**Supplementary Information**

**Identifying Potential Monkeypox Virus Inhibitors: An *In Silico* Study Targeting the A42R Protein**

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Table S1: Docking scores from Autodock Vina and OSIRIS DataWarrior toxicity predictions of shortlisted compounds from TCM, AfroDB, and PubChem that passed ADME predictions. MPXV inhibitor, tecovirimat is included in the table. Table cells are labeled “None” in green, “Low” in yellow, and “High” in red for the toxicity prediction from DataWarrior 5.5.0.

Table S2: Summary of important biological activity predictions for seven potential lead compounds A) ZINC000000899909, B) ZINC000001632866, C) ZINC000015151344, D) ZINC000013378519, E) ZINC000000086470, F) ZINC000095486204, and G) PC11371962 from Prediction of Activity Spectra of Substances (PASS). Pa is potential for activity and Pi is potential of inactivity.

**Supplementary Figures**

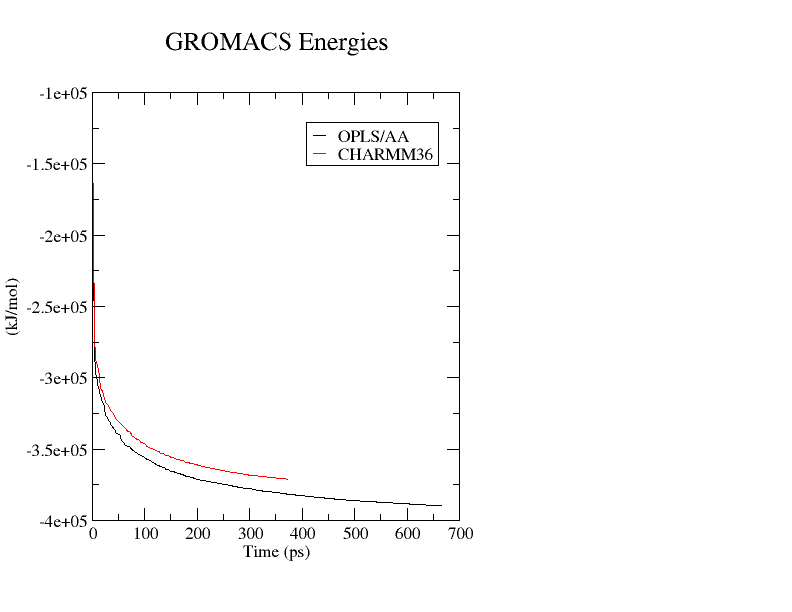


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A)



B)



C)



D)



E)



F)



