Repurposing drugs for senotherapeutic effect: potential senomorphic effects of female synthetic hormones.

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## Supplementary information

### Supplementary Figure Legends

Supplementary Fig. 1: Descriptive data for the drug panel for the senescence screen. A. Type of clinical approval, i.e. compounds approved by the European Medical Association (EMA), the US Food and Drug Administration (FDA) or other countries. B. Research areas linked with each compound. C. Frequency of biological pathways that are targeted by the compounds in the screen. D. Compounds in the panel categorised by target/function.

Supplementary Fig. 2: The chemical structures of compounds that decreased senescent cell load. The chemical structures of compounds that decreased senescent cell load as measured by *CDKN2A* (p16) expression are given above.

Supplementary Fig. 3: Chemical structures of compounds that decreased senescent cell load. The chemical structures of compounds that decreased senescent cell load as measured by SAB staining are given above.

Supplementary Fig. 4: The chemical structures of compounds that increased senescent cell load. The chemical structures of compounds that increased senescent cell load as measured by *CDKN2A* (p16) expression are given above.

Supplementary Fig. 5: Dendrogram indicating structure-function similarity for compounds influencing senescence. Dendrogram constructed using the Tanimoto coefficient to show structural similarity of compounds tested that decreased SAB activity.

Supplementary Fig. 6: Dendrogram indicating structure-function similarity for compounds influencing senescence. Dendrogram constructed using the Tanimoto coefficient to show structural similarity of compounds tested that increased *CDKN2A* gene expression.

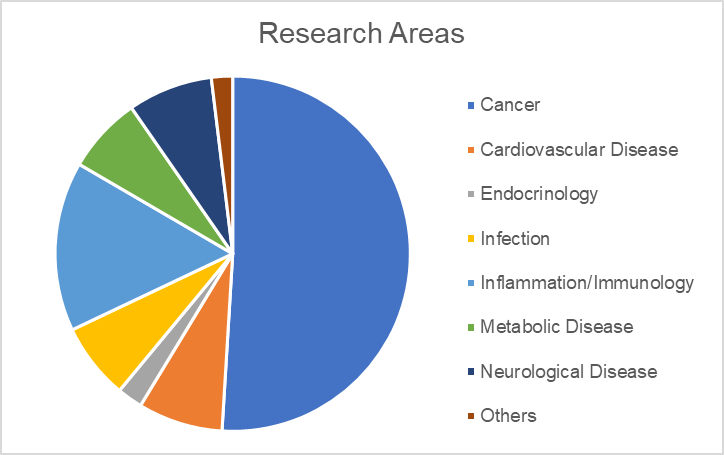
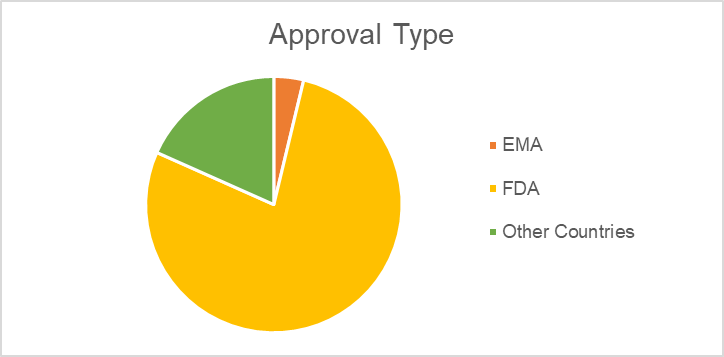
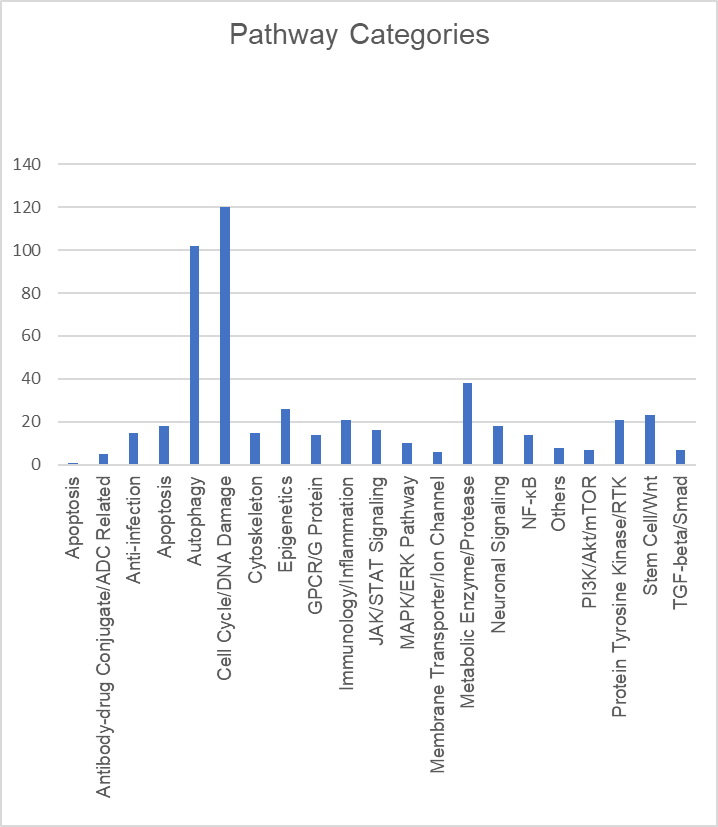
### Supplementary Tables

Supplementary Table 1: Information on compound synonyms, targets and pathways used in a screen for *CDKN2A* gene expression. Information provided from the MedChemExpress FDA Approved Drug Library Plus (MedChemTronica, Stockholm).

