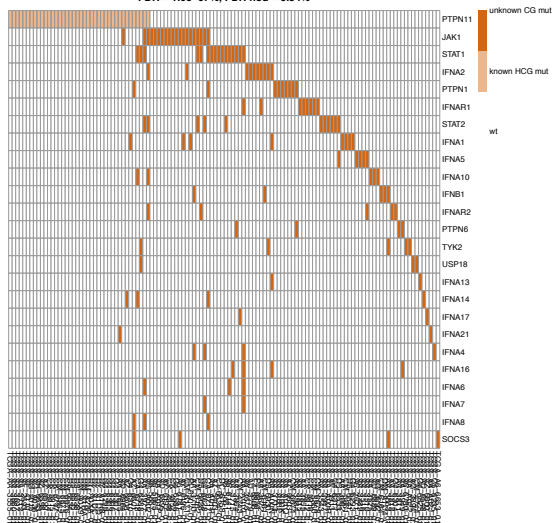
JNK Cascade (TGF Beta Signaling(through TAK1))
 FDR = 0.38%, FDR nod = 0.45%



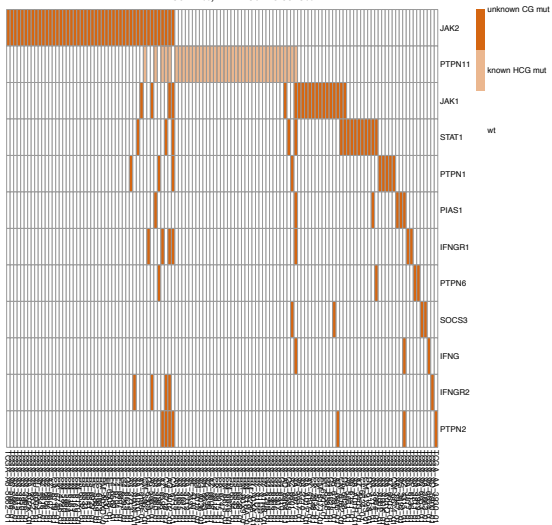
LRR FLII Interacting Protein 1 (LRRFIP1) Activates Type I IFN Production
 FDR = 1.9e-12%, FDR nod = 0.021%



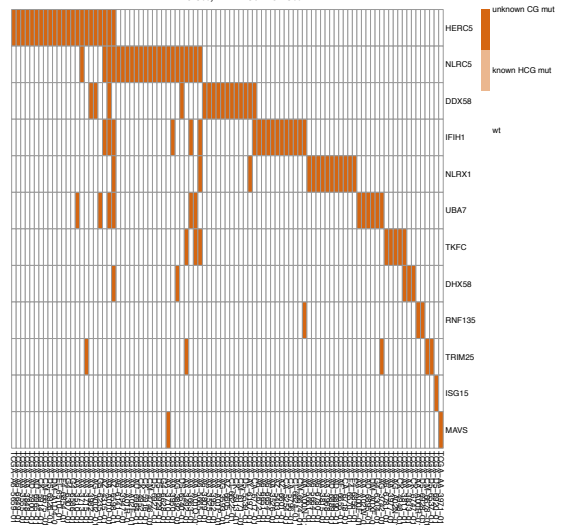
Regulation Of IFNA Signaling
 FDR = 1.9e-07%, FDR nod = 0.54%



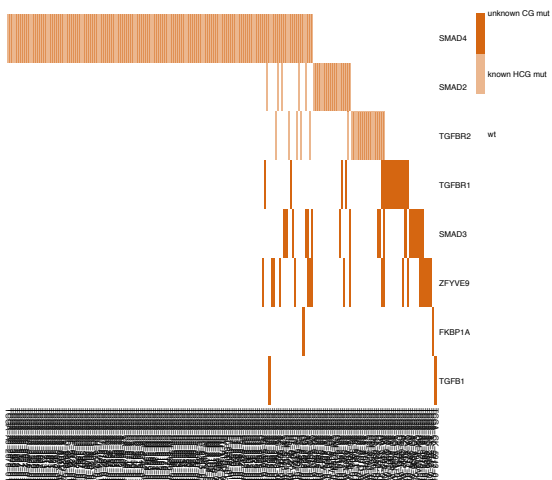
Regulation Of IFNG Signaling
 FDR = 1.5e-11%, FDR nod = 0.0025%



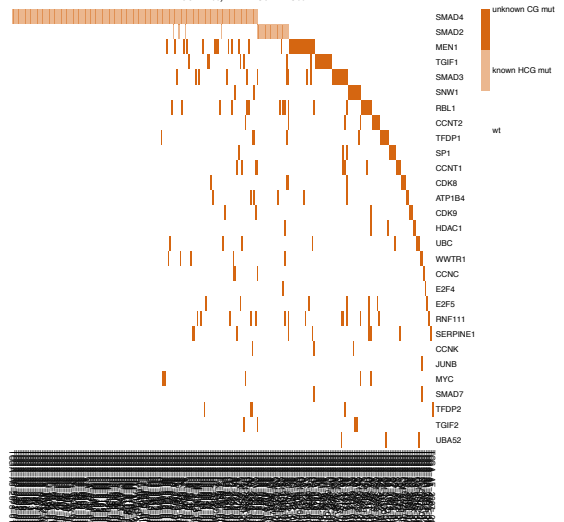
RIG I/MDA5 Mediated Induction Of IFN Alpha/beta Pathways
 FDR = 0.8%, FDR nod = 0.78%



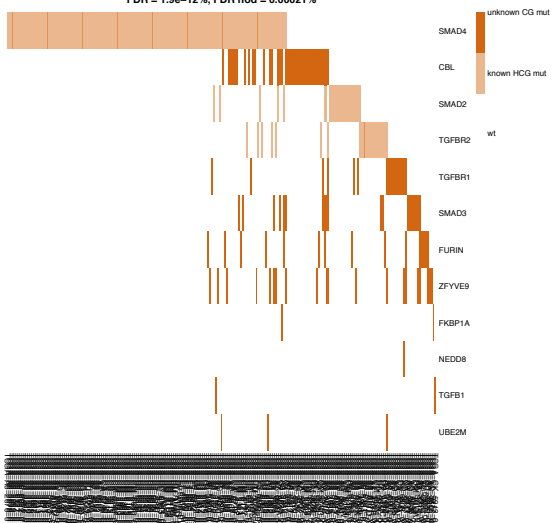
SMAD2/3 MH2 Domain Mutants In Cancer
SMAD2/3 Phosphorylation Motif Mutants In Cancer
TGFBR1 KD Mutants In Cancer
 FDR = 2.1e-12%, FDR nod = 1.9%



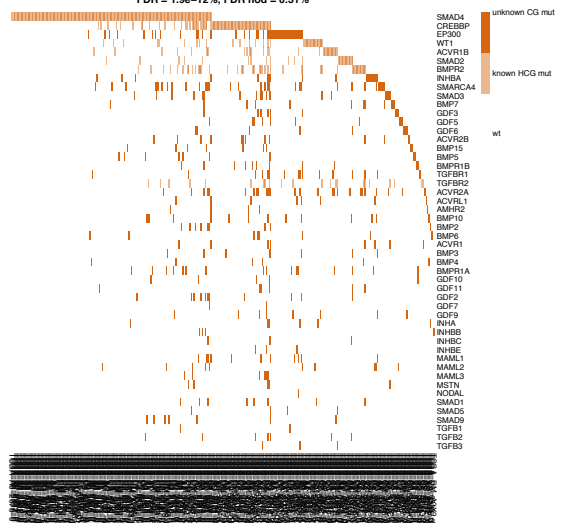
SMAD2/SMAD3:SMAD4 Heterotrimer Regulates Transcription
 FDR = 1.9e-12%, FDR nod = 2.5%



TGF Beta Receptor Signaling Activates SMADs
 FDR = 1.9e-12%, FDR nod = 0.00021%

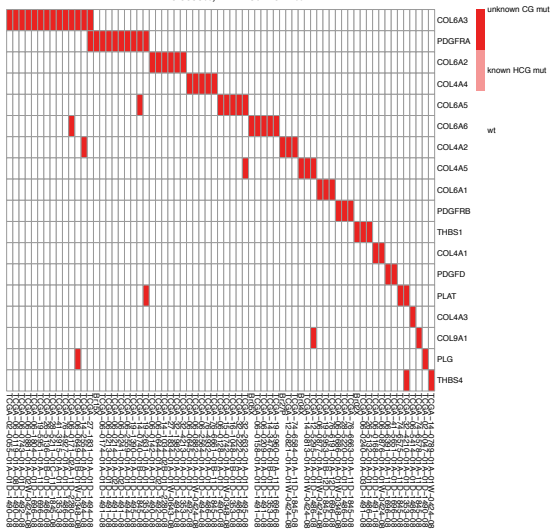


ta Super Family Signaling Pathway(canonical) (TGF Beta BMP Diagram(MolecularVariation))
 FDR = 1.9e-12%, FDR nod = 0.31%

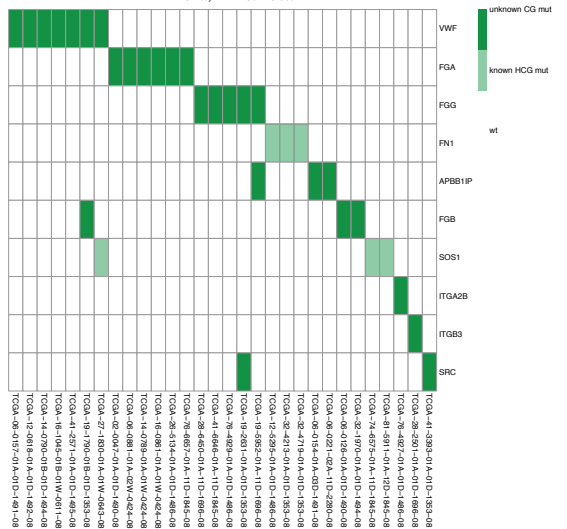


GBM

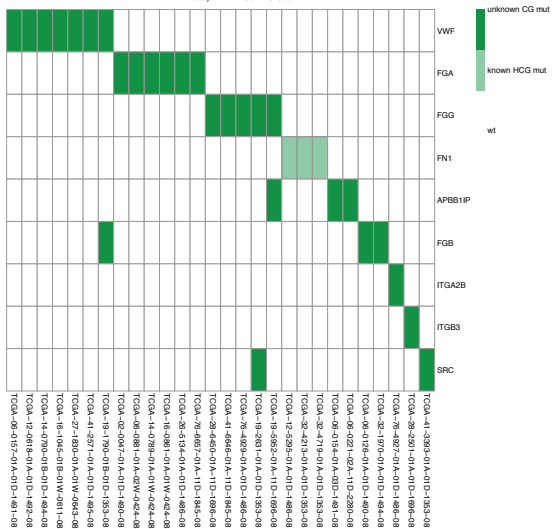
Signaling By PDGF
FDR = 0.0055%, FDR nod = 0.22%



GRB2:SOS Provides Linkage To MAPK Signaling For Integrins
FDR = 3.7%, FDR nod = 3.9%