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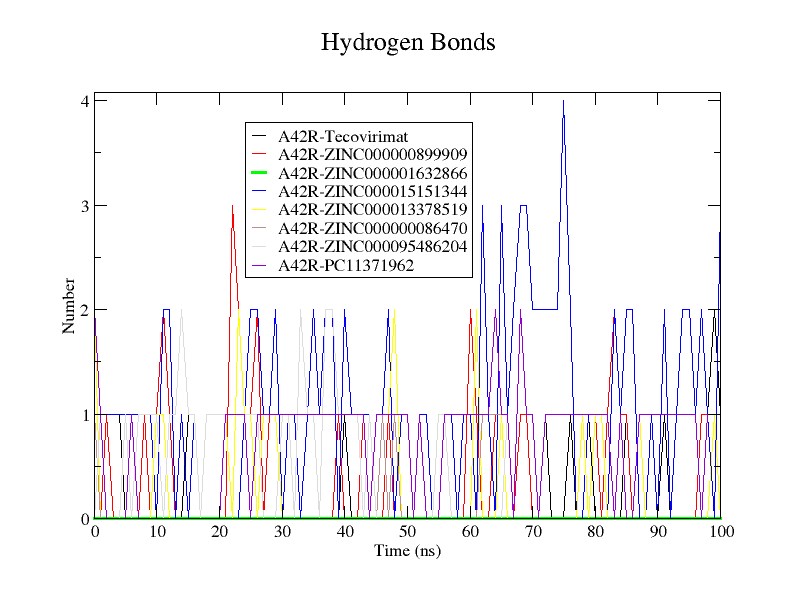
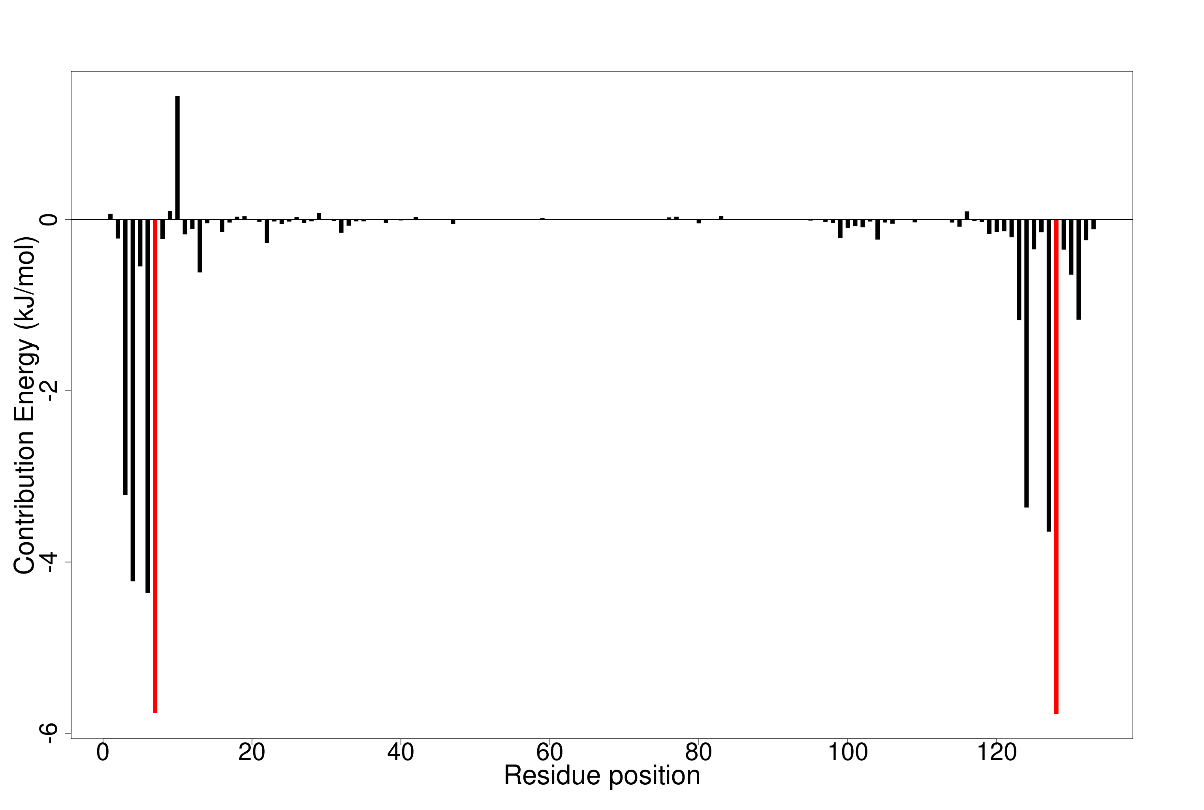