|  |  |  |  |
| --- | --- | --- | --- |
| **Product Name** | **Synonyms** | **Target** | **Pathway** |
| 5-Aminosalicylic Acid | Mesalamine; 5-ASA;Mesalazine | NF-κB; PAK; PPAR | Cell Cycle/DNA Damage; Cytoskeleton; NF-κB |
| 5-Azacytidine | Ladakamycin; 5-AzaC;Azacitidine | Autophagy; DNA Methyltransferase; Nucleoside Antimetabolite/Analog | Autophagy; Cell Cycle/DNA Damage; Epigenetics |
| 5-Fluorouracil | 5-FU | Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| 6-Thioguanine | Thioguanine; 2-Amino-6-purinethiol | Autophagy; Deubiquitinase; SARS-CoV | Anti-infection; Autophagy; Cell Cycle/DNA Damage |
| Abemaciclib (methanesulfonate) | LY2835219 (methanesulfonate) | CDK | Cell Cycle/DNA Damage |
| Acalabrutinib | ACP-196 | Btk | Protein Tyrosine Kinase/RTK |
| Acamprosate (calcium) | Calcium N-acetylhomotaurinate | GABA Receptor | Membrane Transporter/Ion Channel; Neuronal Signalling |
| Aceglutamide | α-N-Acetyl-L-glutamine; N2-Acetylglutamine | Autophagy; Endogenous Metabolite | Autophagy; Metabolic Enzyme/Protease |
| Aclacinomycin A hydrochloride | Aclarubicin hydrochloride | Proteasome; Topoisomerase | Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Allantoin | 5-Ureidohydantoin | Endogenous Metabolite; Imidazoline Receptor | GPCR/G Protein; Metabolic Enzyme/Protease; Neuronal Signalling |
| Alpelisib | BYL-719 | PI3K | PI3K/Akt/mTOR |
| Altretamine | ENT-50852; RB-1515;WR-95704 | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Amlexanox | AA673; Amoxanox; CHX3673 | IKK | NF-κB |
| Amoxapine | CL-67772 | Others | Others |
| Amsacrine | m-AMSA; acridinyl anisidide | Autophagy; Topoisomerase | Autophagy; Cell Cycle/DNA Damage |
| Anethole (trithione) |  | Others | Others |
| Apatinib | YN968D1 | Autophagy; c-Kit; RET; Src; VEGFR | Autophagy; Protein Tyrosine Kinase/RTK |
| Artemisinin | Qinghaosu; NSC 369397 | HCV; Parasite | Anti-infection |
| Artesunate |  | STAT | JAK/STAT Signalling; Stem Cell/Wnt |
| Aspirin | ASA; Acetylsalicylic Acid | Autophagy; COX; Mitophagy | Autophagy; Immunology/Inflammation |
| Atorvastatin (hemicalcium salt) | CI-981; Atorvastatin hemicalcium | Autophagy; HMG-CoA Reductase (HMGCR) | Autophagy; Metabolic Enzyme/Protease |
| Balsalazide |  | Interleukin Related; STAT | Immunology/Inflammation; JAK/STAT Signalling; Stem Cell/Wnt |
| Baricitinib (phosphate) | INCB028050 (phosphate); LY3009104 (phosphate) | JAK | Epigenetics; JAK/STAT Signalling; Stem Cell/Wnt |
| Belinostat | PXD101; PX105684 | Autophagy; HDAC | Autophagy; Cell Cycle/DNA Damage; Epigenetics |
| Belotecan (hydrochloride) | CKD-602 | Topoisomerase | Cell Cycle/DNA Damage |
| Bendamustine (hydrochloride) | SDX-105; EP-3101 | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Bendazol |  | NO Synthase | Immunology/Inflammation |
| Berberine (chloride hydrate) | Natural Yellow 18 (chloride hydrate) | Autophagy; Bacterial; ROS; Topoisomerase | Anti-infection; Autophagy; Cell Cycle/DNA Damage; Protein Tyrosine Kinase/RTK |
| Bexarotene | LGD1069 | Autophagy; RAR/RXR | Autophagy; Metabolic Enzyme/Protease |
| Bezafibrate | BM15075 | PPAR | Cell Cycle/DNA Damage |
| Binimetinib | MEK162; ARRY-162; ARRY-438162 | Autophagy; MEK | Autophagy; MAPK/ERK Pathway |
| Bleomycin (sulfate) |  | Bacterial; DNA/RNA Synthesis | Anti-infection; Cell Cycle/DNA Damage |
| Bortezomib | PS-341; Brotezamide; DPBA; LDP 341; MG 341; Radiciol; NSC 681239 | Apoptosis; Autophagy; Proteasome | Apoptosis; Autophagy; Metabolic Enzyme/Protease |
| Bosutinib | SKI-606 | Autophagy; Bcr-Abl; Src | Autophagy; Protein Tyrosine Kinase/RTK |
| Bremelanotide (Acetate) | PT-141 Acetate | Melanocortin Receptor | GPCR/G Protein; Neuronal Signalling |
| Bromhexine (hydrochloride) |  | Autophagy; Reactive Oxygen Species | Autophagy; Immunology/Inflammation; Metabolic Enzyme/Protease; NF-κB |
| Bucladesine (sodium salt) | Dibutyryl-cAMP sodium salt; DC2797; Sodium dibutyryl cAMP | PKA | Protein Tyrosine Kinase/RTK; Stem Cell/Wnt |
| Bufexamac | Bufexamic acid | HDAC | Cell Cycle/DNA Damage; Epigenetics |
| Busulfan |  | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Cabazitaxel | XRP6258; RPR-116258A; taxoid XRP6258 | Autophagy; Microtubule/Tubulin | Autophagy; Cell Cycle/DNA Damage; Cytoskeleton |
