

| tezomib, 4 Hc | tezomib, 24 Hc | tezomib, 72 Hc | <p>Autophagy</p> <ul style="list-style-type: none"> Chaperone Mediated Autophagy Late endosomal microautophagy Macroautophagy Selective autophagy Autophagy PI3K1-PRKN Mediated Mitophagy Aggrephagy Pexophagy <p>Cell Cycle</p> <ul style="list-style-type: none"> Cell Cycle Checkpoints G2/M Checkpoints G1/S DNA Damage Checkpoints p53-Dependent G1/S DNA damage checkpoint p53-Dependent G1/S DNA Damage Response p53-Independent G1/S DNA damage checkpoint p53-Independent DNA Damage Response <p>Cell Cycle, Mitotic</p> <ul style="list-style-type: none"> Mitotic G2-M Phases G2/M Transition Regulation of PLK1 Activity at G2/M Transition Centrosome maturation Cyclin A/B1/B2 associated events during G2/M transition Use of Cdk2/GTSE1 in G2/M progression after G2 checkpoint FBXL7 down-regulates AURKA during mitotic entry and in early mitosis AURKA Activation by TPX2 Regulation of mitotic cell cycle APC/C-mediated degradation of cell cycle proteins Autodegradation of Cdh1 by Cdh1/APC/C APC/C:Cdh1 mediated degradation of Cdc20 and other APC/C:Cdh1 targeted proteins Conversion from APC/C:Cdc20 to APC/C:Cdh1 in late anaphase Regulation of APC/C activators between G1/S and early anaphase APC/C:Cdh1 mediated degradation of APC/C:Cdc20 mediated degradation of mitotic proteins Mitotic G1 phase and G1/S transition G1/S Transition E2F mediated regulation of DNA replication E2F associated events during G1/S transition G1/S-Specific Transcription <p>M Phase</p> <ul style="list-style-type: none"> Mitotic Metaphase and Anaphase Mitotic Anaphase Mitotic Prometaphase Resolution of Sister Chromatid Cohesion Recruitment of NuMA to mitotic centrosomes EML4 and NUDC in mitotic spindle formation <p>S Phase</p> <ul style="list-style-type: none"> Cyclin A:Cdk2-associated events at S phase entry SCF(Skp2)-mediated degradation of p27/p21 Ubiquitin-dependent degradation of Cyclin D <p>Cell Junction Organization</p> <ul style="list-style-type: none"> Cell-cell junctions Cell-extracellular matrix interactions <p>Cellular responses to stimuli</p> <ul style="list-style-type: none"> Cellular responses to stress Cellular response to hypoxia Oxygen-dependent proline hydroxylation of Hypoxia-inducible Factor Alpha Cellular Senescence Oncogene Induced Senescence HSF1-dependent transcription Cellular response to steroid hormone receptors (SHR) in the presence of lig Regulation of HSF1-mediated heat shock response HSF1 activation HSF1-dependent transactivation Attenuation phase Unfolded Protein Response (UPR) IRE1alpha activates chaperones XBP1(S) activates chaperone genes Heme signaling Cellular response to starvation Response of EIF2AK4 (GCN2) to amino acid deficiency Amino acids regulate mTORC1 Cellular response to chemical stress Detoxification of Reactive Oxygen Species Cytoprotection by HMOX1 KEAP1-NFE2L2 pathway Regulation of BACH1 activity Nuclear events mediated by NFE2L2 <p>Chromatin organization</p> <ul style="list-style-type: none"> Chromatin modifying enzymes RMTs methylate histone arginines <p>DNA Replication</p> <ul style="list-style-type: none"> DNA Damage Bypass Translesion synthesis by Y family DNA polymerases bypasses lesions on DNA template Translesion synthesis by REV1 Translesion Synthesis by POLH Translesion synthesis by POLK Translesion synthesis by POLI Recognition of DNA damage by PCNA-containing replication complex <p>DNA Double-Strand Break Repair</p> <ul style="list-style-type: none"> Homologous Recombination HDR through Homologous Recombination (HRR) or Single Strand Annealing (SSA) HDR through Single Strand Annealing (SSA) HDR through Homologous Recombination (HRR) Phosphorylation of DNA double-strand break ends DNA Double Strand Break Response Recruitment and ATM-mediated phosphorylation of repair and signaling proteins at Fanconi Anemia Pathway Nucleotide Excision Repair Global Genome Nucleotide Excision Repair (GG-NER) DNA Damage Recognition in GG-NER Formation of Incision Complex in GG-NER Gap-filling DNA repair synthesis and ligation in GG-NER <p>DNA Replication Pre-Initiation</p> <ul style="list-style-type: none"> Assembly of the pre-replicative complex Synthesis of DNA Switching of origins