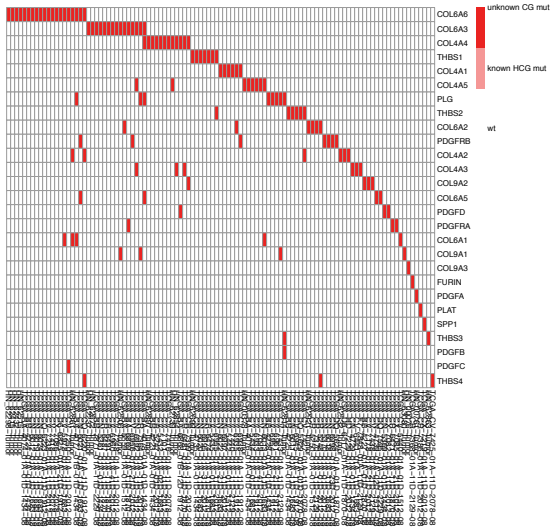


P130Cas Linkage To MAPK Signaling For Integrins
FDR = 1.9%, FDR nod = 3.9%

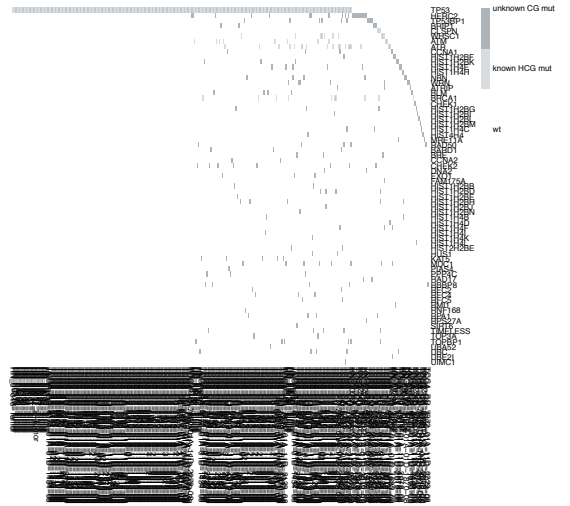


HSNC

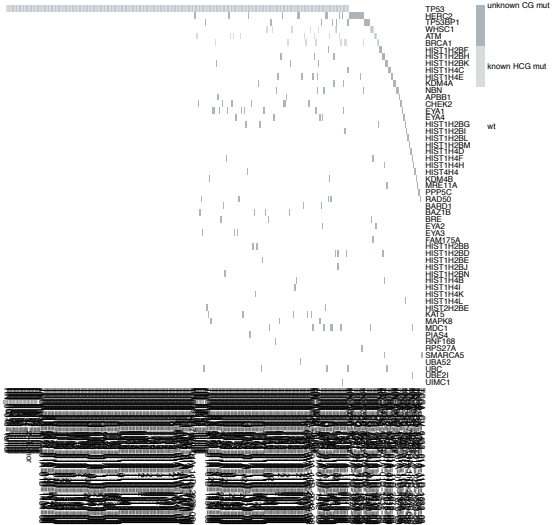
Signaling By PDGF
FDR = 0.65%, FDR nod = 3.1%



G2/M DNA Damage Checkpoint
Processing Of DNA Double Strand Break Ends
FDR = 1.9e-12%, FDR nod = 0.12%

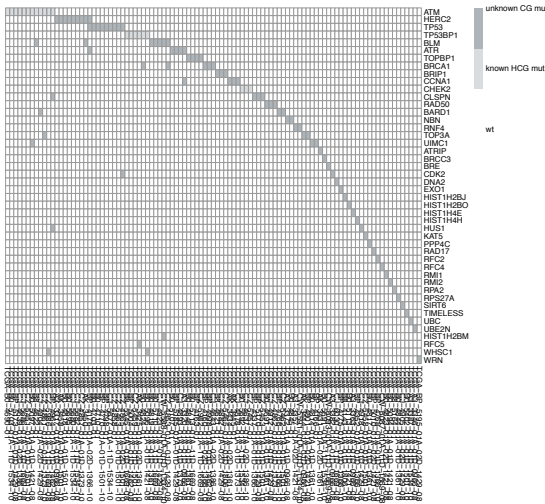


and ATM Mediated Phosphorylation Of Repair And Signaling Proteins At DNA Double Strand Breaks
FDR = 1.9e-12%, FDR nod = 0.028%

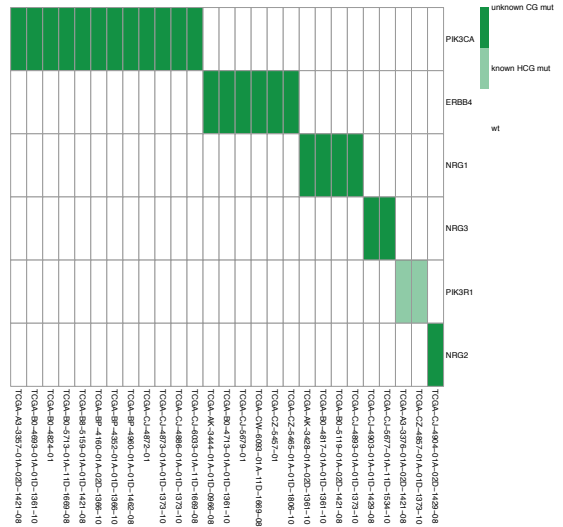


KIRC

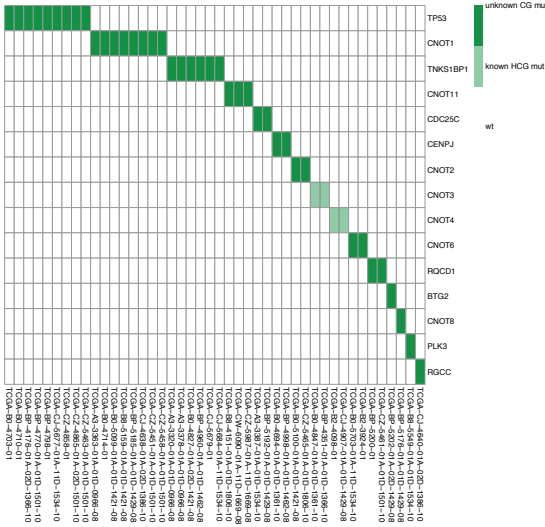
**G2/M DNA Damage Checkpoint
Processing Of DNA Double Strand Break Ends**
FDR = 0.97%, FDR nod = 2.1%



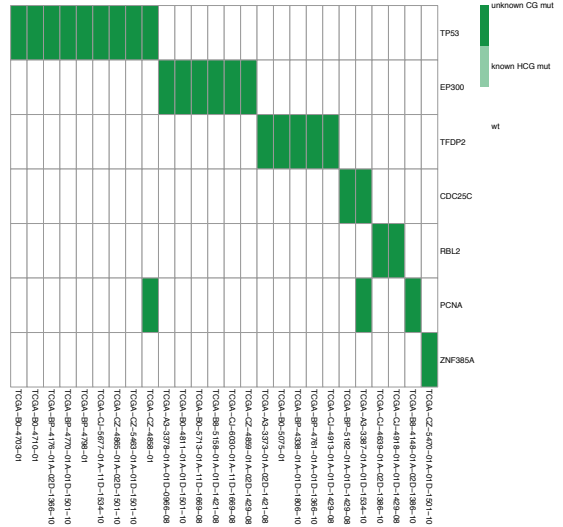
PI3K Events In ERBB4 Signaling
FDR = 4.8%, FDR nod = 3%



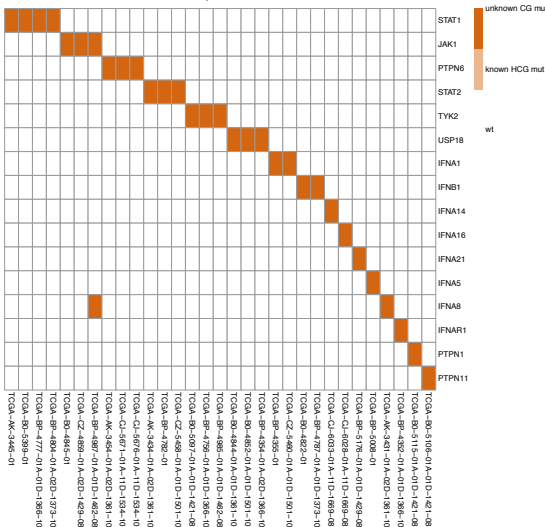
Transcription Of Additional Cell Cycle Genes Whose Exact Role In The P53 Pathway Remain Uncertain
FDR = 0.67%, FDR nod = 0.97%



TP53 Regulates Transcription Of Genes Involved In G2 Cell Cycle Arrest
FDR = 1%, FDR nod = 2.1%

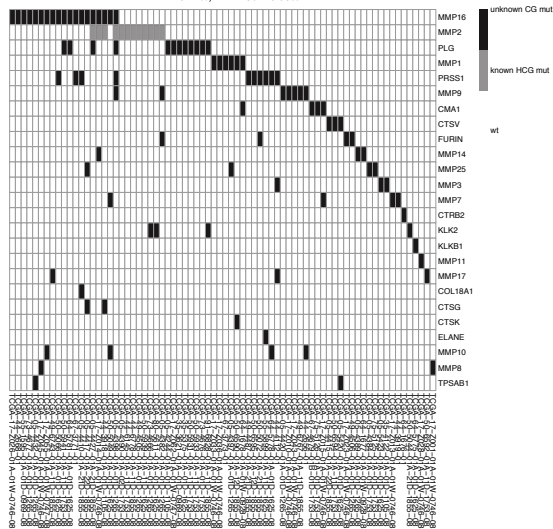


Regulation Of IFNA Signaling
FDR = 1.1%, FDR nod = 2.1%

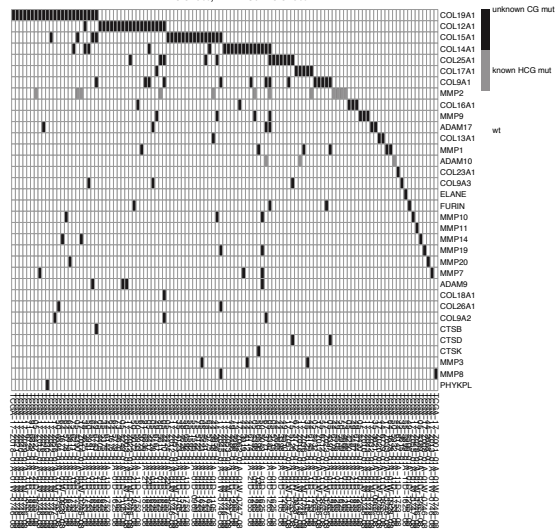


LUAD

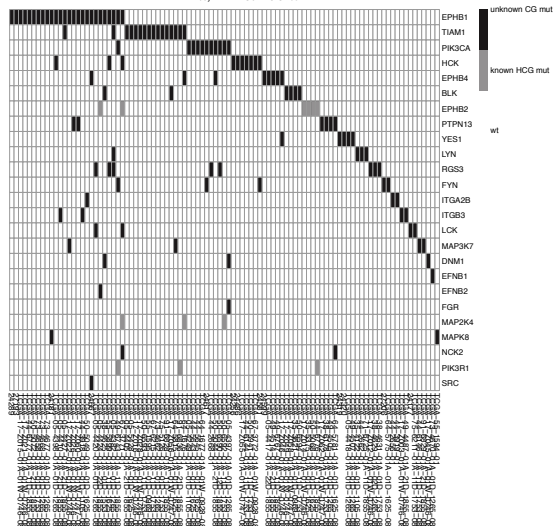
Activation Of Matrix Metalloproteinases
FDR = 0.11%, FDR nod = 0.93%



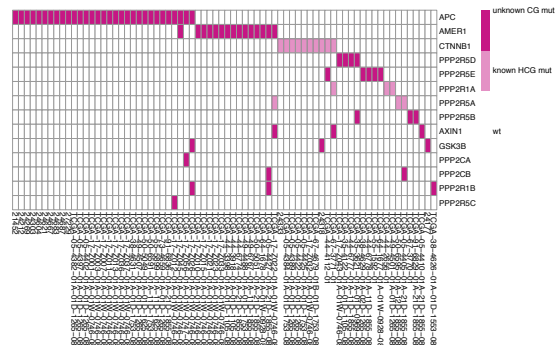
Collagen Degradation
FDR = 0.019%, FDR nod = 0.019%



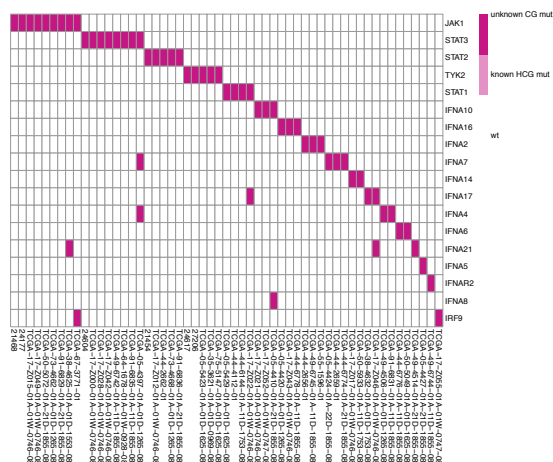
Ephrin B Reverse Signaling
FDR = 2.7%, FDR nod = 0.32%



