Structure-based virtual screening for identification of novel greatwall kinase inhibitors

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Abstract

Over the last few decades, research has substantially enhanced our understanding of cancer biology. Regulating the functioning of mitotic machinery helps to halt cancer progression because uncontrolled cell division is a unifying hallmark of cancer. The complex cell division process is balanced by various kinases and phosphatases. Greatwall kinase (GWL), also known as microtubule-associated serine/threonine kinase-like (MASTL), an AGC family protein kinase required for mitotic control, has received far less attention than Polo-like kinase 1 (PLK1) and Aurora kinases. GWL has emerged as a novel oncogenic candidate in the therapy of several cancer types associated with chromosomal instability (CIN), and poor patient survival where GWL is overexpressed. Hence, identifying novel molecular scaffolds to inhibit the GWL is essential. Therefore, in the current work, structure-based virtual screening was carried out to shortlist the compounds with good efficacy towards the active site of GWL, which led to the identification of 10 compounds with a good binding affinity towards GWL. Compared to Greatwall Kinase Inhibitor-1 (GKI-1), these ten top-scoring compounds have a better docking score and a higher Prime MM-GBSA score with favourable interactions. The results revealed that the compounds Z1526916456, Z1657074241, Z951212238, Z1274223489, and Z241520898 showed good binding affinity and good interactions compared to other selected compounds. Thus, these compounds warrant further confirmation by *in vitro* and *in vivo* studies.

Key words: MASTL, structure-based virtual screening, Cancer, Docking