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Design of Targeted Inhibitors of Polo-like Kinase 1 (Plk1) D.S. DALAFAVE, The College of New Jersey — Computational design of small molecule inhibitors of Polo-like Kinase 1 (Plk1) is presented. Plk1, which regulates cell cycle, is often overexpressed in cancers. Its downregulation was shown to inhibit cancer progression. Most inhibitors of kinases' interact with the highly conserved ATP binding site. This makes the development of Plk1-specific inhibitors challenging, since different kinases have similar ATP sites. However, Plk1 also contains the polo-box domain (PBD), which is absent from other kinases. In this study, the PBD site was used as a target for designed Plk1 inhibitors. Common structural features of experimentally known Plk1 ligands were first identified. The information was used to design putative small molecules that specifically bonded Plk1. Druglikeness and possible toxicities of the designed molecules were determined. Molecules with no implied toxicities and optimal druglikeness were used for docking studies. The docking studies identified several molecules that made stable complexes with the Plk1 PBD site. Possible utilization of the designed molecules in drugs against cancers with overexpressed Plk1 is discussed.

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