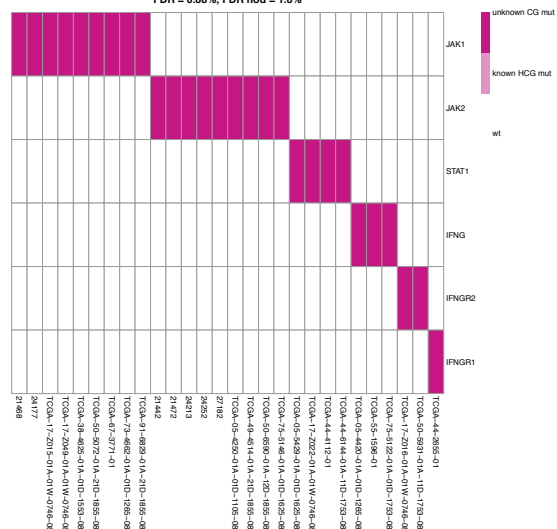
APC Truncation Mutants Have Impaired AXIN Binding
AXIN Missense Mutants Destabilize The Destruction Complex
Beta Catenin Phosphorylation Cascade
Misspliced GSK3beta Mutants Stabilize Beta Catenin
S33 Mutants Of Beta Catenin Aren't Phosphorylated
S37 Mutants Of Beta Catenin Aren't Phosphorylated
S45 Mutants Of Beta Catenin Aren't Phosphorylated
T41 Mutants Of Beta Catenin Aren't Phosphorylated
Truncations Of AMER1 Destabilize The Destruction Complex
FDR = 1.1%, FDR nod = 3.4%



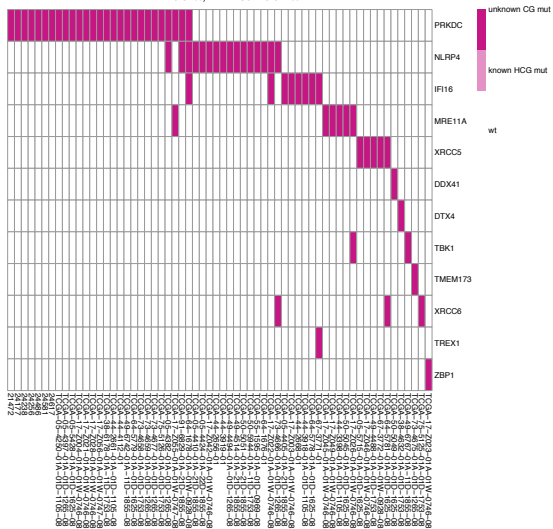
ignaling Pathway(JAK1 TYK2 STAT1 STAT2) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
ignaling Pathway(JAK1 TYK2 STAT1 STAT3) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
a Signaling Pathway(JAK1 TYK2 STAT1) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
a Signaling Pathway(JAK1 TYK2 STAT3) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
FDR = 0.0085%, FDR nod = 0.037%



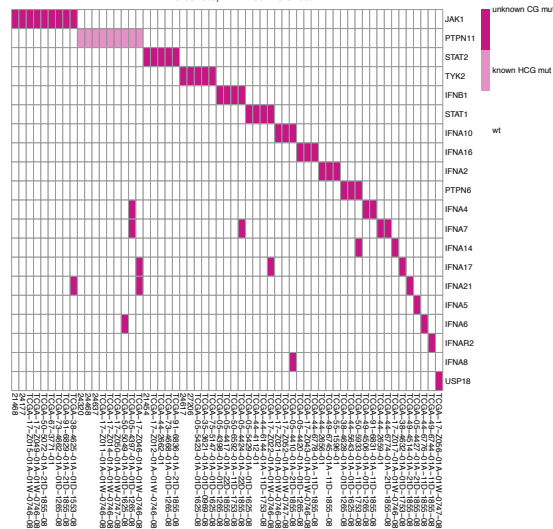
I Gamma Signaling Pathway(JAK1 JAK2 STAT1) (IFN Gamma Signaling(JAK1 JAK2 STAT1))
FDR = 0.88%, FDR nod = 1.8%



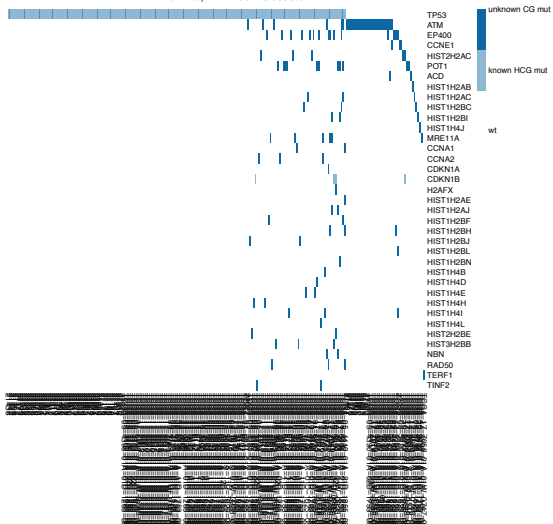
IRF3 Mediated Induction Of Type I IFN
FDR = 0.02%, FDR nod = 0.074%



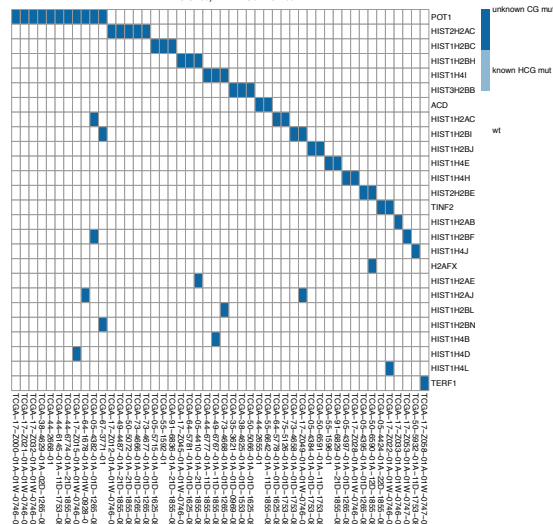
Regulation Of IFNA Signaling
FDR = 0.0013%, FDR nod = 0.019%



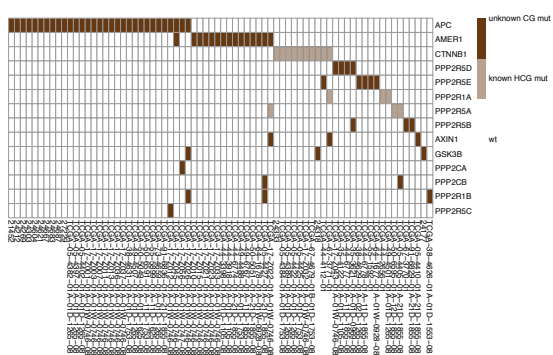
DNA Damage/Telomere Stress Induced Senescence
FDR = 2e-12%, FDR nod = 0.0053%



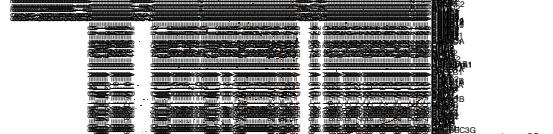
Packaging Of Telomere Ends
FDR = 0.07%, FDR nod = 0.2%



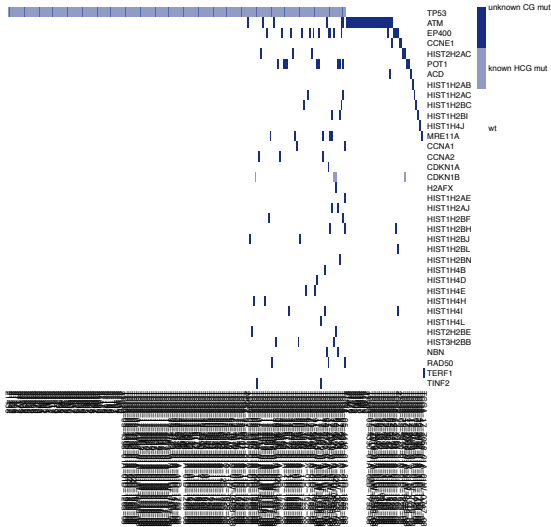
APC Truncation Mutants Have Impaired AXIN Binding
AXIN Missense Mutants Destabilize The Destruction Complex
Beta Catenin Phosphorylation Cascade
Misspliced GSK3beta Mutants Stabilize Beta Catenin
S33 Mutants Of Beta Catenin Aren't Phosphorylated
S37 Mutants Of Beta Catenin Aren't Phosphorylated
S45 Mutants Of Beta Catenin Aren't Phosphorylated
T41 Mutants Of Beta Catenin Aren't Phosphorylated
Truncations Of AMER1 Destabilize The Destruction Complex
FDR = 1.1%, FDR nod = 3.4%



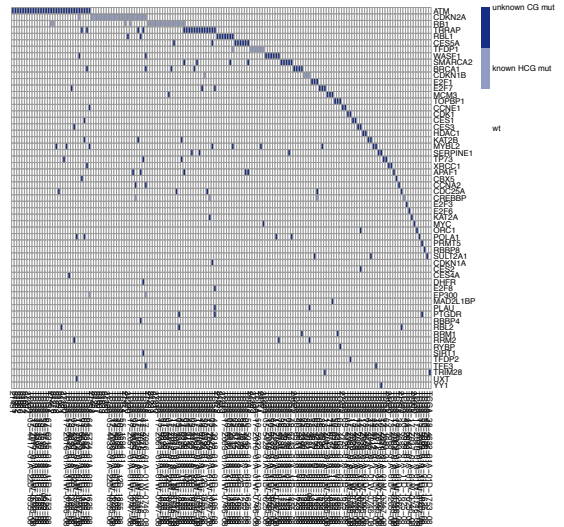
- AUF1 (hnRNP D0) Binds And Destabilizes MRNA
- Autodegradation Of The E3 Ubiquitin Ligase COP1
- CDK Mediated Phosphorylation And Removal Of Cdc6
- CDT1 Association With The CDC6:ORC:origin Complex
- Cross Presentation Of Soluble Exogenous Antigens (endosomes)
- Dectin 1 Mediated Noncanonical NF KB Signaling
- Degradation Of AXIN
- Degradation Of DVL
- Degradation Of GLI1 By The Proteasome
- Degradation Of GLI2 By The Proteasome
- G2/M Checkpoints
- GLI3 Is Processed To GLI3R By The Proteasome
- Hedgehog Ligand Biogenesis
- Hh Mutants That Don't Undergo Autocatalytic Processing Are Degraded By ERAD
- NIK >noncanonical NF KB Signaling
- Orc1 Removal From Chromatin
- Regulation Of Activated PAK 2p34 By Proteasome Mediated Degradation
- Regulation Of Ornithine Decarboxylase (ODC)
- SCF Beta TrCP Mediated Degradation Of Emi1
- The Role Of GTSE1 In G2/M Progression After G2 Checkpoint
- Ubiquitin Dependent Degradation Of Cyclin D1
- Ubiquitin Mediated Degradation Of Phosphorylated Cdc25A



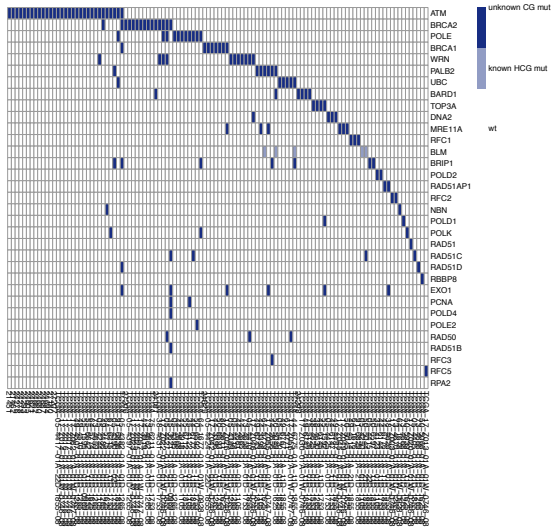
DNA Damage/Telomere Stress Induced Senescence
 FDR = 2e-12%, FDR nod = 0.0053%