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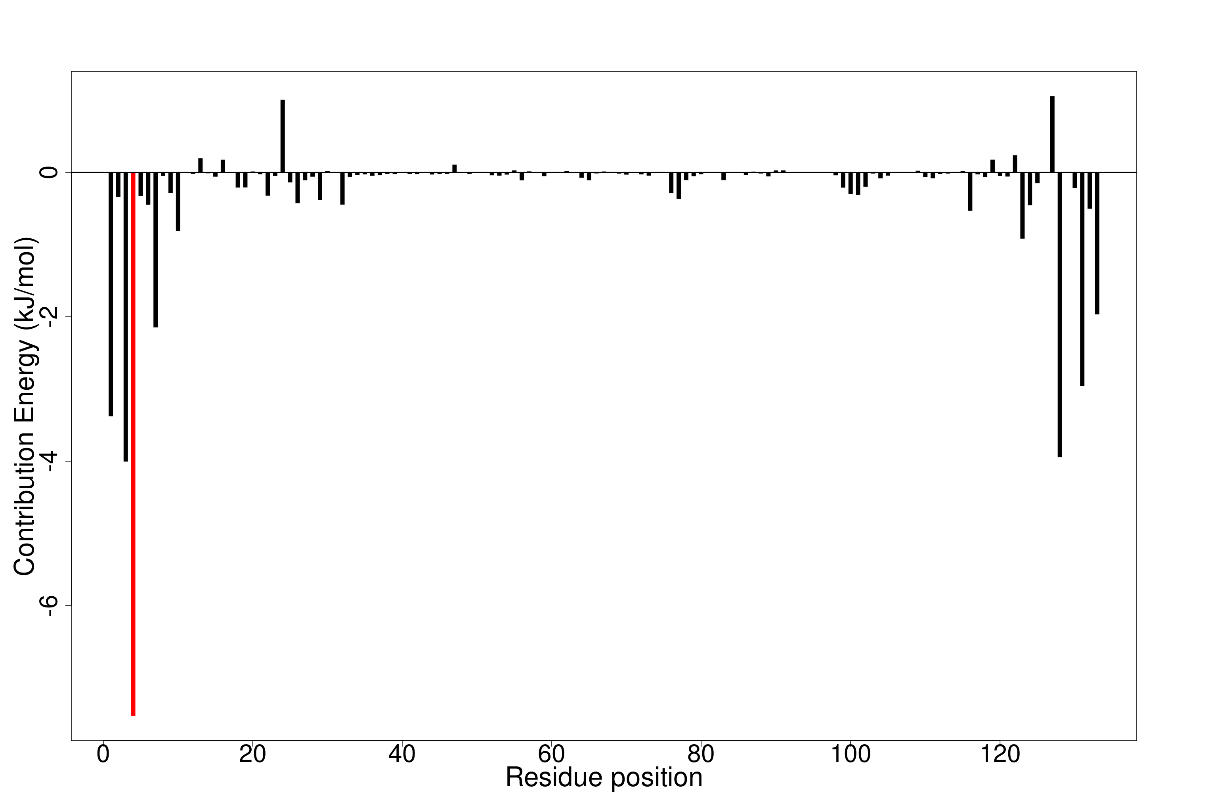
A)