to a post-replicative state Orcl1 represses origin from chromatin CDK-mediated phosphorylation and removal of Cdc6 <p>Developmental Biology</p> <ul style="list-style-type: none"> Gastrulation Formation of paraxial mesoderm Somitogenesis Nervous system development Axon guidance Ephrin signaling EPHB5-mediated forward signaling EPHA-mediated growth cone collapse Ephrin signaling EPH-ephrin mediated repulsion of cells Semaphorin interactions Sema3A PAK dependent Axon repulsion Sema4D in semaphorin signaling Signaling by ROBO receptors Regulation of expression of SLITs and ROBOs <p>Diseases</p> <ul style="list-style-type: none"> Diseases of DNA repair Diseases of DNA Double-Strand Break Repair Defective homologous recombination repair (HRR) due to BRCA1 loss of function Defective HDR through Homologous Recombination Repair (HRR) due to PALB2 loss of function Defective HDR through Homologous Recombination Repair (HRR) due to PALB2 loss of function Diseases of metabolism Defective cobalamin (B12) metabolism Defects in cobalamin (B12) metabolism Diseases of carbohydrate metabolism Diseases of signal transduction by growth factor receptors and second messengers Signaling by ERBB2 in Cancer Constitutive Signaling by Overexpressed ERBB2 Signaling by ERBB2 KD Mutants Signaling by ERBB2 ECD mutants Signaling by ERBB2 TMD/JMD mutants Signaling by EGFR in Cancer Signaling by EGFRVIII in Cancer Constitutive Signaling by EGFRVIII Signaling by Ligand-Responsive EGFR Variants in Cancer Cofactor-dependent signaling by Ligand-Responsive EGFR Cancer Variants Hh mutants abrogate ligand secretion Hh mutants are degraded by ERAD Signaling by KIT in disease Signaling by phosphorylated juxtamembrane, extracellular and kinase domain KIT m Signaling by PDGFRA in cancer Signaling by PDGFRA transmembrane, juxtamembrane and kinase domain mutants Signaling by PDGFRA extracellular domain mutants Signaling by ALK in cancer Signaling by ALK fusions and activated point mutants Disorders of transmembrane transporters ABC transporter disorders Defective CFTR causes cystic fibrosis Infectious disease Bacterial Infection Pathways Uptake and actions of bacterial toxins Listeria monocytogenes entry into host cells InlB-mediated entry of Listeria monocytogenes into host cell Parasitic Infection Pathways Leishmania infection Parasite infection Cell recruitment (pro-inflammatory response) Leishmania parasite growth and survival Viral Infection Pathways HIV Infection HIV Life Cycle Host interactions of HIV factors Influenza Infection Transport of Ribonucleoproteins into the Host Nucleus Influenza Viral RNA Transcription and Replication Export of Viral Ribonucleoproteins from Nucleus NS1 Mediated effects on Host Pathways SARS-CoV Infections SARS-CoV-1 Infection Potential therapeutics for SARS SARS-CoV-2 Infection Respiratory Syncytial Virus Infection Pathway Respiratory syncytial virus (RSV) genome replication, transcription and translation RSV-host interactions <p>Extracellular matrix organization</p> <ul style="list-style-type: none"> Integrin cell surface interactions Non-integrin membrane-ECM interactions <p>Gene expression (Transcription)</p> <ul style="list-style-type: none"> Epigenetic regulation of gene expression Positive epigenetic regulation of rRNA expression ERC6 (CSB) and EMT2 (GSA) positively regulate rRNA expression <p>Gene Silencing by RNA</p> <ul style="list-style-type: none"> PIWI-interacting RNA (piRNA) biogenesis <p>RNA Polymerase II Transcription</p> <ul style="list-style-type: none"> Generic Transcription Pathway Transcriptional Regulation by TP53 Regulates Metabolic Genes Regulation of TP53 Activity TP53 Regulates Transcription of Cell Death Genes TP53 Regulates Transcription of Cell Cycle Genes TP53 Regulates Transcription of DNA Repair Genes Transcriptional regulation by RUNX3 RUNX3 regulates NOTCH signaling Regulation of RUNX3 expression and activity Transcriptional regulation by RUNX2 Regulation of RUNX2 expression and activity RUNX2 regulates bone development Transcriptional regulation by RUNX1 Regulation of RUNX1 Expression and Activity RUNX1 regulates genes involved in megakaryocyte differentiation and platelet function RUNX1 regulates