**Peptidomimetics Targeting Polo-Box Domain of Polo-like kinase 1**

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**Abstract**

The serine/threonine kinase Polo-like kinase 1 (Plk1) is a regulator of multiple stages of mitotic progression. Several Plk1 kinase inhibitors have been uniformly demonstrated to induce mitotic arrest and apoptosis of cancer cells in vitro and in vivo. The PBD is unique to the family of PLKs and therefore it is ideally suited for studying the feasibility of inhibiting PLK1 by selectively influencing its protein-protein interaction. We have tried to develop the short peptidomimetic Plk1 PBD inhibitors with enhanced binding affinity and selectivity against Plk1 PBD from closely related Plk2 and Plk3. To achieve the desired short peptidomimetic agents, a systematic deletion and the N-terminal capping using diverse organic moieties were effected over the most potent 4j peptide, which led to the identification of AB-103 series with improved binding affinity and selectivity. In addition, AB-103 and their PEG-conjugated compounds were evaluated against their cellular uptake, anti-proliferation and Plk1 kinase inhibition by direct incubation with HeLa cells. Finally, improved binding affinity and selectivity of our derived compounds are explained by crystallographic evidences

**Reference**

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