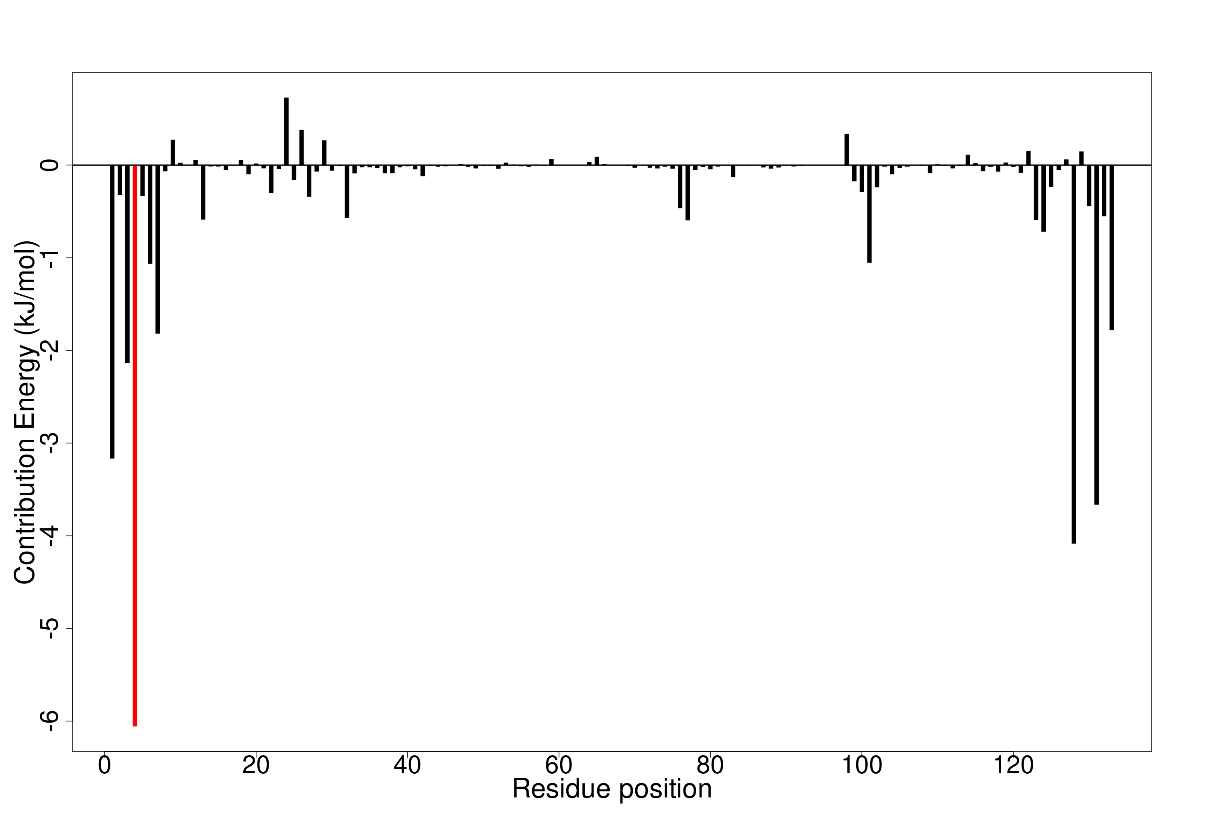
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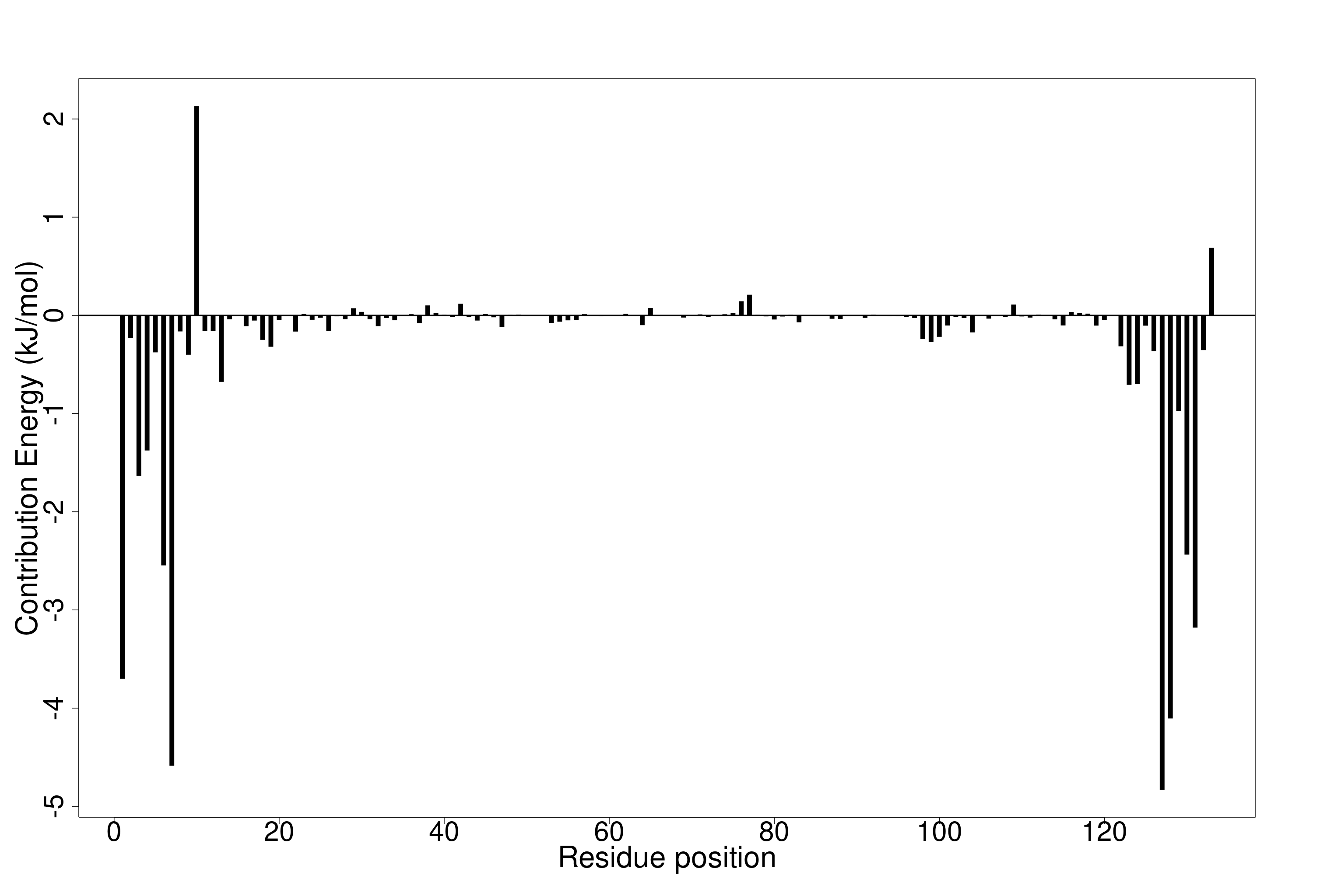
C)