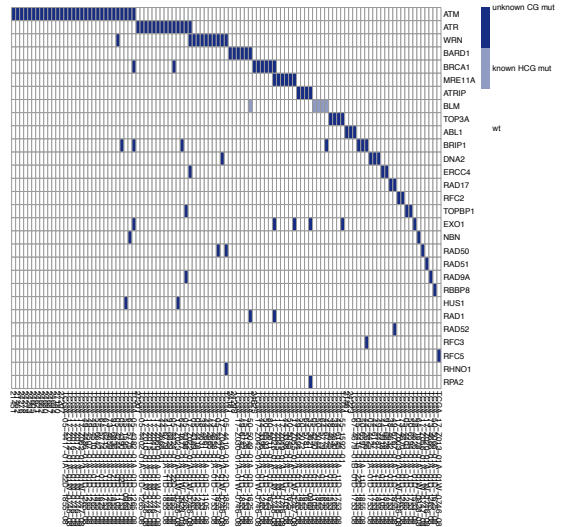
E2F Transcription Factor Network
 FDR = 9.5e-07%, FDR nod = 1.1%



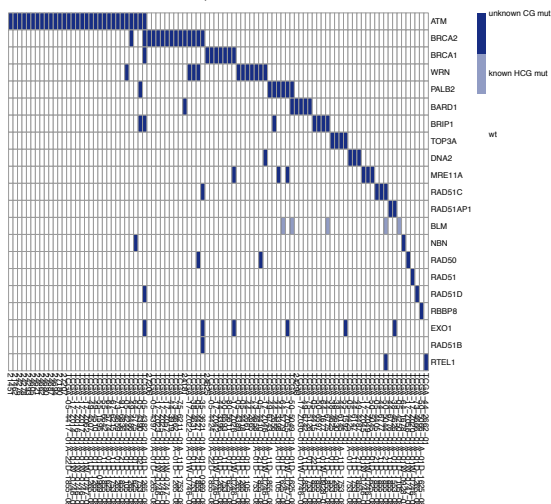
HDR Through Homologous Recombination (HRR)
 FDR = 1.2%, FDR nod = 1.3%



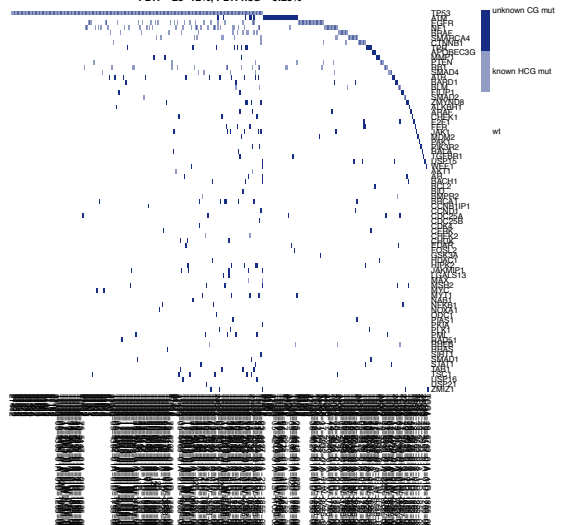
HDR Through Single Strand Annealing (SSA)
 FDR = 0.14%, FDR nod = 0.41%



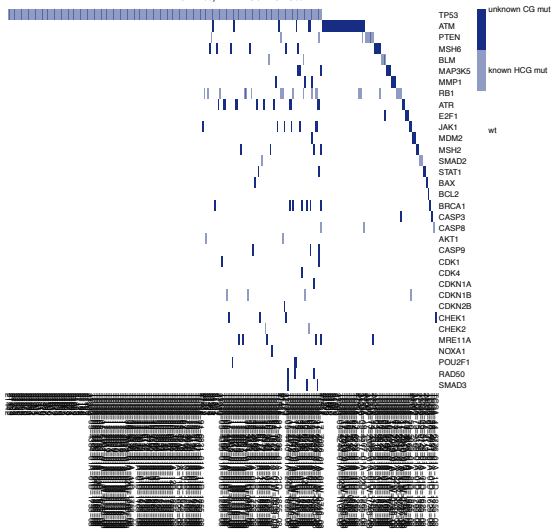
**Homologous DNA Pairing And Strand Exchange
 resolution Of D Loop Structures Through Synthesis Dependent Strand Annealing (SDSA)**
 FDR = 1.1%, FDR nod = 1.1%



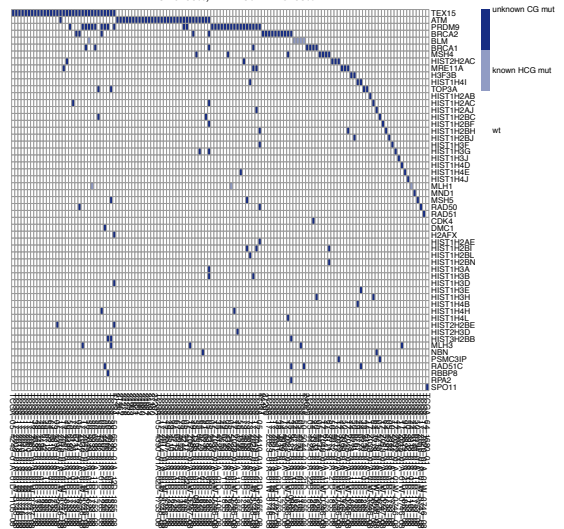
Integrated Breast Cancer Pathway
 FDR = 2e-12%, FDR nod = 0.23%



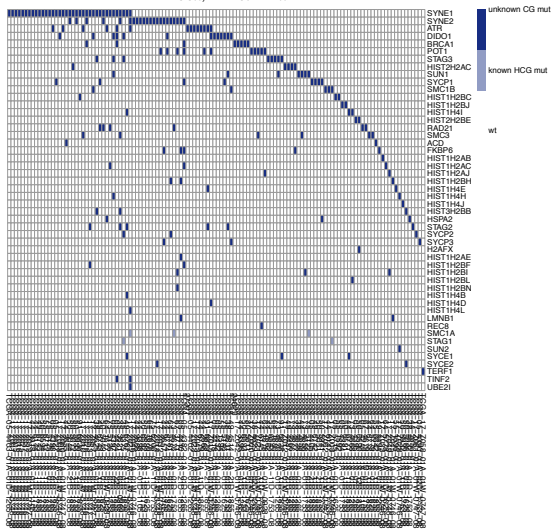
Integrated Cancer Pathway
FDR = 2e-12%, FDR nod = 0.23%



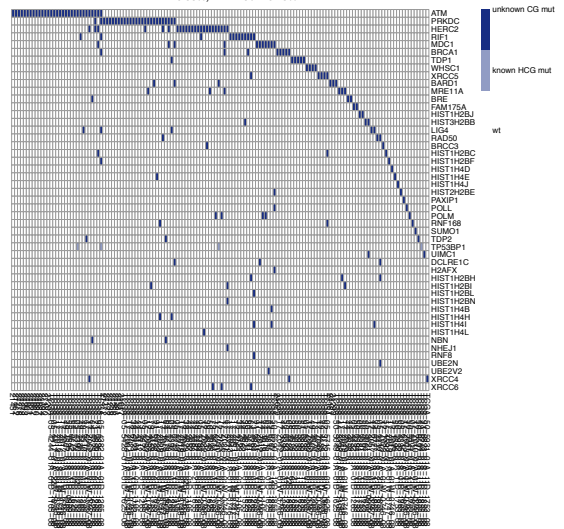
Meiotic Recombination
FDR = 8.2e-06%, FDR nod = 2.7e-05%



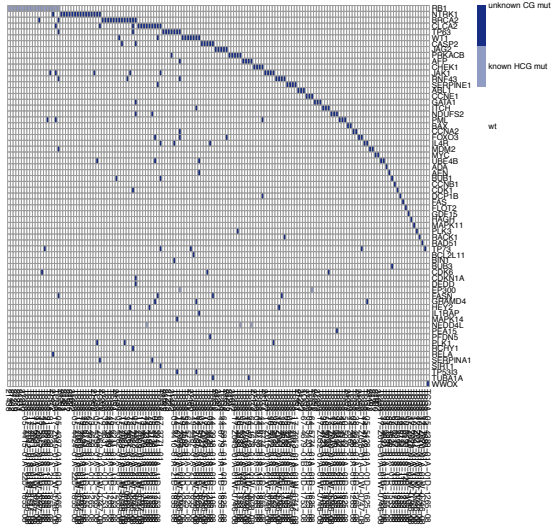
Meiotic Synapsis
FDR = 5.3%, FDR nod = 1.4%



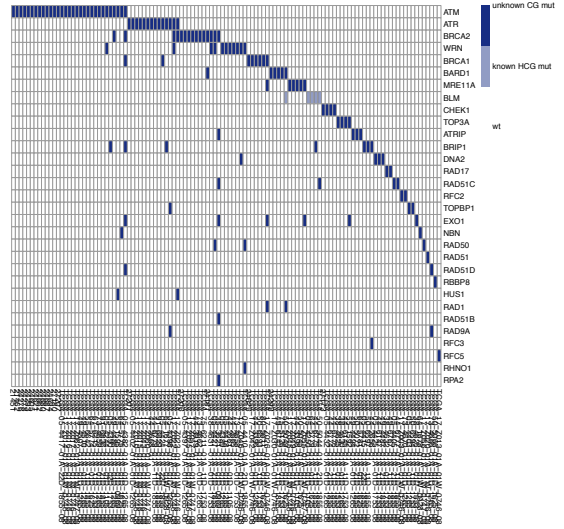
Nonhomologous End Joining (NHEJ)
FDR = 0.35%, FDR nod = 0.23%



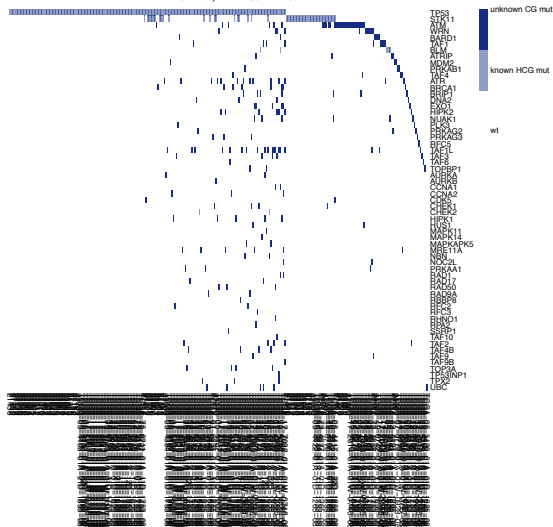
P73 Transcription Factor Network
FDR = 0.11%, FDR nod = 1.2%



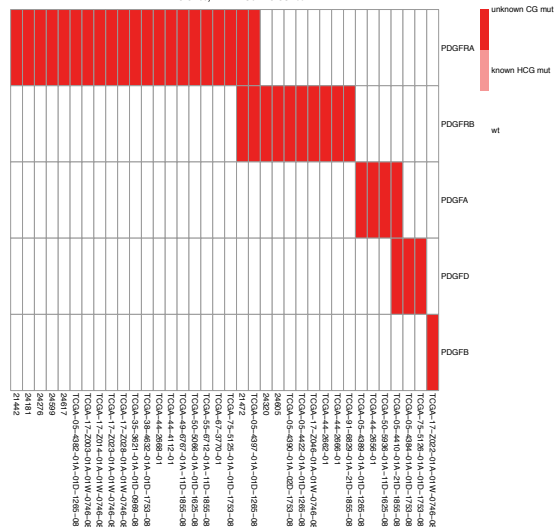
Presynaptic Phase Of Homologous DNA Pairing And Strand Exchange
FDR = 0.13%, FDR nod = 0.23%



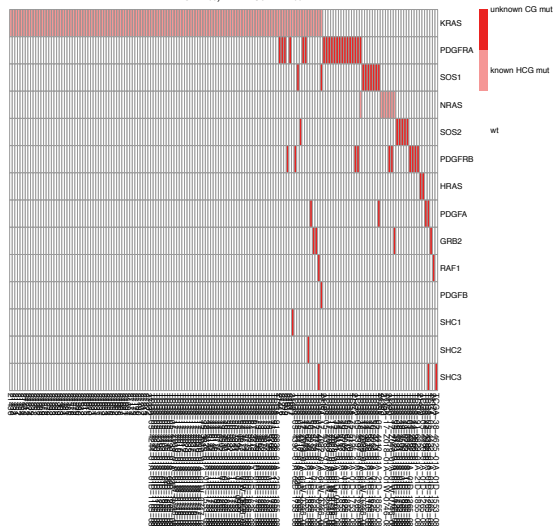
Regulation Of TP53 Activity Through Phosphorylation
FDR = 2e-12%, FDR nod = 1.1%