transcription of genes involved in differentiation of HSCs RUNX1 interacts with co-factors whose precise effect on RUNX1 targets is not known FOXO-mediated transcription <p>Hemostasis</p> <ul style="list-style-type: none"> Cell surface interactions at the vascular wall Factors involved in megakaryocyte development and platelet production Kinases Platelet activation, signaling and aggregation GPVI-mediated activation cascade Response to elevated platelet cytosolic Ca2+ Platelet degranulation <p>Immune System</p> <ul style="list-style-type: none"> Adaptive Immune System Immunoregulatory interactions between a Lymphoid and a non-Lymphoid cell TCR signaling Downstream TCR signaling Phosphorylation of CD3 and TCR zeta chains Translocation of ZAP-70 to Immunological synapse Generation of second messenger molecules Costimulation by the CD28 family PD-1 signaling Class I MHC mediated antigen processing & presentation Antigen processing-Cross presentation ER-Phagosome pathway Cross-presentation of soluble exogenous antigens (endosomes) Antigen processing: Ubiquitination & Proteasome degradation Antigen Presentation: Folding, assembly and peptide loading of class I MHC Signaling by the B Cell Receptor (BCR) Downstream signaling events of B cell Receptor (BCR) Activation of NF-kappaB in B cells Antigen activates B Cell Receptor (BCR) leading to generation of second messenger Cytokine Signaling in Immune system Signaling by Interleukins Interleukin-7 signaling Interleukin-1 family signaling Interleukin-37 signaling Interleukin-1 signaling Interleukin-12 family signaling Interleukin-35 Signaling Interleukin-12 signaling Interleukin-2 family signaling Interleukin-15 signaling Interleukin-2 signaling Interleukin receptor SHC signaling Interleukin-3, Interleukin-5 and GM-CSF signaling Interleukin-4 and Interleukin-13 signaling TNF2 non-canonical NF-kB pathway TNFs bind their physiological receptors NIK-->noncanonical NF-kB signaling IKK receptor superfamily (TNFSF) members mediating non-canonical NF-kB pathway Interferon Signaling Antiviral mechanism by IFN-stimulated genes ISG15 antiviral mechanism PKR-mediated signaling Interferon gamma signaling Interferon alpha/beta signaling Regulation of IFNA/IFNB signaling Growth hormone receptor signaling <p>Innate Immune System</p> <ul style="list-style-type: none"> Toll-like Receptor Cascades Toll Like Receptor 3 (TLR3) Cascade TICAM1, RIP1-mediated IKK complex recruitment TAK1-dependent IKK and NF-kappa-B activation MAP kinase activation TICAM1-dependent activation of IRF3/IRF7 TICAM1, TRAF6-dependent induction of TAK1 complex DDX58/IFIH1-mediated induction of interferon-alpha/beta TRAF3-dependent IRF activation pathway Negative regulators of DDX58/IFIH1 signaling Cytosolic sensors of pathogen-associated DNA Fcgamma receptor (FCGR) dependent phagocytosis Regulation of actin dynamics for phagocytic cup formation Role of phospholipids in phagocytosis DAP12 interactions DAP12 signaling Fc epsilon receptor (FCER1) signaling FCER1 mediated MAPK activation FCER1 mediated Ca2+ mobilization FCER1 mediated NF-kB activation C-type lectin receptors (CLRs) CLEC7A (Dectin-1) signaling Dectin-1 mediated noncanonical NF-kB signaling CLEC7A (Dectin-1) induces NFAT activation Neutrophil degranulation Alpha-protein kinase 1 signaling pathway <p>Metabolism</p> <ul style="list-style-type: none"> Biological oxidations Phase I - Functionalization of compounds Metabolism of amino acids and derivatives Selenoamino acid metabolism Selenocysteine synthesis Metabolism of polyamines Regulation of ornithine decarboxylase (ODC) Metabolism of carbohydrates Glycogen metabolism Glycogen synthesis Metabolism of lipids Phospholipid metabolism PI Metabolism Synthesis of PIPs at the plasma membrane Synthesis of PIPs at the Golgi membrane Synthesis of PIPs at the early endosome membrane Metabolism of nucleotides Nucleotide salvage Metabolism of vitamins and cofactors Metabolism of water-soluble vitamins and cofactors Cobalamin (Cbl, vitamin B12) transport and metabolism Metabolism of cofactors The citric acid (TCA) cycle and respiratory electron transport Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat Formation of ATP by chemiosmotic