| Cabozantinib | XL184; BMS-907351 | c-Kit; c-Met/HGFR; FLT3; TAM Receptor; VEGFR | Protein Tyrosine Kinase/RTK |
| Caffeic acid |  | 5-Lipoxygenase; Endogenous Metabolite; TRP Channel | Membrane Transporter/Ion Channel; Metabolic Enzyme/Protease; Neuronal Signalling |
| Capecitabine |  | DNA/RNA Synthesis; Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| Carbamazepine | CBZ; NSC 169864 | Autophagy; Mitophagy; Sodium Channel | Autophagy; Membrane Transporter/Ion Channel |
| Carmofur | HCFU | Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| Carmustine |  | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Carprofen |  | Autophagy; COX; FAAH | Autophagy; Immunology/Inflammation; Metabolic Enzyme/Protease; Neuronal Signalling |
| Ceritinib | LDK378 | ALK; IGF-1R; Insulin Receptor | Protein Tyrosine Kinase/RTK |
| Chlorambucil | CB-1348; WR-139013 | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Chloroquine (diphosphate) |  | Autophagy; Toll-like Receptor (TLR) | Autophagy; Immunology/Inflammation |
| Chlorpheniramine (maleate) | Chlorphenamine maleate | Histamine Receptor | GPCR/G Protein; Immunology/Inflammation; Neuronal Signalling |
| Chlorzoxazone |  | Cytochrome P450 | Metabolic Enzyme/Protease |
| Choline Fenofibrate | ABT-335 | Cytochrome P450; PPAR | Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Chromocarb | Chromone-2-carboxylic acid | Others | Others |
| Ciprofibrate | Win35833 | PPAR | Cell Cycle/DNA Damage |
| Citalopram (hydrobromide) | (±)-Citalopram hydrobromide; Lu 10-171 | Autophagy; Serotonin Transporter | Autophagy; Neuronal Signalling |
| Citric acid |  | Apoptosis; Endogenous Metabolite | Apoptosis; Metabolic Enzyme/Protease |
| Clioquinol | Iodochlorhydroxyquin | Autophagy; Fungal; Mitophagy | Anti-infection; Autophagy |
| Clofarabine |  | Autophagy; Nucleoside Antimetabolite/Analog | Autophagy; Cell Cycle/DNA Damage |
| Clofibrate |  | PPAR | Cell Cycle/DNA Damage |
| Cobimetinib | GDC-0973; XL518 | MEK | MAPK/ERK Pathway |
| Colchicine |  | Autophagy; Microtubule/Tubulin | Autophagy; Cell Cycle/DNA Damage; Cytoskeleton |
| Conivaptan (hydrochloride) | YM 087 | Vasopressin Receptor | GPCR/G Protein |
| Crizotinib (hydrochloride) | PF-02341066 hydrochloride | ALK; Autophagy; c-Met/HGFR | Autophagy; Protein Tyrosine Kinase/RTK |
| Cytarabine | Cytosine β-D-arabinofuranoside; Cytosine Arabinoside; Ara-C | Autophagy; DNA/RNA Synthesis; Nucleoside Antimetabolite/Analog | Autophagy; Cell Cycle/DNA Damage |
| Dabrafenib | GSK2118436A; GSK2118436 | Raf | MAPK/ERK Pathway |
| Dacarbazine | Imidazole Carboxamide | Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| Dacomitinib | PF-00299804; PF-299804 | EGFR | JAK/STAT Signalling; Protein Tyrosine Kinase/RTK |
| Dasatinib (hydrochloride) | BMS 354825 hydrochloride | Autophagy; Bcr-Abl; Src | Autophagy; Protein Tyrosine Kinase/RTK |
| Daunorubicin (Hydrochloride) | RP 13057 (Hydrochloride); Daunomycin (Hydrochloride); Rubidomycin (Hydrochloride) | ADC Cytotoxin; Autophagy; DNA/RNA Synthesis; Topoisomerase | Antibody-drug Conjugate/ADC Related; Autophagy; Cell Cycle/DNA Damage |
| Decitabine | NSC 127716; 5-Aza-2'-deoxycytidine | DNA Methyltransferase | Epigenetics |
| Deferoxamine (mesylate) | Desferrioxamine B mesylate; DFOM | Amyloid-β; Autophagy; Mitophagy | Autophagy; Neuronal Signalling |
| Dexamethasone | Hexadecadrol; Prednisolone F | Autophagy; Glucocorticoid Receptor; Mitophagy | Autophagy; GPCR/G Protein |
| Diacerein | Diacerhein; Diacetylrhein | Interleukin Related | Immunology/Inflammation |
| Diethylstilboestrol | DES; Diethylstilbestrol; Stilbestrol | Estrogen Receptor/ERR | Others |
| Dimethyl fumarate | DMF | Keap1-Nrf2 | NF-κB |
| Disulfiram | Tetraethylthiuram disulfide; TETD | Aldehyde Dehydrogenase (ALDH); Apoptosis; Interleukin Related | Apoptosis; Immunology/Inflammation; Metabolic Enzyme/Protease |
| Docetaxel | RP-56976 | Microtubule/Tubulin | Cell Cycle/DNA Damage; Cytoskeleton |
| Doxifluridine | Ro 21-9738; 5-Fluoro-5'-deoxyuridine; 5'-DFUR | Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| Doxorubicin (hydrochloride) | Hydroxydaunorubicin (hydrochloride) | ADC Cytotoxin; AMPK; Autophagy; Mitophagy; Topoisomerase | Antibody-drug Conjugate/ADC Related; Autophagy; Cell Cycle/DNA Damage; Epigenetics; PI3K/Akt/mTOR |