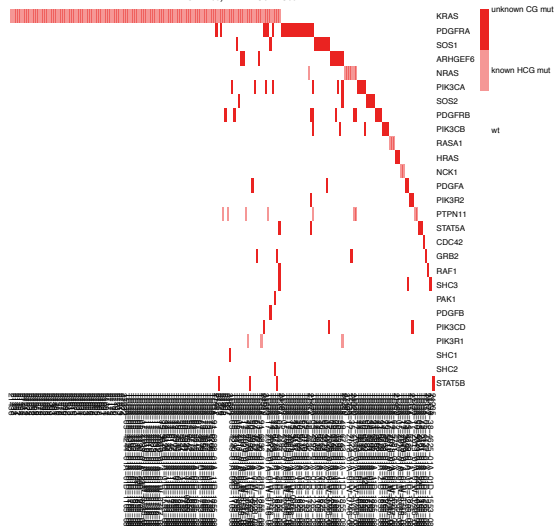
PDGF Receptor Signaling Network
FDR = 0.02%, FDR nod = 0.081%



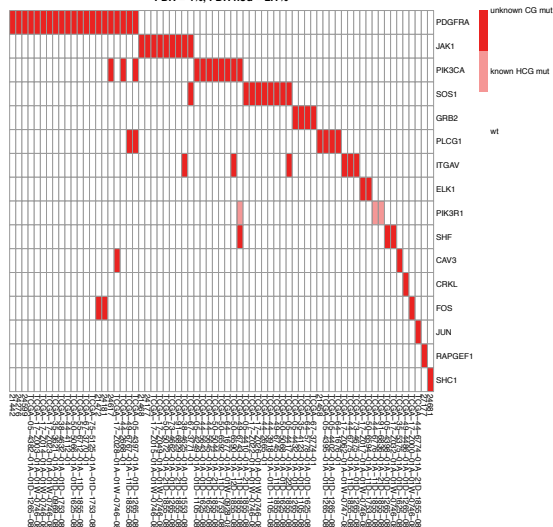
PDGF Signaling Pathway (PDGF Signaling Pathway)
FDR = 2e-12%, FDR nod = 2.2%



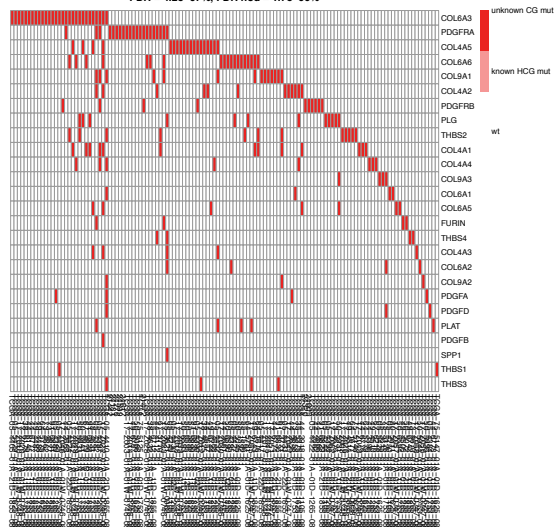
PDGF Signaling Pathway (Mammal) (PDGF Signaling Pathway)
FDR = 2e-12%, FDR nod = 5%



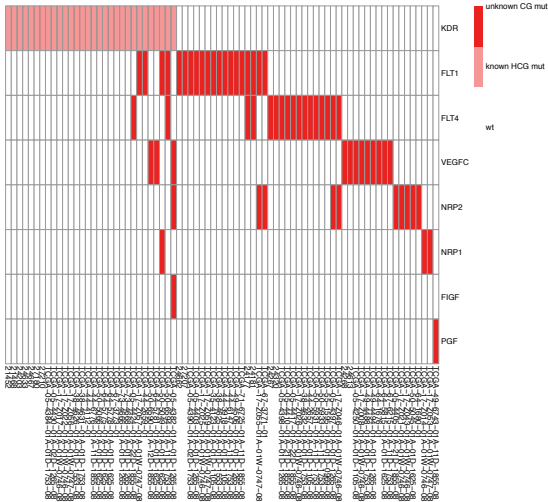
PDGFR Alpha Signaling Pathway
FDR = 4%, FDR nod = 2.1%



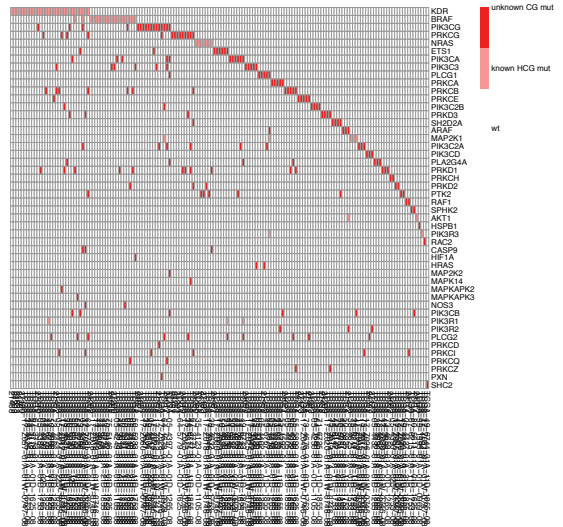
Signaling By PDGF
FDR = 4.2e-07%, FDR nod = 1.7e-06%



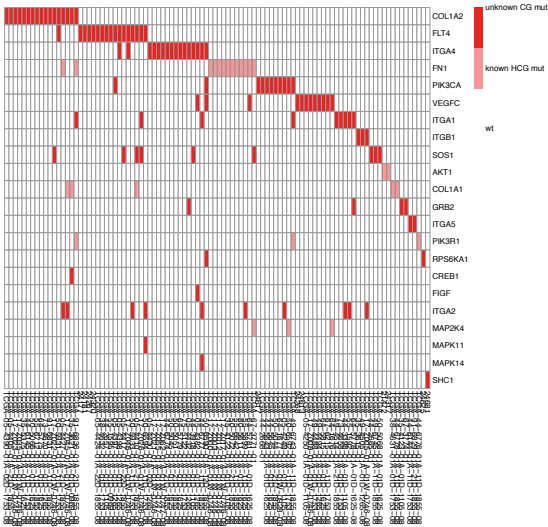
VEGF And VEGFR Signaling Network
VEGF Binds To VEGFR Leading To Receptor Dimerization
FDR = 1.7e-08%, FDR nod = 0.2%



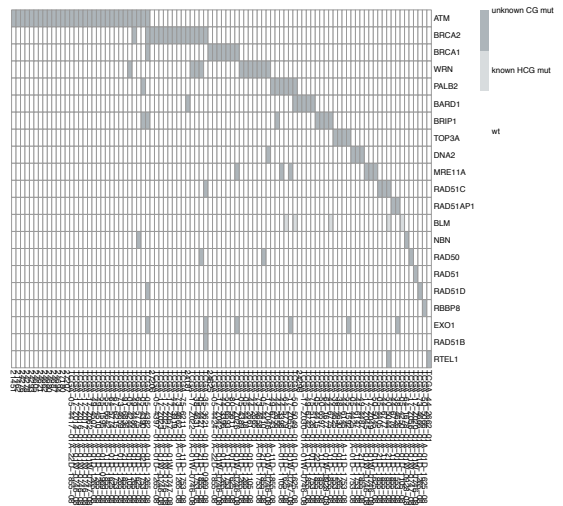
VEGF Signaling Pathway
FDR = 9e-06%, FDR nod = 0.14%



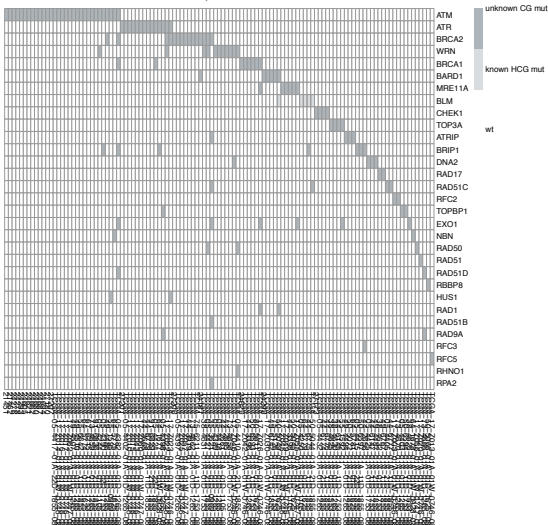
VEGFR3 Signaling In Lymphatic Endothelium
FDR = 5.6%, FDR nod = 0.73%



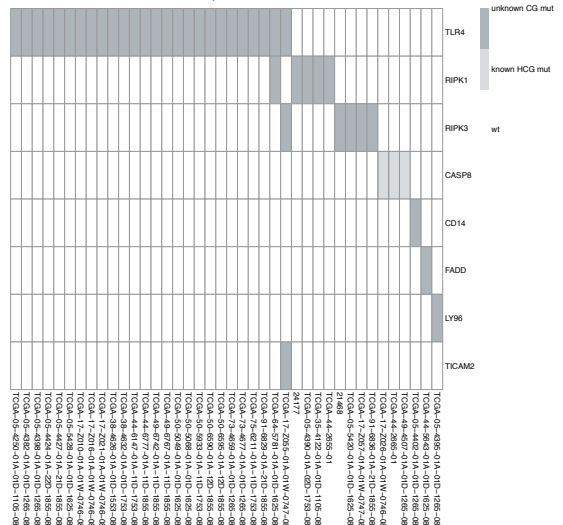
Homologous DNA Pairing And Strand Exchange
evolution Of D Loop Structures Through Synthesis Dependent Strand Annealing (SDSA)
FDR = 1.1%, FDR nod = 1.1%



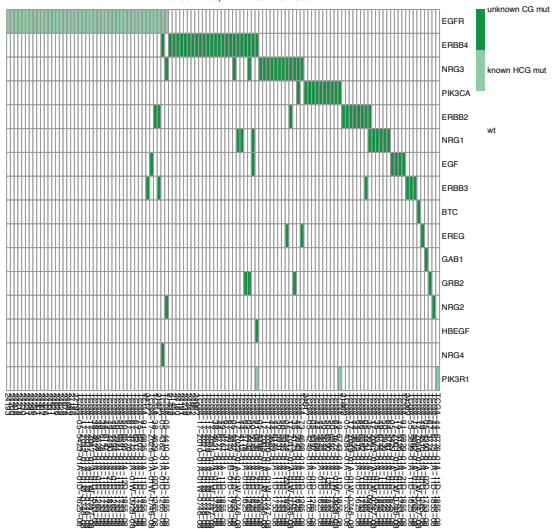
Presynaptic Phase Of Homologous DNA Pairing And Strand Exchange
FDR = 0.13%, FDR nod = 0.23%



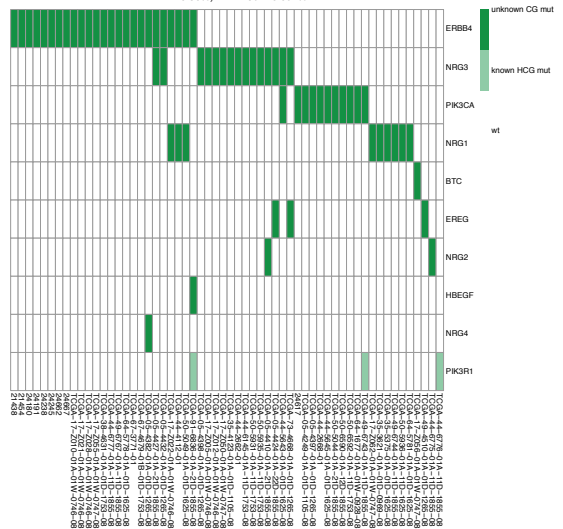
TRIF Mediated Programmed Cell Death
FDR = 0.00019%, FDR nod = 2.7e-05%