coupling Respiratory electron transport Complex I biogenesis <p>Metabolism of RNA</p> <ul style="list-style-type: none"> Mitochondrial RNA degradation FASTK mediated RNA degradation processing and stability of mitochondrial RNAs Nonsense-Mediated Decay (NMD) Nonsense Mediated Decay (NMD) independent of the Exon Junction Complex (EJC) Nonsense Mediated Decay (NMD) enhanced by the Exon Junction Complex (EJC) Regulation of mRNA stability by proteins that bind AU-rich elements AUF1 (hnRNP D0) binds and destabilizes mRNAs rRNA processing rRNA processing in the nucleolus rRNA processing in the nucleus and cytosol rRNA modification in the nucleus and cytosol Major pathway of rRNA processing in the nucleolus and cytosol tRNA processing tRNA processing in the mitochondrion <p>Metabolism of proteins</p> <ul style="list-style-type: none"> Mitochondrial protein degradation Post-translational protein modification SUMOylation SUMO E3 ligases SUMOylate target proteins SUMOylation of DNA damage response and repair proteins SUMOylation of transcription factors SUMOylation of ubiquitylation proteins SUMOylation of transcription cofactors SUMOylation of SUMOylation proteins SUMOylation of intracellular receptors SUMOylation of chromatin organization proteins SUMOylation of RNA binding proteins SUMOylation of DNA replication proteins SUMOylation of DNA methylation proteins SUMOylation of immune response proteins Asparagine N-linked glycosylation N-glycan trimming in the ER and Calnexin/Calreticulin cycle Calnexin/calreticulin cycle Deubiquitination UCH protein domains Ub-specific processing proteases Ovarian tumor-associated proteases Metalloprotease DUBs Protein ubiquitination Synthesis of active ubiquitin: roles of E1 and E2 enzymes Ubiquitin ligases ubiquitinate target proteins Protein methylation Neddylation Carboxyterminal post-translational modifications of tubulin <p>Protein folding</p> <ul style="list-style-type: none"> Post-chaperonin tubulin folding pathway Chaperonin-mediated protein folding Cooperation of Prefoldin and TricC/CT in actin and tubulin folding Prefoldin mediated transfer of substrate to CCT/TricC Formation of tubulin folding intermediates by CCT/TricC <p>Translation</p> <ul style="list-style-type: none"> Eukaryotic Translation Elongation Peptide chain elongation SRP-dependent cotranslational protein targeting to membrane Eukaryotic Translation Initiation L13a-mediated translation silencing of Ceruloplasmin expression Cap-dependent Translational Initiation Activation of the mRNA upon binding of the cap-binding complex and eIFs, and sub Formation of a preinitiation complex Formation of a preinitiation complex, and subsequently, the 43S complex Ribosomal scanning and start codon recognition GTP hydrolysis and joining of the 60S ribosomal subunit Polypeptide translation Termination <p>Neuronal System</p> <ul style="list-style-type: none"> Transmission across Chemical Synapses Neurotransmitter receptors and postsynaptic signal transduction Activation of kainate receptors upon glutamate binding Orogenesis biogenesis and maintenance Cilium Assembly Anchoring of the basal body to the plasma membrane Intraflagellar transport Mitochondrial biogenesis Cristae formation <p>Programmed Cell Death</p> <ul style="list-style-type: none"> Apoptosis Regulation of Apoptosis Regulation of activated PAK-2p34 by proteasome mediated degradation Regulated Necrosis RIPK1-mediated regulated necrosis Regulation of necroptotic cell death <p>Protein localization</p> <ul style="list-style-type: none"> Peroxisomal protein import <p>Signal Transduction</p> <ul style="list-style-type: none"> Death Receptor Signaling p75NTR receptor-mediated signalling p75NTR signals via NF-kB p75NTR recruits signalling complexes NF-kB is activated and signals survival Cell death signalling via NRAGE, NRIF and NADE NRAGE signals death through JNK NRIF signals cell death from the nucleus TNF signaling Regulation of TNFR1 signaling Intracellular signaling by second messengers PI3P activates AKT signaling PTEN Regulation Regulation of PTEN mRNA translation Regulation of PTEN gene transcription Regulation of PTEN stability and activity MAPK family signaling cascades