| Dronedarone | SR 33589 | Autophagy; mAChR | Autophagy; GPCR/G Protein; Neuronal Signalling |
| Duvelisib | IPI-145; INK1197 | PI3K | PI3K/Akt/mTOR |
| Emtricitabine | BW1592 | HIV; Reverse Transcriptase | Anti-infection |
| Enasidenib | AG-221 | Isocitrate Dehydrogenase (IDH) | Metabolic Enzyme/Protease |
| Entacapone |  | COMT | Metabolic Enzyme/Protease; Neuronal Signalling |
| Entrectinib | NMS-E628; RXDX-101 | ALK; Autophagy; ROS; Trk Receptor | Autophagy; Neuronal Signalling; Protein Tyrosine Kinase/RTK |
| Epirubicin (hydrochloride) | 4'-Epidoxorubicin hydrochloride | Topoisomerase | Cell Cycle/DNA Damage |
| Erdosteine | RV 144 | NF-κB | NF-κB |
| Erlotinib | CP-358774; NSC 718781; OSI-774 | Autophagy; EGFR | Autophagy; JAK/STAT Signalling; Protein Tyrosine Kinase/RTK |
| Erlotinib (Hydrochloride) | CP-358774 (Hydrochloride); NSC 718781 (Hydrochloride); OSI-774 (Hydrochloride) | Autophagy; EGFR | Autophagy; JAK/STAT Signalling; Protein Tyrosine Kinase/RTK |
| Estramustine (phosphate sodium) |  | Microtubule/Tubulin | Cell Cycle/DNA Damage; Cytoskeleton |
| Ethamsylate |  | Prostaglandin Receptor | GPCR/G Protein |
| Ethynyl Estradiol | 17α-Ethynylestradiol; Ethynylestradiol | Endogenous Metabolite; Estrogen Receptor/ERR | Metabolic Enzyme/Protease; Others |
| Etoposide | VP-16; VP-16-213 | Apoptosis; Autophagy; Mitophagy; Topoisomerase | Apoptosis; Autophagy; Cell Cycle/DNA Damage |
| Ezetimibe | SCH 58235 | Autophagy; Keap1-Nrf2 | Autophagy; NF-κB |
| Fasudil (Hydrochloride) | HA-1077 (Hydrochloride); AT-877 (Hydrochloride) | Autophagy; Calcium Channel; ROCK | Autophagy; Cell Cycle/DNA Damage; Membrane Transporter/Ion Channel; Neuronal Signalling; Stem Cell/Wnt; TGF-beta/Smad |
| Favipiravir | T-705 | DNA/RNA Synthesis | Cell Cycle/DNA Damage |
| Fenofibrate |  | Autophagy; Cytochrome P450; PPAR | Autophagy; Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Fenofibric acid | FNF acid | COX; PPAR | Cell Cycle/DNA Damage; Immunology/Inflammation |
| Fingolimod | FTY720 free base | LPL Receptor; PAK | Cell Cycle/DNA Damage; Cytoskeleton; GPCR/G Protein |
| Floxuridine | 5-Fluorouracil 2'-deoxyriboside | Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| Flubendazole |  | Apoptosis; Microtubule/Tubulin; Parasite | Anti-infection; Apoptosis; Cell Cycle/DNA Damage; Cytoskeleton |
| Fludarabine | F-ara-A; NSC 118218 | DNA/RNA Synthesis; Nucleoside Antimetabolite/Analog; STAT | Cell Cycle/DNA Damage; JAK/STAT Signalling; Stem Cell/Wnt |
| Fluvastatin (sodium) | XU 62320 sodium | Autophagy; HMG-CoA Reductase (HMGCR) | Autophagy; Metabolic Enzyme/Protease |
| Folic acid | Vitamin B9; Vitamin M | DNA/RNA Synthesis; Endogenous Metabolite | Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Forodesine (hydrochloride) | BCX-1777; Immucillin-H hydrochloride | Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| Fostamatinib Disodium | R788(Disodium) | Syk | Protein Tyrosine Kinase/RTK |
| Gefitinib (hydrochloride) | ZD-1839 hydrochloride | EGFR | JAK/STAT Signalling; Protein Tyrosine Kinase/RTK |
| Gemcitabine | NSC 613327; LY188011 | Autophagy; DNA/RNA Synthesis; Nucleoside Antimetabolite/Analog | Autophagy; Cell Cycle/DNA Damage |
| Gemfibrozil | CI-719 | Cytochrome P450; PPAR | Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Glasdegib | PF-04449913 | Smo | Stem Cell/Wnt |
| Glycerol phenylbutyrate | HPN-100 | Others | Others |
| Homoharringtonine | Omacetaxine mepesuccinate; HHT | STAT | JAK/STAT Signalling; Stem Cell/Wnt |
| Hydrocortisone | Cortisol | Endogenous Metabolite; Glucocorticoid Receptor | GPCR/G Protein; Metabolic Enzyme/Protease |
| Hydroxychloroquine sulfate | HCQ sulfate | Autophagy; Parasite; Toll‑like Receptor (TLR) | Anti-infection; Autophagy; Immunology/Inflammation |
| Hydroxyfasudil | HA-1100 | ROCK | Cell Cycle/DNA Damage; Stem Cell/Wnt; TGF-beta/Smad |
| Hydroxyurea | Hydroxycarbamide | Apoptosis; Autophagy; DNA/RNA Synthesis | Apoptosis; Autophagy; Cell Cycle/DNA Damage |
| Ibuprofen | (±)-Ibuprofen | COX | Immunology/Inflammation |
| Idarubicin (hydrochloride) | 4-Demethoxydaunorubicin hydrochloride | Autophagy; Topoisomerase | Autophagy; Cell Cycle/DNA Damage |
| Idelalisib | CAL-101; GS-1101 | Autophagy; PI3K | Autophagy; PI3K/Akt/mTOR |
