CBCHFX 10 (7) 1109 – 1264 (2009) · ISSN 1439-4227 · Vol. 10 · No. 7 · May 4, 2009

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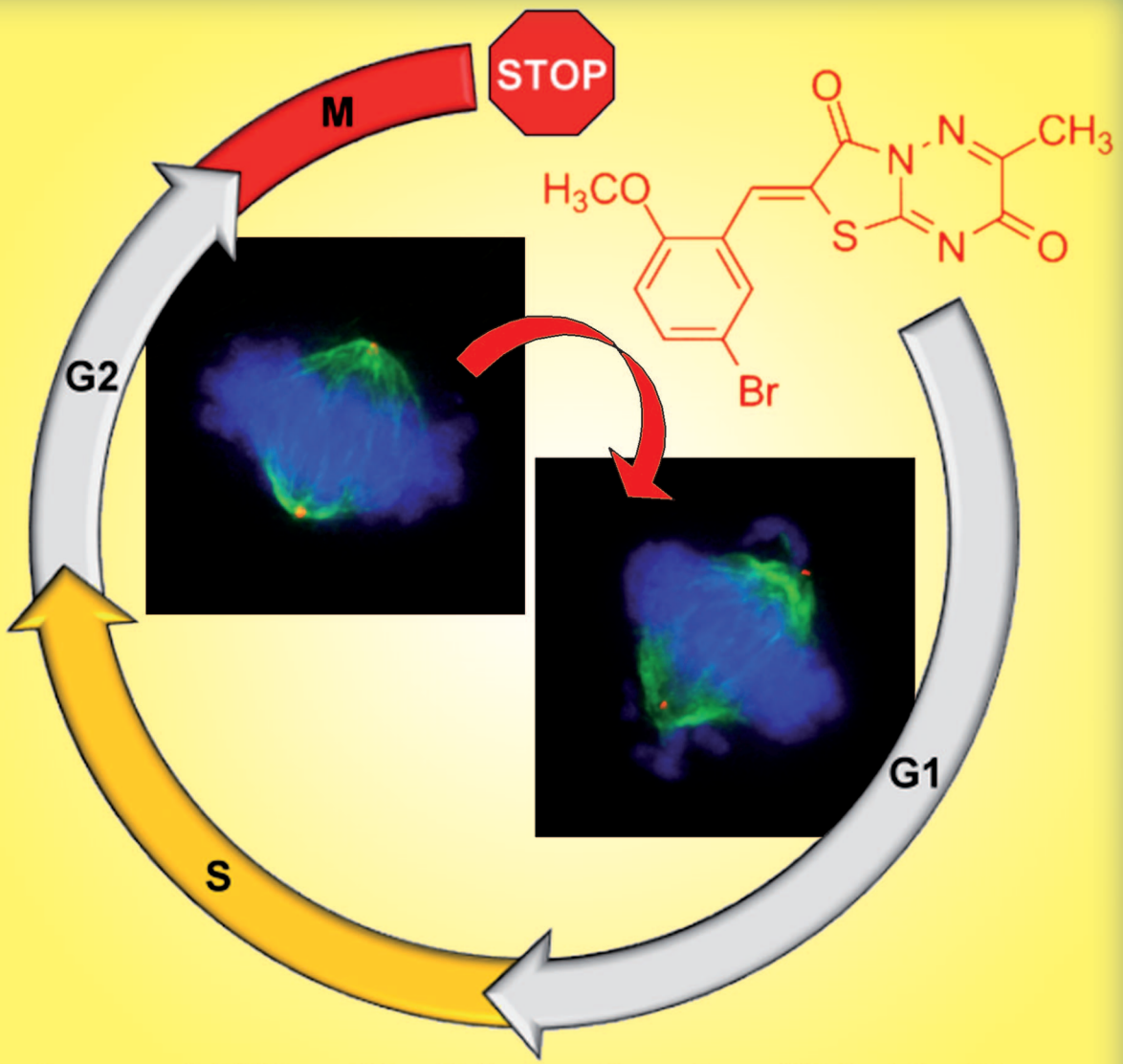
A EUROPEAN JOURNAL

CHEMBIOCHEM

OF CHEMICAL BIOLOGY



Poloxipan: an Inhibitor of the Polo-Box Domains of Polo-Like Kinases

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Review: The Plant Cytochrome CYP74 Family (A. Santino)

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Cover Picture

Wolfgang Reindl, Juping Yuan, Andrea Krämer, Klaus Strebhardt*, and Thorsten Berg*

The cover picture shows the small molecule Poloxipan, a pan-specific inhibitor of polo-like kinases (Plks), and its effects on human cancer cells. Most inhibitors of protein kinases such as Plk1, which is a key player in mitosis, inhibit the enzyme ATP-binding pocket. Due to the conserved nature of the ATP-binding pocket in protein kinases, this approach is frequently associated with specificity problems. In addition to their catalytic domain, polo-like kinases contain a unique protein–protein interaction domain dubbed "polo-box domain", which is used by the enzymes to bind to their respective intracellular anchoring sites. On p. 1145 ff. of this issue, Berg, Strebhardt et al. explore the concept of inhibiting Plk1 by targeting the function of its polo-box domain with Poloxipan, and find that the molecule induces mitotic arrest accompanied by a characteristic cellular phenotype called "chromosome congression defects". This phenotype is represented by failure of one or more chromosomes to congress to the metaphase plate of mitotic cells, and is distinct from the phenotype observed with ATP-competitive inhibitors of Plk1.