D)



E)



F)

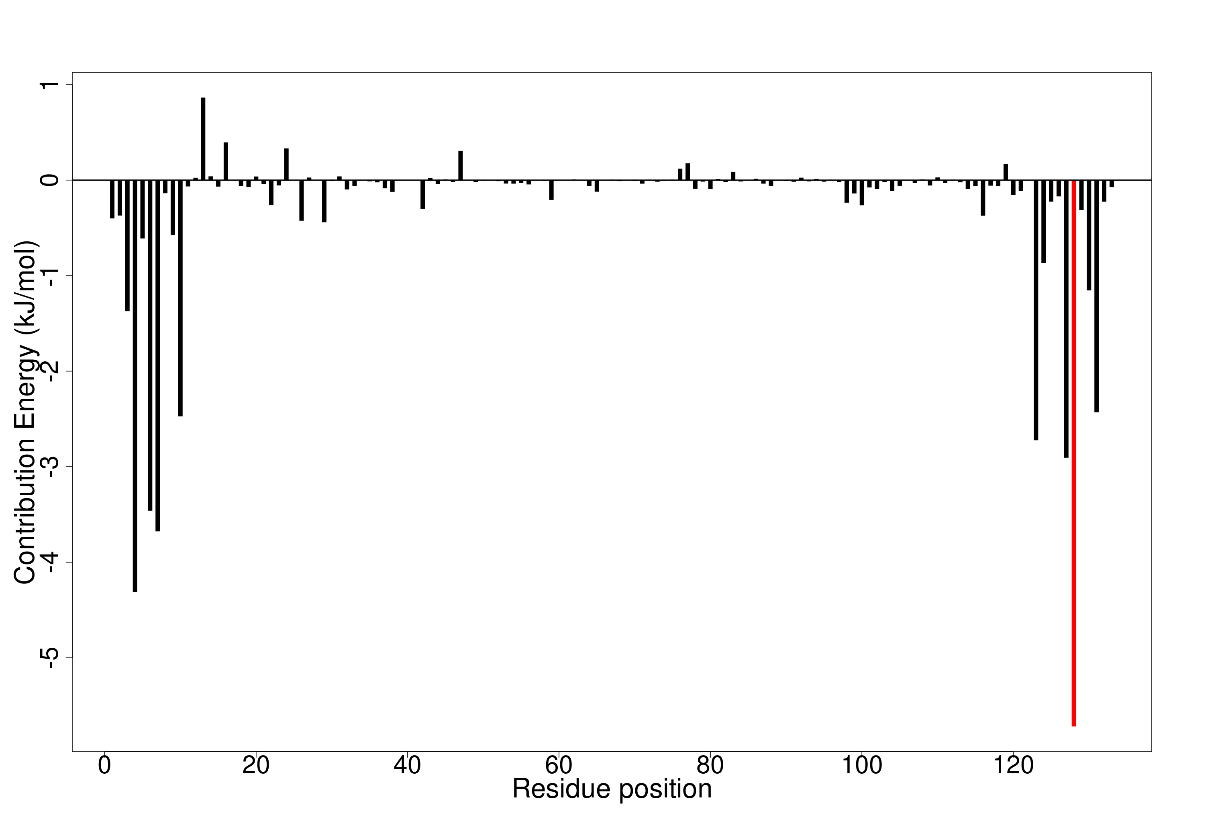


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**Supplementary Tables**

Table S1: Docking scores from Autodock Vina and OSIRIS DataWarrior toxicity predictions of shortlisted compounds from TCM, AfroDB, and PubChem that passed ADME predictions. MPXV inhibitor, tecovirimat is included in the table. Table cells are labeled “None” in green, “Low” in yellow, and “High” in red for the toxicity prediction from DataWarrior 5.5.0.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Compound** | **Binding Energy (kcal/mol)** | **Mutagenic** | **Tumorigenic** | **Reproductive Effective** | **Irritant** |
| ZINC000095486204 | -8.3 | none | high | low | none |
| ZINC000013378519 | -8.1 | none | none | none | none |
| ZINC000001632866 | -8 | low | high | none | none |
| ZINC000015151344 | -7.9 | none | none | none | none |
| ZINC000000899909 | -7.8 | none | none | high | none |
| ZINC000095909830 | -7.8 | none | none | none | none |
| ZINC000095913878 | -7.8 | none | none | none | none |
| ZINC000000689683 | -7.7 | none | none | none | none |
| ZINC000000897930 | -7.7 | none | none | none | none |
| ZINC000013375730 | -7.7 | none | none | high | none |
| ZINC000028702248 | -7.7 | low | high | high | high |
| ZINC000059589174 | -7.7 | none | none | high | none |
| ZINC000085594093 | -7.6 | low | none | high | high |
| ZINC000000086470 | -7.6 | none | none | high | none |
| ZINC000000134782 | -7.4 | none | none | none | none |
| ZINC000031852149 | -7.3 | none | high | none | high |
| ZINC000095485910 | -7.3 | high | high | none | none |
| Pub11371962 | -7.2 | none | none | high | none |
