

CDK4

Cyclin dependent kinase 4 also known as cell division protein kinase 4 is an enzyme that in humans is encoded by the CDK4 gene. CDK4 is a member of the cyclin-dependent kinase family.

Cyclin-dependent kinases 4 and 6 (CDK4/6) play critical roles in the **G1** to **S** checkpoint of the **cell cycle** and have been shown to be overactive in several human **cancers**. Small-molecule inhibitors of CDK4/**CDK6** have demonstrated significant efficacy against many **solid tumors**. Since CDK4/6 inhibition is thought to induce cell cycle arrest at the G1/S checkpoint, much interest has been focused on combining CDK4/6 inhibitors with cytotoxic agents active against the S or **M phase** of the cell cycle to enhance therapeutic efficacy. However, it remains unclear how best to combine these two classes of drugs to avoid their potentially antagonistic effects.

Jin et al. tested various combinations of highly selective and potent CDK4/6 inhibitors with commonly used cytotoxic drugs in several cancer cell lines derived from lung, breast and brain cancers, for their cell-killing effects as compared to monotherapy. All combinations, either concurrent or sequential, failed to enhance cell-killing effects. Importantly, in certain schedules, especially pre-treatment with a CDK4/6 inhibitor, combining these drugs resulted in reduced cytotoxicity of cytotoxic agents. These findings urge cautions when combining these two classes of agents in clinical settings ¹⁾.

¹⁾
Jin D, Tran N, Thomas N, Tran DD. Combining CDK4/6 inhibitors ribociclib and palbociclib with cytotoxic agents does not enhance cytotoxicity. PLoS One. 2019 Oct 10;14(10):e0223555. doi: 10.1371/journal.pone.0223555. eCollection 2019. PubMed PMID: 31600301.

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