| Imatinib | STI571; CGP-57148B | Autophagy; Bcr-Abl; c-Kit; PDGFR | Autophagy; Protein Tyrosine Kinase/RTK |
| Indomethacin | Indometacin | Autophagy; COX | Autophagy; Immunology/Inflammation |
| Irinotecan (hydrochloride) | CPT-11 hydrochloride; Camptothecin 11 hydrochloride | Autophagy; Topoisomerase | Autophagy; Cell Cycle/DNA Damage |
| Isotretinoin | 13-cis-Retinoic acid | Autophagy; Endogenous Metabolite; RAR/RXR | Autophagy; Metabolic Enzyme/Protease |
| Ixabepilone | Azaepothilone B; BMS 247550;BMS 247550-1 | Apoptosis; Microtubule/Tubulin | Apoptosis; Cell Cycle/DNA Damage; Cytoskeleton |
| Lamivudine | BCH-189 | HIV; Reverse Transcriptase | Anti-infection |
| Lanatoside C |  | Autophagy | Autophagy |
| Lapatinib | GW572016 | Autophagy; EGFR | Autophagy; JAK/STAT Signalling; Protein Tyrosine Kinase/RTK |
| LCZ696 | Sacubitril mixture with Valsartan | Angiotensin Receptor; JNK; Neprilysin; NF-κB; p38 MAPK | GPCR/G Protein; MAPK/ERK Pathway; Metabolic Enzyme/Protease; NF-κB |
| L-Epinephrine (Bitartrate) | (-)-Epinephrine (+)-bitartrate salt; L-Adrenaline (+)-bitartrate salt | Adrenergic Receptor | GPCR/G Protein; Neuronal Signalling |
| Levoleucovorin (Calcium) | Calcium levofolinate; CL307782 | Antifolate | Cell Cycle/DNA Damage |
| Lidocaine (hydrochloride) | Lignocaine hydrochloride | ERK; MEK; NF-κB; Sodium Channel | MAPK/ERK Pathway; Membrane Transporter/Ion Channel; NF-κB; Stem Cell/Wnt |
| Loperamide (hydrochloride) | R-18553 (hydrochloride) | Autophagy; Opioid Receptor | Autophagy; GPCR/G Protein; Neuronal Signalling |
| Lovastatin | Mevinolin | Autophagy; HMG-CoA Reductase (HMGCR) | Autophagy; Metabolic Enzyme/Protease |
| Melphalan | L-PAM | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Memantine (hydrochloride) | D-145 (hydrochloride) | Autophagy; Cytochrome P450; iGluR | Autophagy; Membrane Transporter/Ion Channel; Metabolic Enzyme/Protease; Neuronal Signalling |
| Metformin (hydrochloride) | 1,1-Dimethylbiguanide hydrochloride | AMPK; Autophagy; Mitophagy | Autophagy; Epigenetics; PI3K/Akt/mTOR |
| Methotrexate | Amethopterin; CL14377;WR19039 | ADC Cytotoxin; Antifolate | Antibody-drug Conjugate/ADC Related; Cell Cycle/DNA Damage |
| Methylthiouracil | MTU | ERK; Interleukin Related; NF-κB; TNF Receptor | Apoptosis; Immunology/Inflammation; MAPK/ERK Pathway; NF-κB; Stem Cell/Wnt |
| Metyrapone | Su-4885 | Autophagy; Cytochrome P450 | Autophagy; Metabolic Enzyme/Protease |
| Mifepristone | RU486; RU 38486 | Autophagy; Glucocorticoid Receptor; Progesterone Receptor | Autophagy; GPCR/G Protein; Others |
| Miltefosine | HePC; Hexadecyl phosphocholine | Akt; HIV | Anti-infection; PI3K/Akt/mTOR |
| Mitomycin C | Ametycine | ADC Cytotoxin; Autophagy; DNA Alkylator/Crosslinker; DNA/RNA Synthesis | Antibody-drug Conjugate/ADC Related; Autophagy; Cell Cycle/DNA Damage |
| Mitoxantrone | Mitozantrone | PKC; Topoisomerase | Cell Cycle/DNA Damage; Epigenetics; TGF-beta/Smad |
| Mizoribine | NSC 289637; HE 69 | HSP | Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Montelukast (sodium) | MK0476 | Autophagy; Leukotriene Receptor | Autophagy; GPCR/G Protein |
| Mycophenolic acid | Mycophenolate | Others | Others |
| Nedaplatin | NSC 375101D | DNA/RNA Synthesis | Cell Cycle/DNA Damage |
| Nefopam (hydrochloride) | Fenazoxine hydrochloride | β-catenin | Stem Cell/Wnt |
| Nelarabine | 506U78; GW 506U78; Nelzarabine | Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| Neratinib | HKI-272 | EGFR | JAK/STAT Signalling; Protein Tyrosine Kinase/RTK |
| Niclosamide | BAY2353 | STAT | JAK/STAT Signalling; Stem Cell/Wnt |
| Nicotinamide | Niacinamide; Nicotinic acid amide; Vitamin B3 | Endogenous Metabolite; Sirtuin | Cell Cycle/DNA Damage; Epigenetics; Metabolic Enzyme/Protease |
| Nifuroxazide |  | STAT | JAK/STAT Signalling; Stem Cell/Wnt |
| Niraparib | MK-4827 | PARP | Cell Cycle/DNA Damage; Epigenetics |
| Nitisinone | NTBC; Nitisone;SC0735 | Reactive Oxygen Species | Immunology/Inflammation; Metabolic Enzyme/Protease; NF-κB |
| Olaparib | AZD2281; KU0059436 | Autophagy; Mitophagy; PARP | Autophagy; Cell Cycle/DNA Damage; Epigenetics |
| Opicapone | BIA 9-1067 | COMT | Metabolic Enzyme/Protease; Neuronal Signalling |