| ZINC000048998695 | -7.2 | none | none | none | none |
| ZINC000095486327 | -7.1 | none | high | none | none |
| ZINC000014557836 | -7 | none | none | none | none |
| ZINC000038658035 | -7 | none | none | none | none |
| Pub11360575 | -7 | none | none | low | none |
| Pub129016384 | -7 | none | none | high | none |
| Tecovirimat | -6.7 | none | none | high | none |

Table S2: Summary of important biological activity predictions for seven potential lead compounds A) ZINC000000899909, B) ZINC000001632866, C) ZINC000015151344, D) ZINC000013378519, E) ZINC000000086470, F) ZINC000095486204, and G) PC11371962 from Prediction of Activity Spectra of Substances (PASS). Pa is potential for activity and Pi is potential of inactivity.

**A**.

|  |  |  |
| --- | --- | --- |
| **ZINC000000899909** | | |
| Activity | Pa | Pi |
| RELA expression inhibitor | 0,623 | 0,003 |
| JAK2 expression inhibitor | 0,527 | 0,047 |
| Anticarcinogenic | 0,470 | 0,022 |
| HCV IRES inhibitor | 0,437 | 0,017 |
| APOA1 expression enhancer | 0,443 | 0,047 |
| Pin1 inhibitor | 0,361 | 0,112 |
| Topoisomerase I inhibitor | 0,272 | 0,018 |
| Topoisomerase II inhibitor | 0,147 | 0,035 |
| RNA directed DNA polymerase inhibitor | 0,275 | 0,038 |
| DNA directed RNA polymerase inhibitor | 0,209 | 0,033 |
| Antiviral (Herpes) | 0,438 | 0,021 |
| Antiviral (Rhinovirus) | 0,383 | 0,111 |
| Antiviral (Hepatitis B) | 0,212 | 0,075 |
| Viral entry inhibitor | 0,217 | 0,098 |
| Antiviral (HIV) | 0,132 | 0,090 |
| Antiviral | 0,164 | 0,142 |
| HIV-2 reverse transcriptase inhibitor | 0,217 | 0,027 |
| HIV-1 integrase inhibitor | 0,082 | 0,065 |

