**Figure S1:** Doxorubicininhibition of cellular proliferation



**Figure S1:** Doxorubicincellular toxicity



**Table S1:** *Euphorbia ingens* compounds drug candidate test

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **S/N** | **Compound** | **MF** | **MW**  **(g/mol)** | **HBD** | **HBA** | **Mol**  **LogP** | **Lipinski’s**  **Rule**  **(Violation)** | **BBB** | **CYP**  **2D6** | **CYP**  **3A4** | **TPSA** |
|  | 1-Decene | C10H20 | 140.27 | 0 | 0 | 4.68 | Yes; 1 | yes | No | No | 0 |
|  | (1R,7S,E)-7-Isopropyl-4,10-dimethylenecyclodec-5-enol | C15H24O | 220.35 | 1 | 1 | 3.46 | Yes; 0 | yes | No | No | 20.23 |
|  | 11-Oxoandrosterone | C19H28O3 | 304.4 | 1 | 3 |  | Yes; 0 | yes | No | No | 54.37 |
|  | 17.beta.-Hydroxy-6.alpha.-pentyl-4-nor-3,5-secoandrostan-3-oic acid, methyl ester | C24H42O3 | 378.6 | 1 | 3 | 2.71 | Yes; 1 | yes | No | No | 46.53 |
|  | 1-Dodecene | C12H24 | 168.32 | 0 | 0 | 5.25 | Yes; 1 | No | No | No | 0 |
|  | 1-Heneicosanol | C21H44O | 312.6 | 1 | 1 | 5.62 | Yes; 1 | No | No | No | 20.23 |
|  | 1-Octadecene | C18H36 | 252.5 | 0 | 0 | 6.77 | Yes; 1 | No | No | No | 0 |
|  | 1-Tridecene | C13H26 | 182.35 | 0 | 0 | 5.52 | Yes; 1 | No | No | No | 0 |
|  | 2,4-Di-tert-butylphenol | C14H22O | 206.32 | 1 | 1 | 3.87 | Yes; 0 | yes | No | No | 20.23 |
|  | 2-Bornanol | C10H18O | 154.25 | 1 | 1 | 4.73 | Yes; 0 | yes | No | No | 20.23 |
|  | 6-Pentylidene-4,5-secoandrostane-4,17.beta.-diol | C24H42O2 | 362.6 | 2 | 2 | 2.45 | Yes; 1 | yes | yes | No | 40.46 |
|  | Andrographolide | C20H30O5 | 350.4 | 3 | 5 | 1.98 | yes 0 | No | No | No | 86.99 |
|  | Bicyclo[3.1.1]hept-3-en-2-one | C7H8O | 108.14 | 0 | 1 | 1.24 | yes 0 | yes | No | No | 17.07 |
|  | Bicyclo[3.1.1]heptan-3-ol | C7H12O | 112.17 | 1 | 1 | 1.49 | yes 0 | yes | No | No | 20.23 |
|  | Ferruginol | C20H30O | 286.5 | 1 | 1 | 4.92 | Yes; 1 | yes | yes | No | 20.23 |
|  | Octadecyl trifluoroacetate | C20H37F3O2 | 366.5 | 0 | 5 | 5.47 | Yes; 1 | No | No | No | 26.30 |
|  | Prasterone | C19H28O2 | 288.4 | 1 | 2 | 3.59 | yes 0 | yes | No | No | 37.3 |
|  | Squalene | C30H50 | 410.7 | 0 | 0 | 3.59 | yes 0 | No | No | No | 0 |

**Table S2:** *E. ingens* compounds targets

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **S/N** | **Compound** | **Targets** | | **Total** |
|  |  | **Swiss TargetPrediction** | **BindingDB** |  |
|  | 1-Dodecene | - | - | 0 |
|  | 1-Heneicosanol | TRPM8, CA2, CA1, CA4, AR, ESR1, SHBG, NR1I3, NR1H4, UGT2B7, GPBAR1, CDC25B, CDC25A, ESR2, CNR1, POLA1, HSD11B1, SHH, ACHE, SQLE, CNR2, FAAH | - | 22 |
|  | 1-Octadecene | ACACB, CYP24A1, SLC6A4 | - | 3 |
|  | 1-Tridecene | - | - | 0 |
|  | Octadecyl trifluoroacetate | ACHE | - | 1 |
|  | Squalene | CNR2, SQLE, PPARA, BACE1, PTGES | MAOB | 6 |
|  | Andrographolide | PRKCA, TTL, PRKCD, IL6, ADAM17, GLUL, GPBAR1, FABP1, AR, PDCD4, EPHX2, WEE1, POLA1, JAK1, SLC5A4, SLC5A1, BRD4, CREBBP, PYGL, DPP4, PRKCE, IMPDH1, IMPDH2, PDE10A, PGR, CDK2, CDK1, LRRK2, GABRB3 GABRA3 GABRG2, GABRB3 GABRG2 GABRA1, GABRB3 GABRG2 GABRA5,  GABRA2 GABRB3 GABRG2, ROCK2, ROCK1, OPRM1, NR3C2, CA7, CA12, CHEK1, ERN1, MKNK2, CDC42BPA, G6PD, JAK2, MAP2K1, MMP9, ACVRL1, ITGAL, ICAM1, ITGB2, CDK9, CHRNA4 | PRKCA, TTL, PRKCD, NR1H4, PRKCE | 55 |
|  |  |  |  | **87** |

