Approach 1: We select overlapping features between PKM2 and ERK2 with p-value <0.05. Additional features with lowest p-value for PKM2 and ERK2 individually without presence in overlapping list are also provided.

|  |  |  |
| --- | --- | --- |
| Overlapping Features | Additional PKM2 | Additional ERK2 |
| NumAromaticRings | FpDensityMorgan1 | Chi4v |
| RingCount | SMR\_VSA9 | AvgIpc |
| fr\_thiazole | MolLogP | Chi3v |
| BertzCT | fr\_nitro | PEOE\_VSA3 |
| BalabanJ | fr\_nitro\_arom | Chi2v |
| SlogP\_VSA3 | VSA\_EState6 | NumHAcceptors |
| SlogP\_VSA5 | NumAromaticCarbocycles | BCUT2D\_MWHI |
| HeavyAtomMolWt | fr\_benzene | VSA\_EState1 |
| SlogP\_VSA6 | fr\_amide | NumHeteroatoms |
| VSA\_EState5 | SlogP\_VSA10 | VSA\_EState9 |
| fr\_C\_O | EState\_VSA7 | EState\_VSA6 |
| fr\_C\_O\_noCOO |  | BCUT2D\_MRHI |
| MolWt |  | fr\_sulfonamd |
| ExactMolWt |  | fr\_thiophene |
| FractionCSP3 |  | PEOE\_VSA5 |
| Ipc |  |  |
| SlogP\_VSA8 |  |  |
| LabuteASA |  |  |
| PEOE\_VSA4 |  |  |

Approach 2: We distinguish between kinase inhibition for PKM2 and ERK2 individually. We simply evaluate per column (0 vs. 1) based on the features that detect the largest difference between kinase inhibition or no inhibition. Yellow = 20 most relevant features. Blue = more features with p < 0.05.

|  |  |
| --- | --- |
| Features for PKM2 | Features for ERK2 |
| NumAromaticRings | FpDensityMorgan1 |
| RingCount | SMR\_VSA9 |
| fr\_thiazole | SlogP\_VSA6 |
| BertzCT | SlogP\_VSA8 |
| BalabanJ | NumAromaticRings |
| Chi4v | RingCount |
| AvgIpc | MolLogP |
| Chi3v | fr\_C\_O |
| PEOE\_VSA3 | fr\_C\_O\_noCOO |
| Chi2v | fr\_nitro |
| NumHAcceptors | fr\_nitro\_arom |
| BCUT2D\_MWHI | PEOE\_VSA4 |
| VSA\_EState1 | VSA\_EState6 |
| NumHeteroatoms | SlogP\_VSA5 |
| VSA\_EState9 | NumAromaticCarbocycles |
| EState\_VSA6 | fr\_benzene |
| BCUT2D\_MRHI | fr\_thiazole |
| fr\_sulfonamd | fr\_amide |
| fr\_thiophene | VSA\_EState5 |
| PEOE\_VSA5 | SlogP\_VSA10 |
| SlogP\_VSA3 | EState\_VSA7 |
| Chi1v | SlogP\_VSA3 |
| SMR\_VSA10 | BertzCT |
| BCUT2D\_MWLOW | BCUT2D\_LOGPHI |
| SlogP\_VSA5 | SMR\_VSA7 |
| NumHDonors | BalabanJ |
| NHOHCount | FpDensityMorgan2 |
| HeavyAtomMolWt | SMR\_VSA5 |
| NumAromaticHeterocycles | EState\_VSA2 |
| SlogP\_VSA6 | Ipc |
| VSA\_EState5 | MolMR |
| EState\_VSA3 | HeavyAtomMolWt |
| fr\_C\_O | fr\_aniline |
| fr\_C\_O\_noCOO | fr\_aryl\_methyl |
| fr\_furan | fr\_alkyl\_halide |
| MolWt | FractionCSP3 |
| ExactMolWt | MolWt |
| FractionCSP3 | ExactMolWt |
| BCUT2D\_MRLOW | Chi1 |
| VSA\_EState10 | fr\_Ar\_NH |
| Ipc | fr\_Nhpyrrole |
| PEOE\_VSA1 | LabuteASA |
| NOCount | EState\_VSA4 |
| PEOE\_VSA14 |  |
| MinEStateIndex |  |
| SlogP\_VSA12 |  |
| VSA\_EState2 |  |
| SlogP\_VSA1 |  |
| Chi0v |  |
| SlogP\_VSA8 |  |
| LabuteASA |  |
| PEOE\_VSA4 |  |