**B**.

|  |  |  |
| --- | --- | --- |
| **ZINC000001632866** | | |
| Activity | Pa | Pi |
| JAK2 expression inhibitor | 0,860 | 0,004 |
| Vasoprotector | 0,748 | 0,008 |
| Lipoprotein lipase inhibitor | 0,444 | 0,060 |
| RELA expression inhibitor | 0,493 | 0,012 |
| Pin1 inhibitor | 0,661 | 0,011 |
| Antiviral (Picornavirus) | 0,459 | 0,071 |
| Antiviral (Adenovirus) | 0,387 | 0,035 |
| Antiviral (CMV) | 0,299 | 0,030 |
| Antiviral (Poxvirus) | 0,315 | 0,052 |
| Viral entry inhibitor | 0,267 | 0,019 |
| Antiviral (Influenza) | 0,309 | 0,083 |
| Antiviral (Herpes) | 0,303 | 0,089 |
| Antiviral (Parainfluenza) | 0,059 | 0,015 |
| Antiviral (Rhinovirus) | 0,295 | 0,265 |
| HIV-2 reverse transcriptase inhibitor | 0,320 | 0,007 |
| HIV-1 integrase (Overall Integration) inhibitor | 0,205 | 0,013 |
| HIV fusion inhibitor | 0,019 | 0,003 |
| HCV IRES inhibitor | 0,292 | 0,096 |
| DNA directed DNA polymerase inhibitor | 0,132 | 0,052 |
| DNA polymerase I inhibitor | 0,243 | 0,167 |
| RNA-directed RNA polymerase inhibitor | 0,446 | 0,026 |

**C.**

|  |  |  |
| --- | --- | --- |
| **ZINC000015151344** | | |
| Activity | Pa | Pi |
| JAK2 expression inhibitor | 0,796 | 0,008 |
| Pin1 inhibitor | 0,636 | 0,013 |
| Vasoprotector | 0,607 | 0,019 |
| RELA expression inhibitor | 0,468 | 0,016 |
| RNA-directed RNA polymerase inhibitor | 0,414 | 0,043 |
| APOA1 expression enhancer | 0,420 | 0,059 |
| Antiviral (Adenovirus) | 0,381 | 0,037 |
| Antiviral (Influenza) | 0,388 | 0,050 |
| Antiviral (Picornavirus) | 0,386 | 0,121 |
| Antiviral (Herpes) | 0,322 | 0,077 |
| HCV IRES inhibitor | 0,315 | 0,072 |
| Antiviral (CMV) | 0,228 | 0,115 |
| Viral entry inhibitor | 0,214 | 0,109 |
| Antiviral (Poxvirus) | 0,215 | 0,136 |
| Antiviral (Hepatitis B) | 0,183 | 0,110 |
| Antiviral (HIV) | 0,133 | 0,088 |
| Antiviral (Rhinovirus) | 0,296 | 0,262 |
| Antiviral | 0,161 | 0,146 |
| HIV-2 reverse transcriptase inhibitor | 0,248 | 0,018 |
| HIV-1 integrase (Strand Transfer) inhibitor | 0,137 | 0,016 |
| HIV-1 integrase (3'-Processing) inhibitor | 0,134 | 0,017 |
| HIV-1 integrase inhibitor | 0,116 | 0,025 |
| HIV-1 integrase (Overall Integration) inhibitor | 0,105 | 0,055 |