| Orotic acid | 6-Carboxyuracil; Vitamin B13 | Endogenous Metabolite; Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Osalmid | Oxaphenamide; 4'-Hydroxysalicylanilide | HBV | Anti-infection |
| Paclitaxel | Taxol | ADC Cytotoxin; Autophagy; Microtubule/Tubulin | Antibody-drug Conjugate/ADC Related; Autophagy; Cell Cycle/DNA Damage; Cytoskeleton |
| Palbociclib (hydrochloride) | PD 0332991 hydrochloride | CDK | Cell Cycle/DNA Damage |
| Pamidronic acid |  | Wnt; β-catenin | Stem Cell/Wnt |
| Panobinostat | LBH589; NVP-LBH589 | Autophagy; HDAC | Autophagy; Cell Cycle/DNA Damage; Epigenetics |
| Pazopanib | GW786034 | Autophagy; c-Kit; FGFR; PDGFR; VEGFR | Autophagy; Protein Tyrosine Kinase/RTK |
| Pazopanib (Hydrochloride) | GW786034 (Hydrochloride) | Autophagy; c-Fms; c-Kit; FGFR; PDGFR; VEGFR | Autophagy; Protein Tyrosine Kinase/RTK |
| Peficitinib | ASP015K; JNJ-54781532 | JAK | Epigenetics; JAK/STAT Signalling; Stem Cell/Wnt |
| Pemetrexed (disodium hemipenta hydrate) | LY231514 (disodium hemipenta hydrate) | Antifolate; Autophagy | Autophagy; Cell Cycle/DNA Damage |
| Penfluridol | R-16341 | Autophagy; Calcium Channel | Autophagy; Membrane Transporter/Ion Channel; Neuronal Signalling |
| Pexidartinib | PLX-3397 | c-Fms; c-Kit | Protein Tyrosine Kinase/RTK |
| Phenindione | Rectadione | Others | Others |
| Pioglitazone | U 72107 | PPAR | Cell Cycle/DNA Damage |
| Pipobroman |  | Others | Others |
| Pirfenidone | AMR69 | TGF-beta/Smad | Stem Cell/Wnt; TGF-beta/Smad |
| Pixantrone (dimaleate) | BBR 2778 dimaleate | Topoisomerase | Cell Cycle/DNA Damage |
| Podofilox | Podophyllotoxin | Microtubule/Tubulin | Cell Cycle/DNA Damage; Cytoskeleton |
| Ponatinib | AP24534 | Autophagy; Bcr-Abl; FGFR; PDGFR; Src; VEGFR | Autophagy; Protein Tyrosine Kinase/RTK |
| Pralatrexate |  | Antifolate | Cell Cycle/DNA Damage |
| Pranlukast | ONO-1078 | Leukotriene Receptor | GPCR/G Protein |
| Procarbazine (Hydrochloride) |  | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Propranolol (hydrochloride) |  | Adrenergic Receptor; Autophagy | Autophagy; GPCR/G Protein; Neuronal Signalling |
| Pyrimethamine | Pirimecidan; Pirimetamin; RP 4753 | Antifolate; Parasite | Anti-infection; Cell Cycle/DNA Damage |
| Pyrvinium pamoate | Pyrvinium embonate | Wnt | Stem Cell/Wnt |
| Quinapril (hydrochloride) | CI-906 | Angiotensin-converting Enzyme (ACE) | Metabolic Enzyme/Protease |
| Raloxifene (hydrochloride) | LY156758 hydrochloride; LY139481 hydrochloride | Autophagy; Estrogen Receptor/ERR | Autophagy; Others |
| Raltitrexed | ZD1694; D1694; ICI-D1694 | Nucleoside Antimetabolite/Analog; Thymidylate Synthase | Apoptosis; Cell Cycle/DNA Damage |
| Rasagiline (mesylate) | AGN1135 (mesylate); TVP1012 (mesylate) | Autophagy; Monoamine Oxidase | Autophagy; Neuronal Signalling |
| Regorafenib (monohydrate) | BAY 73-4506 monohydrate | Autophagy; PDGFR; Raf; RET; VEGFR | Autophagy; MAPK/ERK Pathway; Protein Tyrosine Kinase/RTK |
| Resveratrol | SRT 501; trans-Resveratrol | Autophagy; IKK; Mitophagy; Sirtuin | Autophagy; Cell Cycle/DNA Damage; Epigenetics; NF-κB |
| Retinoic acid | ATRA; Tretinoin; Vitamin A acid; all-trans-Retinoic acid | Autophagy; Endogenous Metabolite; PPAR; RAR/RXR | Autophagy; Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Ribociclib | LEE011 | CDK | Cell Cycle/DNA Damage |
| Ripasudil | K-115 | ROCK | Cell Cycle/DNA Damage; Stem Cell/Wnt; TGF-beta/Smad |
| Rosiglitazone | BRL 49653 | Autophagy; PPAR; TRP Channel | Autophagy; Cell Cycle/DNA Damage; Membrane Transporter/Ion Channel; Neuronal Signalling |
| Rucaparib (phosphate) | AG-014699 phosphate; PF-01367338 phosphate | PARP | Cell Cycle/DNA Damage; Epigenetics |
| Ruxolitinib | INCB018424 | Autophagy; JAK; Mitophagy | Autophagy; Epigenetics; JAK/STAT Signalling; Stem Cell/Wnt |
| Salicylic acid | 2-Hydroxybenzoic acid | Autophagy; COX; Endogenous Metabolite; Mitophagy | Autophagy; Immunology/Inflammation; Metabolic Enzyme/Protease |
| Selumetinib | AZD6244; ARRY-142886 | MEK | MAPK/ERK Pathway |
| Sertraline (hydrochloride) |  | Serotonin Transporter | Neuronal Signalling |
| Sildenafil | UK-92480 | Autophagy; Phosphodiesterase (PDE) | Autophagy; Metabolic Enzyme/Protease |
| Silibinin | Silybin; Silibinin A; Silymarin I | Autophagy; Reactive Oxygen Species | Autophagy; Immunology/Inflammation; Metabolic Enzyme/Protease; NF-κB |