**Table S4:** *Euphorbia ingens*-prostate cancer common genes

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **S/N** | **Symbol** | **Entrez** | **Species** | **Description** |
|  | CNR2 | 1269 | Human | cannabinoid receptor 2 |
|  | FAAH | 2166 | Human | fatty acid amide hydrolase |
|  | JAK1 | 3716 | Human | Janus kinase 1 |
|  | NR1I3 | 9970 | Human | nuclear receptor subfamily 1 group I member 3 |
|  | GLUL | 2752 | Human | glutamate-ammonia ligase |
|  | HSD11B1 | 3290 | Human | hydroxysteroid 11-beta dehydrogenase 1 |
|  | CDC42BPA | 8476 | Human | CDC42 binding protein kinase alpha |
|  | ADAM17 | 6868 | Human | ADAM metallopeptidase domain 17 |
|  | ROCK2 | 9475 | Human | Rho associated coiled-coil containing protein kinase 2 |
|  | PRKCE | 5581 | Human | protein kinase C epsilon |
|  | FABP1 | 2168 | Human | fatty acid binding protein 1] |
|  | TTL | 150465 | Human | tubulin tyrosine ligase |
|  | DPP4 | 1803 | Human | dipeptidyl peptidase 4 |
|  | TRPM8 | 79054 | Human | transient receptor potential cation channel subfamily M member 8 |
|  | CDC25A | 993 | Human | cell division cycle 25A |
|  | IMPDH2 | 3615 | Human | inosine monophosphate dehydrogenase 2 |
|  | PRKCD | 5580 | Human | protein kinase C delta |
|  | UGT2B7 | 7364 | Human | UDP glucuronosyltransferase family 2 member B7 |
|  | NR3C2 | 4306 | Human | nuclear receptor subfamily 3 group C member 2 |
|  | CNR1 | 1268 | Human | cannabinoid receptor 1 |
|  | ESR1 | 2099 | Human | estrogen receptor 1 |
|  | OPRM1 | 4988 | Human | opioid receptor mu 1 |
|  | PDE10A | 10846 | Human | phosphodiesterase 10A |
|  | IL6 | 3569 | Human | interleukin 6 |
|  | ACHE | 43 | Human | acetylcholinesterase (Cartwright blood group)] |
|  | SHH | 6469 | Human | sonic hedgehog signaling molecule |
|  | EPHX2 | 2053 | Human | epoxide hydrolase 2 |
|  | CA1 | 759 | Human | carbonic anhydrase 1 |
|  | CA2 | 760 | Human | carbonic anhydrase 2 |
|  | SQLE | 6713 | Human | squalene epoxidase |
|  | JAK2 | 3717 | Human | Janus kinase 2 |
|  | CDK9 | 1025 | Human | cyclin dependent kinase 9 |
|  | PTGES | 9536 | Human | prostaglandin E synthase |
|  | CDK1 | 983 | Human | cyclin dependent kinase 1 |
|  | PDCD4 | 27250 | Human | programmed cell death 4 |
|  | WEE1 | 7465 | Human | WEE1 G2 checkpoint kinase |
|  | PGR | 5241 | Human | progesterone receptor |
|  | BACE1 | 23621 | Human | beta-secretase 1 |
|  | CHEK1 | 1111 | Human | checkpoint kinase 1 |
|  | ACVRL1 | 94 | Human | activin A receptor like type 1 |
|  | CDK2 | 1017 | Human | cyclin dependent kinase 2 |
|  | NR1H4 | 9971 | Human | nuclear receptor subfamily 1 group H member 4 |
|  | ACACB | 32 | Human | acetyl-CoA carboxylase beta |
|  | PYGL | 5836 | Human | glycogen phosphorylase L |
|  | ESR2 | 2100 | Human | estrogen receptor 2 |
|  | CA12 | 771 | Human | carbonic anhydrase 12 |
|  | MAP2K1 | 5604 | Human | mitogen-activated protein kinase kinase 1 |
|  | CREBBP | 1387 | Human | CREB binding protein |
|  | SHBG | 6462 | Human | sex hormone binding globulin |
|  | SLC6A4 | 6532 | Human | solute carrier family 6 member 4 |
|  | CA4 | 762 | Human | carbonic anhydrase 4 |
|  | ERN1 | 2081 | Human | endoplasmic reticulum to nucleus signaling 1 |
|  | PRKCA | 5578 | Human | protein kinase C alpha |
|  | ROCK1 | 6093 | Human | Rho associated coiled-coil containing protein kinase 1 |
|  | MKNK2 | 2872 | Human | MAPK interacting serine/threonine kinase 2 |
|  | BRD4 | 23476 | Human | bromodomain containing 4 |
|  | CDC25B | 994 | Human | cell division cycle 25B |
|  | MMP9 | 4318 | Human | matrix metallopeptidase 9 |
|  | CYP24A1 | 1591 | Human | cytochrome P450 family 24 subfamily A member 1 |
|  | SLC5A1 | 6523 | Human | solute carrier family 5 member 1 |
|  | PPARA | 5465 | Human | peroxisome proliferator activated receptor alpha |
|  | POLA1 | 5422 | Human | DNA polymerase alpha 1, catalytic subunit |
|  | MAOB | 4129 | Human | monoamine oxidase B |
|  | AR | 367 | Human | androgen receptor |
|  | G6PD | 2539 | Human | glucose-6-phosphate dehydrogenase |