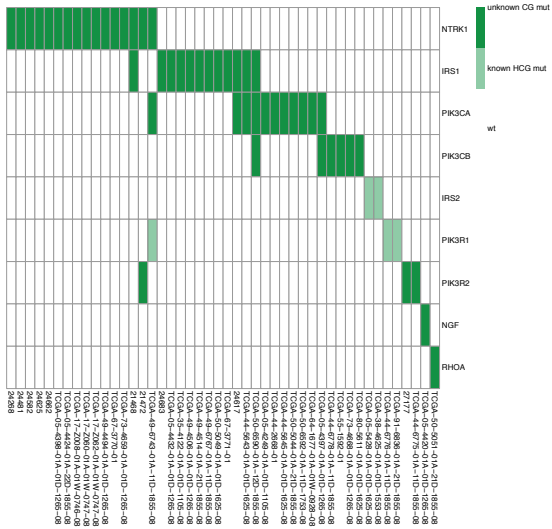
PI3K Events In ERBB2 Signaling
FDR = 9.6e-12%, FDR nod = 0.18%



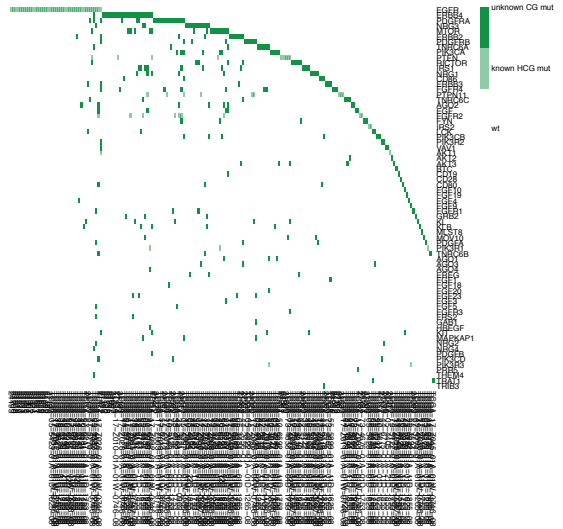
PI3K Events In ERBB4 Signaling
FDR = 0.56%, FDR nod = 0.091%



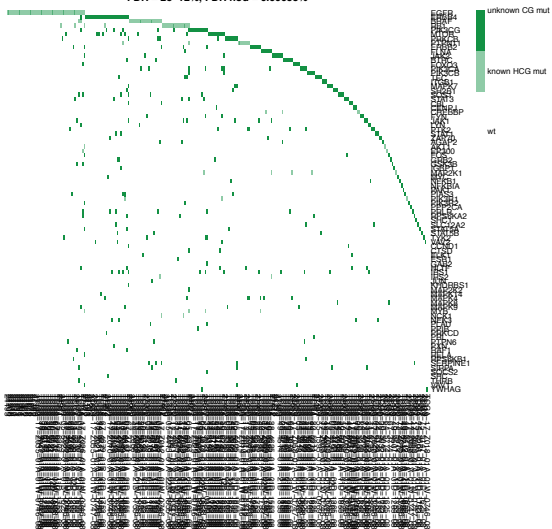
PI3K/AKT Activation
FDR = 5.5%, FDR nod = 0.23%



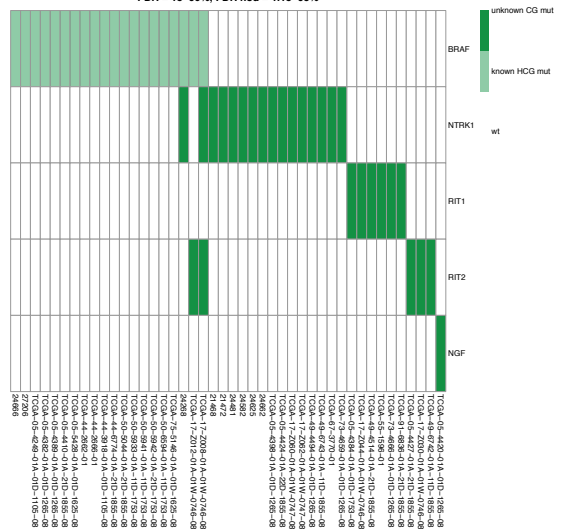
PIP3 Activates AKT Signaling
FDR = 1.6e-10%, FDR nod = 1.4%



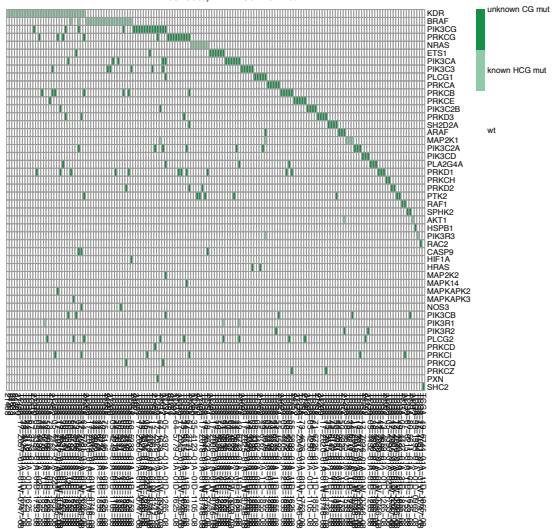
Prolactin
FDR = 2e-12%, FDR nod = 0.00055%



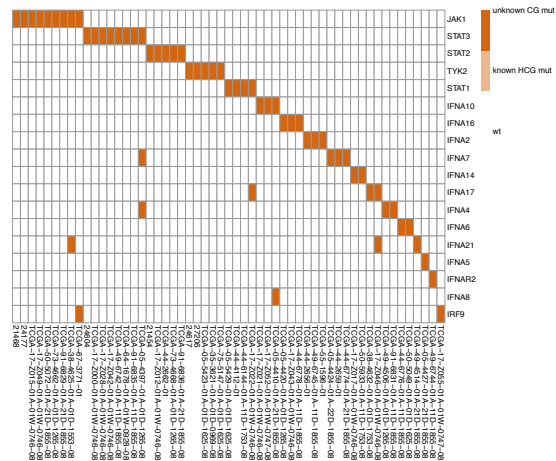
Signaling To P38 Via RIT And RIN
FDR = 1e-09%, FDR nod = 1.1e-05%



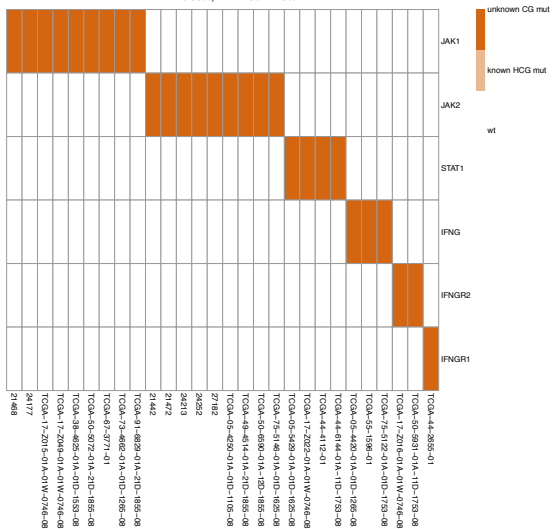
VEGF Signaling Pathway
FDR = 9e-06%, FDR nod = 0.14%



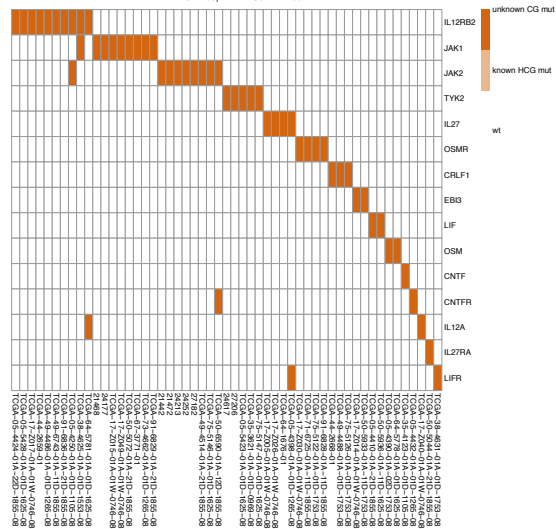
**ignaling Pathway(JAK1 TYK2 STAT1 STAT2) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
ignaling Pathway(JAK1 TYK2 STAT1 STAT3) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
ia Signaling Pathway(JAK1 TYK2 STAT1) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))
ia Signaling Pathway(JAK1 TYK2 STAT3) (IFN Alpha Signaling(JAK1 TYK2 STAT1 STAT2 STAT3))**
FDR = 0.0085%, FDR nod = 0.037%



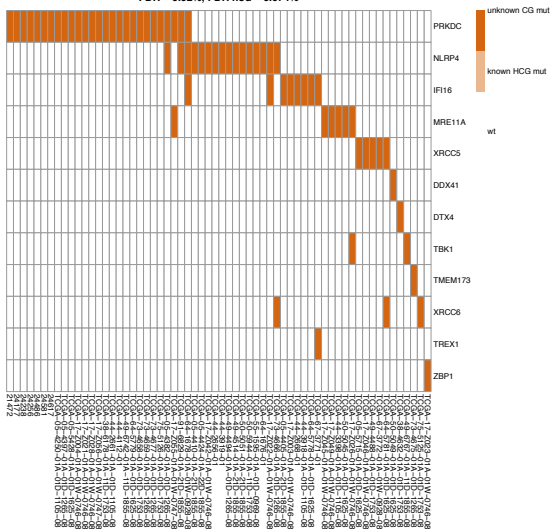
Gamma Signaling Pathway(JAK1 JAK2 STAT1) (IFN Gamma Signaling(JAK1 JAK2 STAT1))
FDR = 0.88%, FDR nod = 1.8%



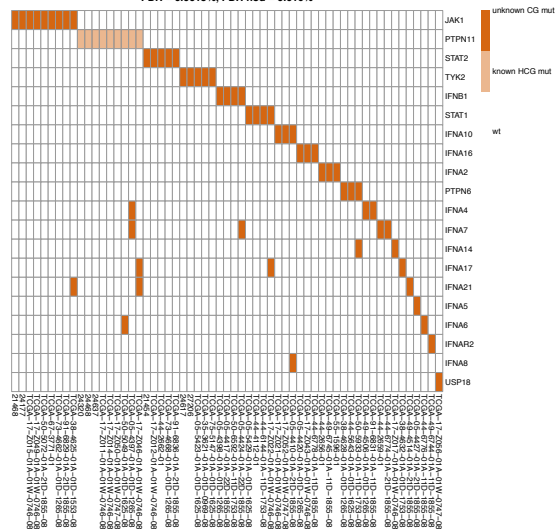
IL 6 Type Cytokine Receptor Ligand Interactions
FDR = 0.74%, FDR nod = 1.4%



IRF3 Mediated Induction of Type I IFN
FDR = 0.02%, FDR nod = 0.074%



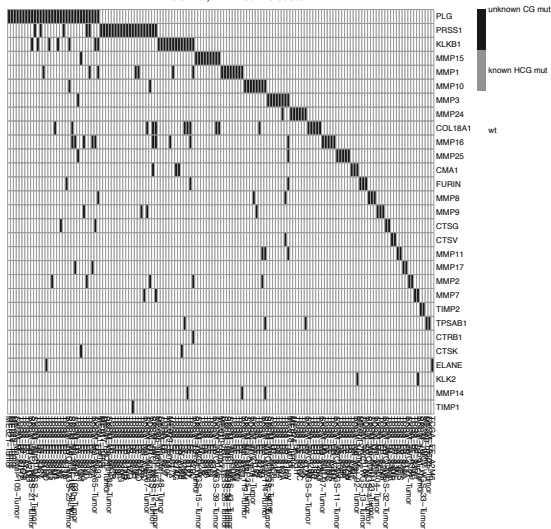
Regulation of IFN Alpha Signaling
FDR = 0.0013%, FDR nod = 0.019%