| Sitagliptin | MK0431 | Autophagy; Dipeptidyl Peptidase | Autophagy; Metabolic Enzyme/Protease |
| Sodium phenylbutyrate | Sodium 4-phenylbutyrate; TriButyrate | Autophagy; HDAC | Autophagy; Cell Cycle/DNA Damage; Epigenetics |
| Sorafenib | Bay 43-9006 | Autophagy; FLT3; Raf; VEGFR | Autophagy; MAPK/ERK Pathway; Protein Tyrosine Kinase/RTK |
| Sulfasalazine | NSC 667219 | Autophagy; NF-κB | Autophagy; NF-κB |
| Sunitinib | SU 11248 | Autophagy; Mitophagy; PDGFR; VEGFR | Autophagy; Protein Tyrosine Kinase/RTK |
| Tacrolimus (monohydrate) | FK506 (monohydrate); Fujimycin (monohydrate); FR900506 (monohydrate) | Autophagy; FKBP; Phosphatase | Apoptosis; Autophagy; Immunology/Inflammation; Metabolic Enzyme/Protease |
| Talazoparib | BMN-673; LT-673 | PARP | Cell Cycle/DNA Damage; Epigenetics |
| Tamoxifen | ICI47699; Z-Tamoxifen; trans-Tamoxifen | Autophagy; Oestrogen Receptor/ERR | Autophagy; Others |
| Taurodeoxychloic Acid (sodium hydrate) | Sodium taurodeoxycholate monohydrate | Apoptosis; Caspase | Apoptosis |
| Tegafur | FT 207; NSC 148958 | Nucleoside Antimetabolite/Analog | Cell Cycle/DNA Damage |
| Telmisartan | BIBR 277 | Angiotensin Receptor; Autophagy | Autophagy; GPCR/G Protein |
| Temozolomide | NSC 362856; CCRG 81045; TMZ | Autophagy; DNA Alkylator/Crosslinker | Autophagy; Cell Cycle/DNA Damage |
| Temsirolimus | CCI-779 | Autophagy; mTOR | Autophagy; PI3K/Akt/mTOR |
| Teniposide | VM26 | Topoisomerase | Cell Cycle/DNA Damage |
| Teprenone | Geranylgeranylacetone | HSP | Cell Cycle/DNA Damage; Metabolic Enzyme/Protease |
| Terazosin (hydrochloride dihydrate) |  | Adrenergic Receptor | GPCR/G Protein; Neuronal Signalling |
| Theophylline | 1,3-Dimethylxanthine; Theo-24 | Adenosine Receptor; Autophagy; Endogenous Metabolite; Phosphodiesterase (PDE) | Autophagy; GPCR/G Protein; Metabolic Enzyme/Protease |
| Thio-TEPA |  | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Tofacitinib (citrate) | Tasocitinib citrate; CP-690550 citrate | JAK | Epigenetics; JAK/STAT Signalling; Stem Cell/Wnt |
| Topotecan (Hydrochloride) | SKF 104864A (Hydrochloride); NSC 609669 (Hydrochloride) | Autophagy; Topoisomerase | Autophagy; Cell Cycle/DNA Damage |
| Trametinib (DMSO solvate) | GSK-1120212 (DMSO solvate); JTP-74057 (DMSO solvate) | MEK | MAPK/ERK Pathway |
| Tranylcypromine (hemisulfate) | dl-Tranylcypromine hemisulfate; trans-2-Phenylcyclopropylamine hemisulfate salt | Histone Demethylase; Monoamine Oxidase | Epigenetics; Neuronal Signalling |
| Triclabendazole | CGA89317 | Microtubule/Tubulin | Cell Cycle/DNA Damage; Cytoskeleton |
| Trifluridine | Trifluorothymidine; 5-Trifluorothymidine; TFT | HSV; Nucleoside Antimetabolite/Analog; Thymidylate Synthase | Anti-infection; Apoptosis; Cell Cycle/DNA Damage |
| Trimethoprim |  | Antifolate | Cell Cycle/DNA Damage |
| Troglitazone | CS-045 | Autophagy; PPAR | Autophagy; Cell Cycle/DNA Damage |
| Troxipide |  | Others | Others |
| Tucidinostat | Chidamide; HBI-8000;CS 055 | HDAC | Cell Cycle/DNA Damage; Epigenetics |
| Upadacitinib | ABT-494 | JAK | Epigenetics; JAK/STAT Signalling; Stem Cell/Wnt |
| VAL-083 | Dianhydrodulcitol; Dianhydrogalactitol | DNA Alkylator/Crosslinker | Cell Cycle/DNA Damage |
| Valproic acid (sodium salt) | Sodium Valproate | Autophagy; HDAC; Mitophagy | Autophagy; Cell Cycle/DNA Damage; Epigenetics |
| Valpromide |  | Others | Others |
| Valrubicin | AD-32 | PKC | Epigenetics; TGF-beta/Smad |
| Vemurafenib | PLX4032; RG7204; RO5185426 | Autophagy; Raf | Autophagy; MAPK/ERK Pathway |
| Venetoclax | ABT-199; GDC-0199 | Autophagy; Bcl-2 Family | Apoptosis; Autophagy |
| Vidarabine | Ara-A; Adenine Arabinoside; 9-β-D-Arabinofuranosyladenine | HSV; Nucleoside Antimetabolite/Analog | Anti-infection; Cell Cycle/DNA Damage |
| Vinblastine (sulfate) | Vincaleukoblastine sulfate salt | Autophagy; Microtubule/Tubulin | Autophagy; Cell Cycle/DNA Damage; Cytoskeleton |
| Vinorelbine (ditartrate) | KW-2307; Nor-5'-anhydrovinblastine ditartrate | Autophagy; Microtubule/Tubulin | Autophagy; Cell Cycle/DNA Damage; Cytoskeleton |
| Vorinostat | SAHA | Autophagy; HDAC; Mitophagy | Autophagy; Cell Cycle/DNA Damage; Epigenetics |
| Zidovudine | Azidothymidine; AZT; ZDV | CRISPR/Cas9; HIV | Anti-infection; Cell Cycle/DNA Damage |