MAPK1/MAPK3 signaling RAF/MAP kinase cascade Regulation of RAS by GAPs RAF activation MEK2K and MAPK activation Negative regulation of MAPK pathway RAS processing MAPK/ERK1 signaling Signaling by GPCR GPCR downstream signalling G alpha (q) signalling events G alpha (12/13) signalling events G alpha (s) signalling events GPCR1 signaling G alpha (i) signalling events GPCR ligand binding Class A/1 (Rhodopsin-like receptors) Class B/2 (Secretin family receptors) Signaling by Hedgehog Hedgehog ligand biogenesis Hedgehog off state Degradation of GLI1 by the proteasome Degradation of GLI2 by the proteasome GLI3 is processed to GLI3R by the proteasome Hedgehog on state Signaling by NOTCH Signaling by NOTCH1 Activated NOTCH1 Transmits Signal to the Nucleus Signaling by NOTCH2 NOTCH2 Activation and Transmission of Signal to the Nucleus Signaling by NOTCH3 NOTCH3 Activation and Transmission of Signal to the Nucleus NOTCH3 Intracellular Domain Regulates Transcription Signaling by NOTCH4 Negative regulation of NOTCH4 signaling Signaling by Non-Receptor Tyrosine Kinases Signaling by PTK6 PI3K Regulates RHO GTPases, RAS GTPase and MAP kinases Signaling by Nuclear Receptors ESR-mediated signaling Extra-nuclear estrogen signaling Estrogen-dependent nuclear events downstream of ESR-membrane signaling Signaling by Tyrosine Kinases Signaling by ERBB2 Downregulation of ERBB2 signaling Signaling by SCF-KIT Regulation of KIT signaling Signaling by EGFR EGFR downregulation Signaling by FGFR Downstream signaling of activated FGFR1 Negative regulation of FGFR1 signaling Signaling by FGFR2 Downstream signaling of activated FGFR2 Negative regulation of FGFR2 signaling FGFR2 alternative splicing Signaling by FGFR3 Downstream signaling of activated FGFR3 Negative regulation of FGFR3 signaling Signaling by FGFR4 Downstream signaling of activated FGFR4 Negative regulation of FGFR4 signaling Signaling by VEGF VEGFA-VEGFR2 pathway VEGFR2 mediated vascular permeability VEGFR2 mediated cell proliferation Signaling by MET Negative regulation of MET activity Signaling by Rho GTPases, Mito GTPases and RHOBTB3 Signaling by Rho GTPases RHO GTPase cycle RHOA GTPase cycle RHOB GTPase cycle RHO C GTPase cycle RHO C2 GTPase cycle RAC1 GTPase cycle RAC2 GTPase cycle RHO GTPase cycle RHOH GTPase cycle RHOI GTPase cycle RHOJ GTPase cycle RAC3 GTPase cycle RHOV GTPase cycle RHO GTPase cycle RND3 GTPase cycle RND2 GTPase cycle RND1 GTPase cycle RHOBTB3 GTPase cycle Signaling by TGF-beta family members Signaling by TGF-beta Receptor Complex Transcriptional activity of SMAD2/SMAD3:SMAD4 heterotrimer Downregulation of SMAD2/3:SMAD4 heterotrimer transcriptional activity SMAD2/3:SMAD4 heterotrimer regulates transcription Signaling by WNT Degradation of beta-catenin by the destruction complex TCF dependent signaling in response to WNT Formation of the beta-catenin:TCF transactivating complex Destruction of the beta-catenin transactivating complex Degradation of AXIN Degradation of DVL Beta-catenin independent WNT signaling Ca2+ pathway PCP/Asymmetric localization of PCP proteins WNT5A-dependent internalization of FZD4 <p>Transport and Trafficking</p> <ul style="list-style-type: none"> Transport of small molecules ABC-1 family proteins mediated transport Iron uptake and transport Plasma lipoprotein assembly, remodeling, and clearance Plasma lipoprotein clearance VLDLR internalisation and degradation SLC-mediated transmembrane transport Transport of bile salts and organic acids, metal ions and amine compounds <p>Vesicle-mediated transport</p> <ul style="list-style-type: none"> Membrane Trafficking Gap junction trafficking and regulation Gap junction trafficking ER to Golgi Anterograde Transport COP1-mediated anterograde transport Trans-Golgi Network Vesicle Budding Golgi Associated Vesicle Biogenesis Intra-Golgi and retrograde Golgi-to-ER traffic Golgi-to-ER retrograde transport COP1-dependent Golgi-to-ER retrograde traffic COP1-independent Golgi-to-ER retrograde traffic Clathrin-mediated endocytosis Cargo recognition for clathrin-mediated endocytosis Regulation of trafficking Endosomal Sorting Complex Required For Transport (ESCRT) |
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