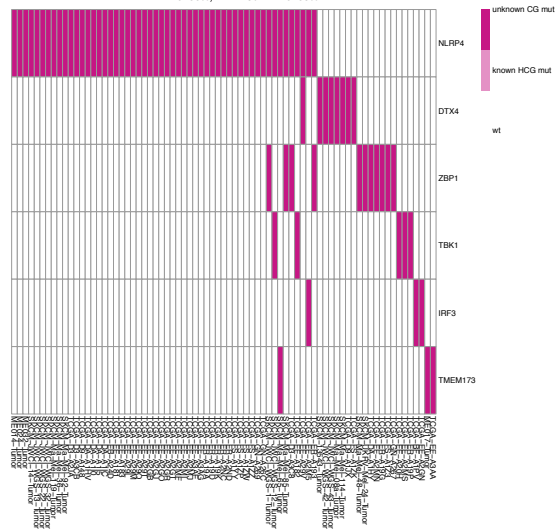
PRAD

SKCM

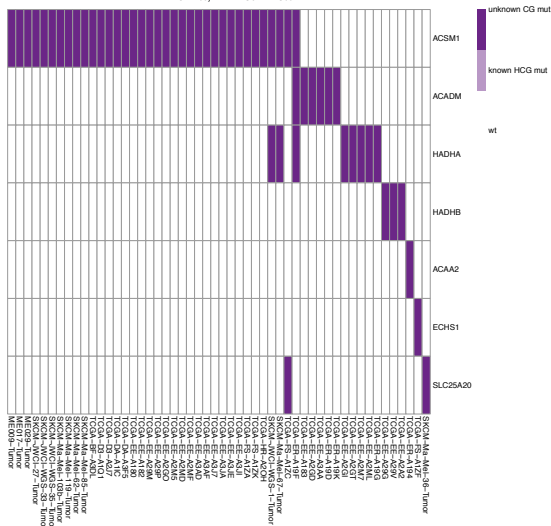
Activation Of Matrix Metalloproteinases
FDR = 0.022%, FDR nod = 0.093%



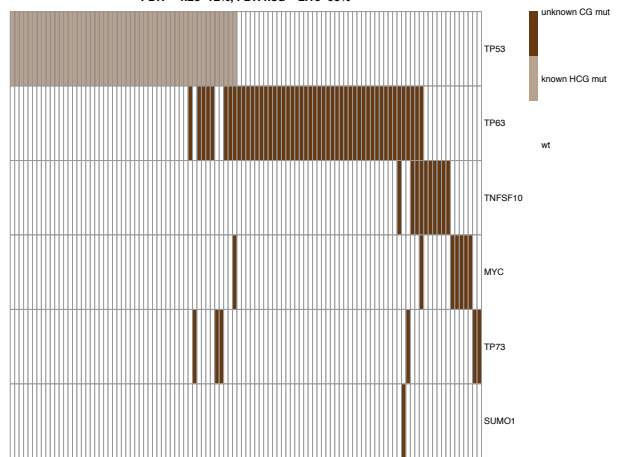
IRF3 Mediated Activation Of Type 1 IFN
FDR = 1.2e-06%, FDR nod = 1.2e-05%



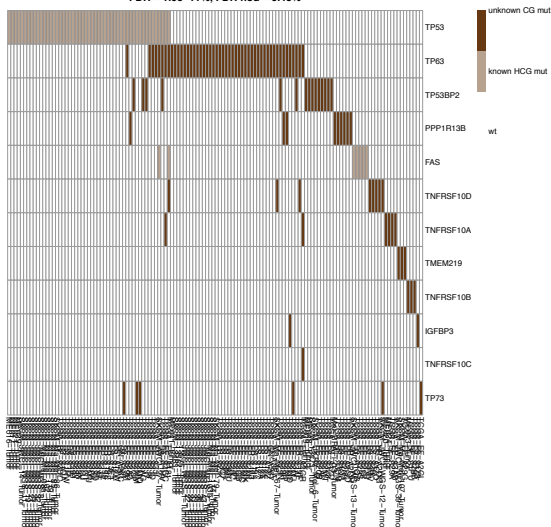
Mitochondrial Beta Oxidation Of Medium Chain Saturated Fatty Acids
FDR = 0.42%, FDR nod = 1.5%



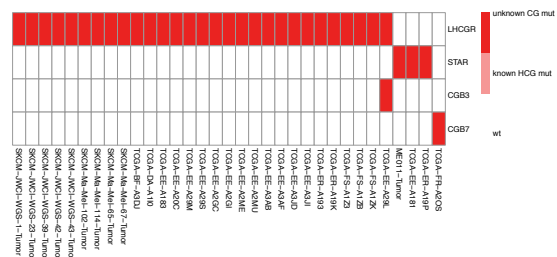
TP53 Network
FDR = 4.2e-12%, FDR nod = 2.1e-05%



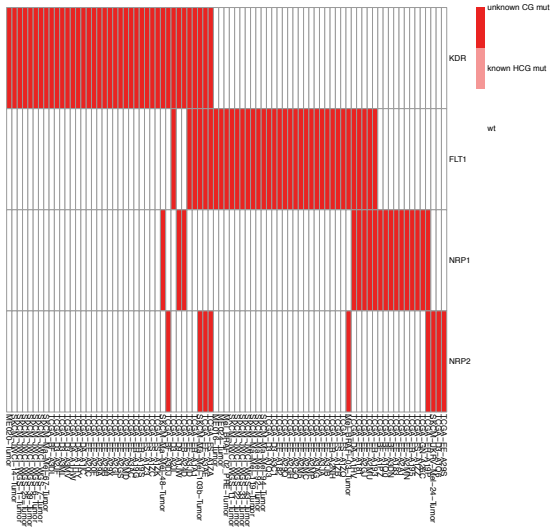
TP53 Regulates Transcription Of Death Receptors And Ligands
FDR = 1.6e-11%, FDR nod = 0.43%



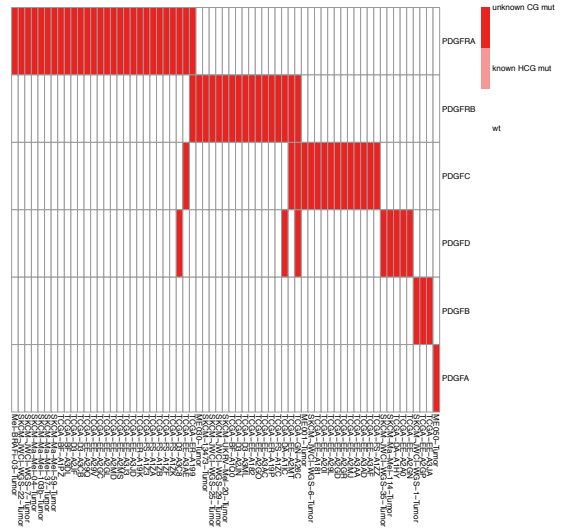
[CGB Protein Results In Increased Activity Of LHCGR Protein]
 e Results In Decreased Activity Of PTGS2 Protein] Inhibits The Reaction [CGB Protein Results In Increased Chen
 [3, 2 F]quinazoline 1.3 Diamine Binds To F2R Protein] Promotes The Reaction [CGB Protein Results In Increased I
 ne Inhibits The Reaction [CGB Protein Results In Increased Chemical Synthesis Of Androgens]
 itrazine Inhibits The Reaction [CGB Protein Results In Increased Secretion Of Cyclic AMP]
 forsin Promotes The Reaction [CGB Protein Results In Increased Abundance Of Cyclic AMP]
 Reaction [[Gonadotropins, Equine Co Treated With CGB Protein] Results In Increased Abundance Of Progesterone
 inhibits The Reaction [[CGB Protein Co Treated With Colforsin] Results In Increased Abundance Of Cyclic AMP]
 Protein Promotes The Reaction [CGB Protein Results In Increased Abundance Of Progesterone]
 e Metabolite Inhibits The Reaction [CGB Protein Results In Increased Abundance Of Testosterone]
 se Chloride Inhibits The Reaction [CGB Protein Results In Increased Expression Of STAR Protein]
 terone Promotes The Reaction [CGB Protein Results In Increased Expression Of VEGFA MRNA]
 one Enanthate Inhibits The Reaction [CGB Protein Results In Increased Abundance Of Androgens]
 FDR = 0.19%, FDR nod = 0.72%



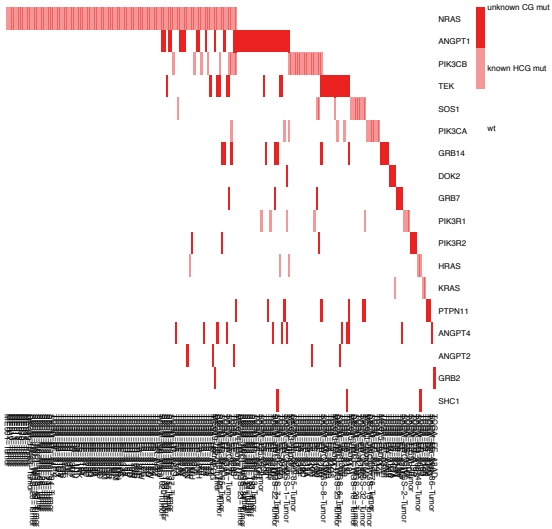
Neurophilin Interactions With VEGF And VEGFR
FDR = 0.05%, FDR nod = 0.21%



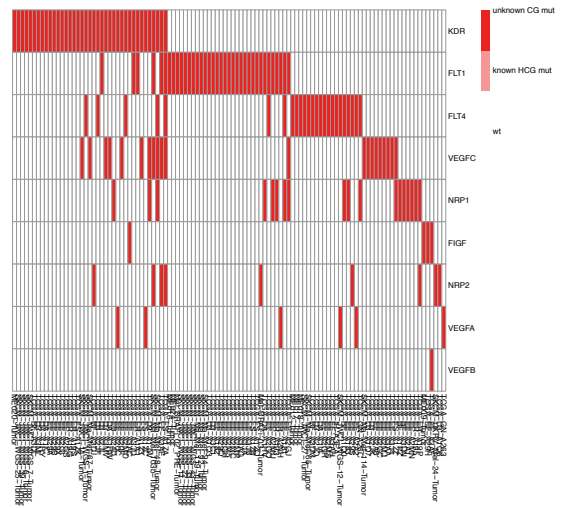
PDGF Receptor Signaling Network
FDR = 0.82%, FDR nod = 2.7%



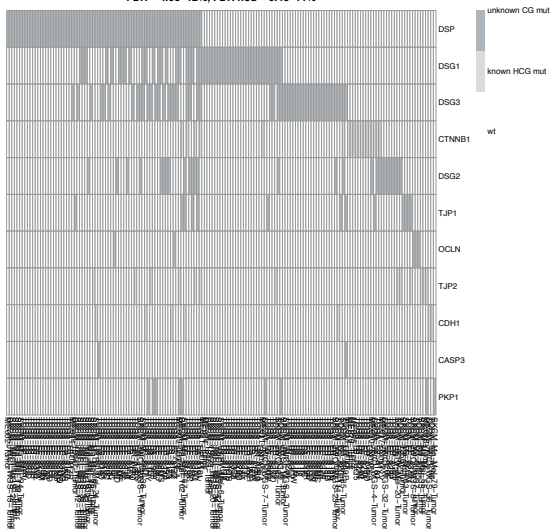
Tie2 Signaling
FDR = 5.6e-12%, FDR nod = 3.7%



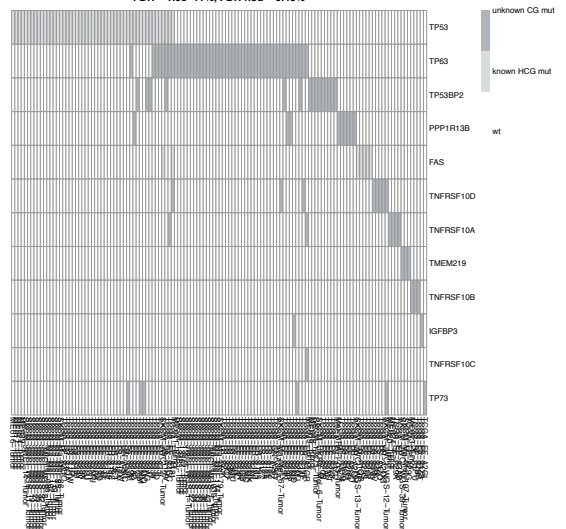
VEGF And VEGFR Signaling Network
VEGF Binds To VEGFR Leading To Receptor Dimerization
FDR = 0.71%, FDR nod = 2.3%