**D.**

|  |  |  |
| --- | --- | --- |
| **ZINC000013378519** | | |
| Activity | Pa | Pi |
| JAK2 expression inhibitor | 0,902 | 0,003 |
| Pin1 inhibitor | 0,575 | 0,023 |
| Vasoprotector | 0,544 | 0,029 |
| Anticarcinogenic | 0,355 | 0,040 |
| Topoisomerase I inhibitor | 0,175 | 0,043 |
| RNA directed DNA polymerase inhibitor | 0,221 | 0,069 |
| DNA polymerase I inhibitor | 0,247 | 0,157 |
| RELA expression inhibitor | 0,544 | 0,006 |
| Topoisomerase II inhibitor | 0,146 | 0,035 |
| Antiviral (Herpes) | 0,316 | 0,080 |
| Viral entry inhibitor | 0,231 | 0,063 |
| Antiviral (Influenza) | 0,233 | 0,152 |
| HIV-1 integrase inhibitor | 0,110 | 0,030 |
| Antiviral (Hepatitis B) | 0,176 | 0,122 |
| HIV-1 integrase (Overall Integration) inhibitor | 0,146 | 0,028 |
| HIV-2 reverse transcriptase inhibitor | 0,156 | 0,060 |
| HIV-1 integrase (3'-Processing) inhibitor | 0,099 | 0,026 |
| HIV-1 integrase (Strand Transfer) inhibitor | 0,084 | 0,033 |

**E.**

|  |  |  |
| --- | --- | --- |
| **ZINC000000086470** | | |
| Activity | Pa | Pi |
| RELA expression inhibitor | 0,647 | 0,003 |
| Antiviral (Rhinovirus) | 0,568 | 0,009 |
| Anticarcinogenic | 0,553 | 0,015 |
| Antiviral (Herpes) | 0,452 | 0,018 |
| RNA directed DNA polymerase inhibitor | 0,421 | 0,016 |
| JAK2 expression inhibitor | 0,398 | 0,086 |
| Viral entry inhibitor | 0,297 | 0,007 |
| Antiviral (Influenza) | 0,343 | 0,067 |
| Antiviral (Hepatitis B) | 0,308 | 0,031 |
| Topoisomerase I inhibitor | 0,285 | 0,016 |
| Pin1 inhibitor | 0,360 | 0,113 |
| DNA directed RNA polymerase inhibitor | 0,235 | 0,027 |
| Vasoprotector | 0,319 | 0,137 |
| Topoisomerase II inhibitor | 0,123 | 0,046 |
| Antiviral | 0,158 | 0,152 |

**F.**

|  |  |  |
| --- | --- | --- |
| **ZINC000095486204** | | |
| Activity | Pa | Pi |
| JAK2 expression inhibitor | 0,620 | 0,029 |
| DNA polymerase I inhibitor | 0,553 | 0,005 |
| Pin1 inhibitor | 0,490 | 0,045 |
| RELA expression inhibitor | 0,370 | 0,047 |
| APOA1 expression enhancer | 0,362 | 0,104 |
| RNA directed DNA polymerase inhibitor | 0,264 | 0,043 |
| Vasoprotector | 0,326 | 0,129 |
| Viral entry inhibitor | 0,228 | 0,070 |
| DNA directed DNA polymerase inhibitor | 0,141 | 0,043 |
| Cancer associated disorders treatment | 0,257 | 0,162 |
| Anticarcinogenic | 0,190 | 0,132 |
| Topoisomerase I inhibitor | 0,113 | 0,084 |

**G.**

|  |  |  |
| --- | --- | --- |
| **PC11371962** | | |
| Activity | Pa | Pi |
| RNA-directed RNA polymerase inhibitor | 0,393 | 0,059 |
| DNA polymerase I inhibitor | 0,344 | 0,034 |
| Topoisomerase I inhibitor | 0,280 | 0,017 |
| Vasoprotector | 0,319 | 0,137 |
| 3C-like protease (Human coronavirus) inhibitor | 0,247 | 0,080 |
| Antiviral (Hepatitis) | 0,146 | 0,037 |
| JAK2 expression inhibitor | 0,263 | 0,164 |
| Pin1 inhibitor | 0,269 | 0,201 |
| RELA expression inhibitor | 0,222 | 0,199 |