### Supplementary Figures

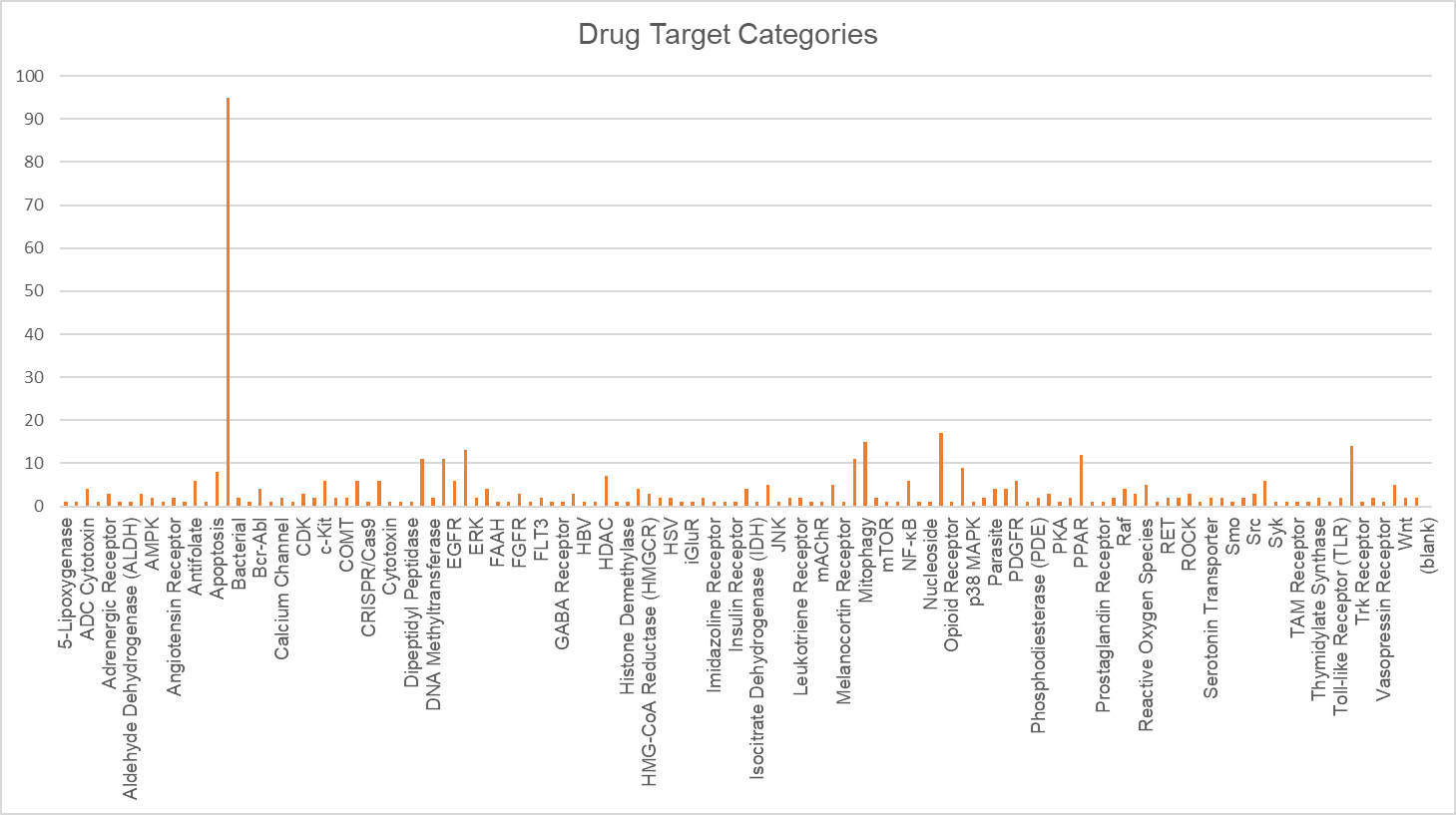
#### Supplementary Fig. 1



**a)**

**b)**

**c)**



**d)**

#### Supplementary Fig. 2

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| 5-Azacytidine | Abemaciclib (methanesulfonate) | Acalabrutinib | Balsalazide | Bendazol |
| Diagram  Description automatically generated | A picture containing outdoor object  Description automatically generated | A picture containing outdoor object, web  Description automatically generated | A picture containing screenshot, diagram, design  Description automatically generated | Icon  Description automatically generated |
| Bexarotene | Bortezomib | Bosutinib | Cabozantinib | Carmofur |
| A picture containing shape  Description automatically generated | A picture containing diagram, design  Description automatically generated | A picture containing outdoor object, honeycomb  Description automatically generated | A picture containing outdoor object  Description automatically generated | Carmofur Chemical Structure |
| Chlorpheniramine (maleate) | Chlorzoxazone | Chromocarb | Clofarabine | Conivaptan (hydrochloride) |
| Diagram  Description automatically generated | Diagram  Description automatically generated | Icon  Description automatically generated | Clofarabine Chemical Structure | A picture containing honeycomb  Description automatically generated |

Note this figure continues onto the following page

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Erlotinib | Dexamethasone | Diethylstilboestrol | Dimethyl fumarate | Dronedarone |
| Erlotinib Chemical Structure | Diagram  Description automatically generated | Diethylstilbestrol Chemical Structure | Dimethyl fumarate Chemical Structure | A picture containing map, text  Description automatically generated |
| Ethynyl estradiol | Methylthiouracil | Metyrapone | Nefopam (hydrochloride) | Nelarabine |
| Shape, arrow  Description automatically generated | Methylthiouracil Chemical Structure | Icon  Description automatically generated | A picture containing sketch, symmetry, diagram, design  Description automatically generated | Nelarabine Chemical Structure |
| Niraparib | Osalmid | Penfluridol | Sodium 4-phenylbutyrate | Topotecan (Hydrochloride) |
| Niraparib Chemical Structure |  | Penfluridol Chemical Structure | Icon  Description automatically generated | A picture containing diagram  Description automatically generated |

#### Supplementary Fig. 3

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Aspirin | Cabozantinib | Carmofur | Chlorpheniramine (maleate) | Ethynyl estradiol |
| Shape  Description automatically generated | A picture containing outdoor object  Description automatically generated | A picture containing diagram  Description automatically generated | Diagram  Description automatically generated | A picture containing diagram, design  Description automatically generated |
| Levonorgestrel | Metyrapone | Penfluridol | Diethylstilboestrol | Sodium 4-phenylbutyrate |
| Diagram, icon  Description automatically generated | Icon  Description automatically generated | A picture containing outdoor object  Description automatically generated | Shape  Description automatically generated | Icon  Description automatically generated |

#### Supplementary Fig. 4

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Atorvastatin  (hemicalcium salt) | Chlorambucil | Cobimetinib | Doxorubicin (hydrochloride) | Gemfibrozil |
| Shape  Description automatically generated | Diagram  Description automatically generated | A picture containing outdoor object  Description automatically generated | A picture containing honeycomb  Description automatically generated | Shape, arrow  Description automatically generated |
| Homoharringtonine | Imatinib | Tucidinostat |  |  |
| Shape  Description automatically generated | A picture containing honeycomb, outdoor object  Description automatically generated | Shape, arrow  Description automatically generated |  |  |

#### Supplementary Fig. 5

A picture containing text, screenshot, line, font

Description automatically generated

#### Supplementary Fig. 6

Chart

Description automatically generated