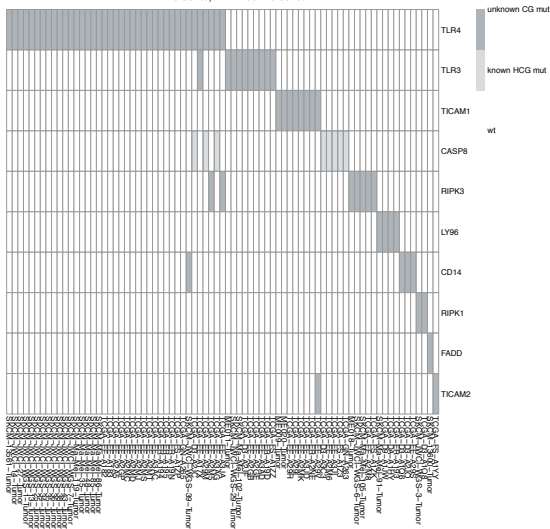
Apoptotic Cleavage Of Cell Adhesion Proteins
FDR = 4.6e-12%, FDR nod = 9.4e-11%



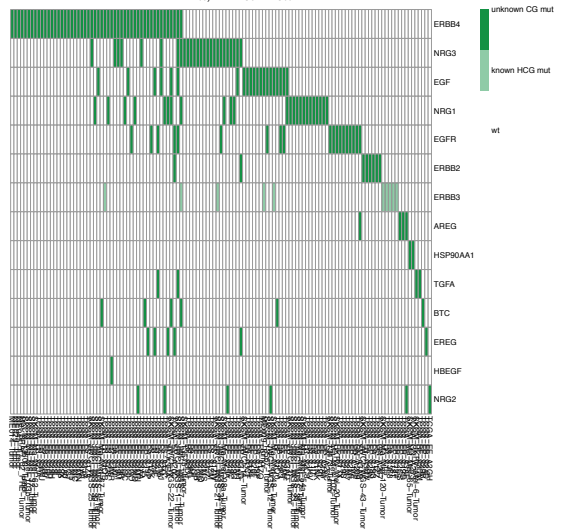
TP53 Regulates Transcription Of Death Receptors And Ligands
FDR = 1.6e-11%, FDR nod = 0.43%



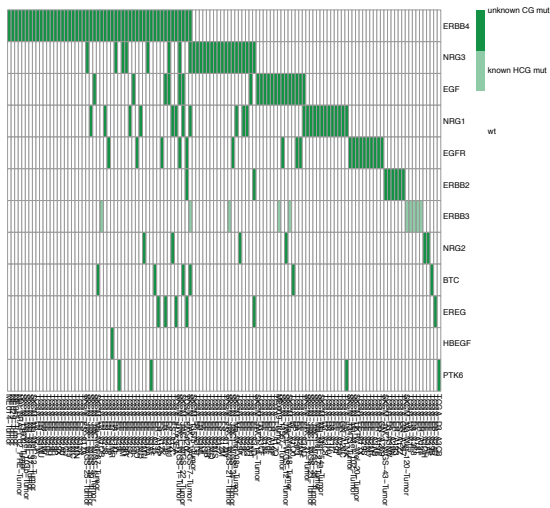
TRIF Mediated Programmed Cell Death
FDR = 0.007%, FDR nod = 0.001%



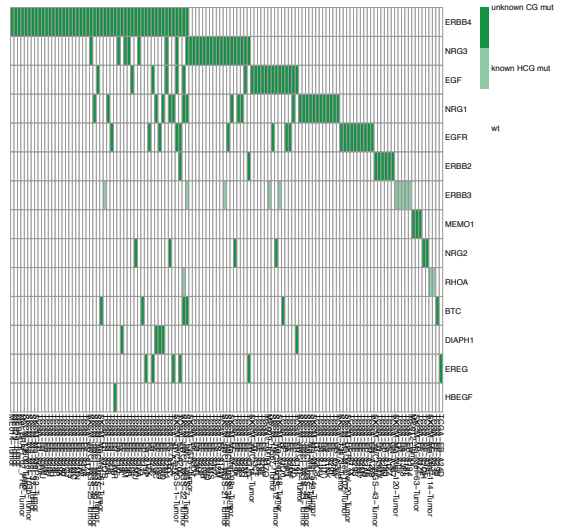
ErbB Receptor Signaling Network
FDR = 1.1%, FDR nod = 1.5%



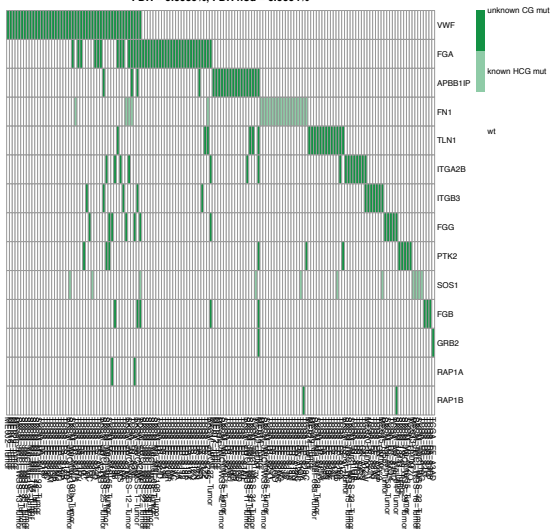
ERBB2 Activates PTK6 Signaling
Signaling By ERBB4
FDR = 0.43%, FDR nod = 0.48%



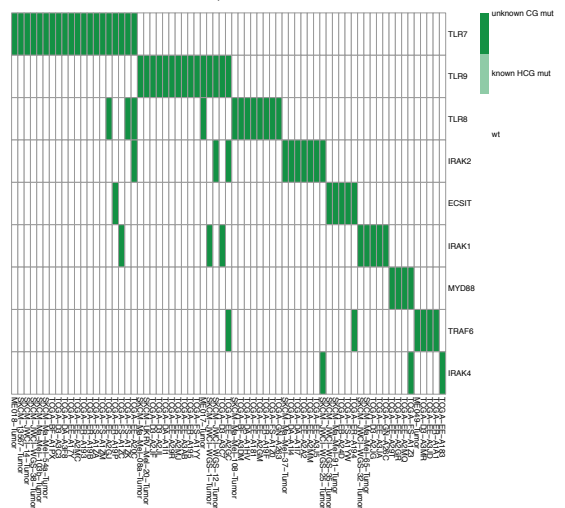
ERBB2 Regulates Cell Motility
FDR = 3.5%, FDR nod = 4.6%



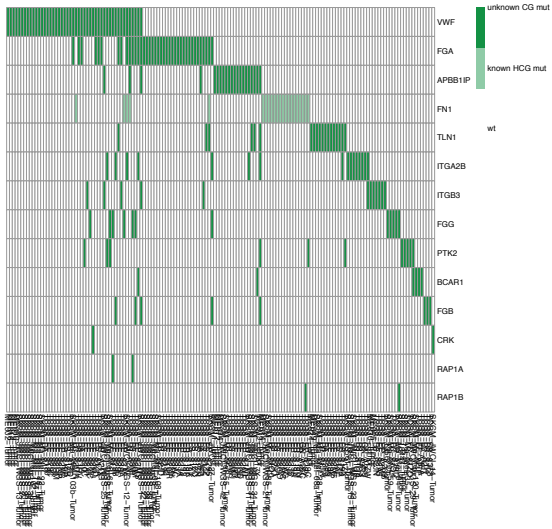
GRB2:SOS Provides Linkage To MAPK Signaling For Integrins
FDR = 0.0059%, FDR nod = 0.0064%



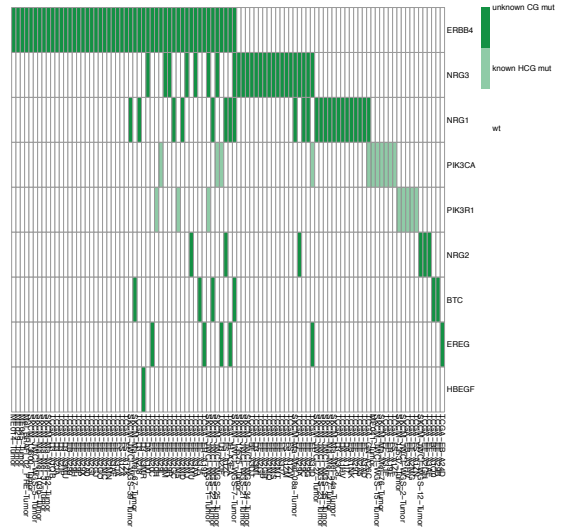
MyD88 Dependent Cascade Initiated On Endosome
TRAF6 Mediated Induction Of NFkB And MAP Kinases Upon TLR7/8 Or 9 Activation
FDR = 0.85%, FDR nod = 2.7%



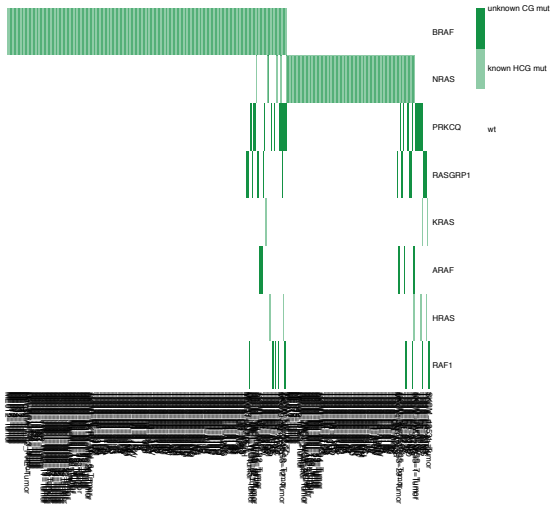
P130Cas Linkage To MAPK Signaling For Integrins
 FDR = 0.0074%, FDR nod = 0.066%



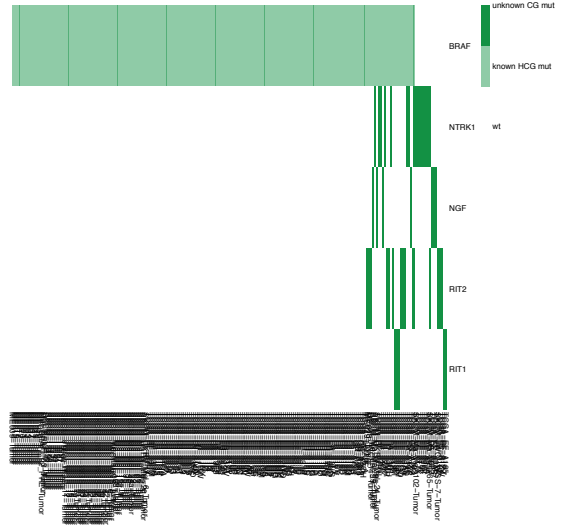
PI3K Events In ERBB4 Signaling
 FDR = 1.1%, FDR nod = 0.02%



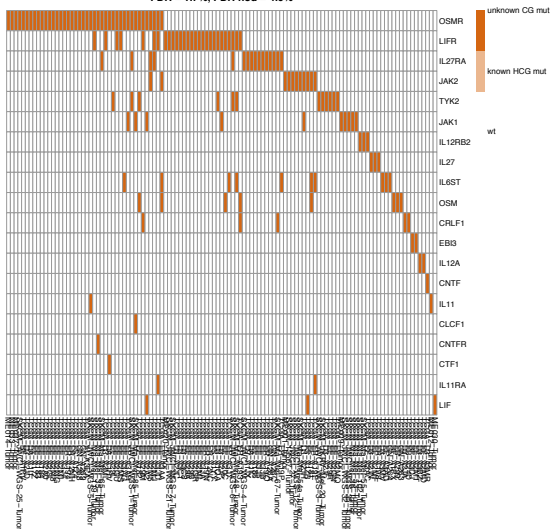
f Activation Signaling (through RasGRP) (CD4 T Cell Receptor Signaling (ERK Cascade))
Raf Activation Signaling (through RasGRP) (CD4 T Cell Receptor Signaling)
 FDR = 3.9e-12%, FDR nod = 1.1%



Signalling To P38 Via RIT And RIN
 FDR = 3.9e-12%, FDR nod = 7.5e-05%



IL 6 Type Cytokine Receptor Ligand Interactions
 FDR = 1.7%, FDR nod = 4.6%



IRF3 Mediated Activation Of Type 1 IFN
 FDR = 1.2e-06%, FDR nod = 1.2e-05%

