Targeting CDK9 with Wogonin as a therapeutic strategy for chronic myeloid leukemia

Yingjie Qing
Xiangyuan Wang
Hongzheng Wang
Po Hu
Hui Li
Xiaoxuan Yu
Mengyuan Zhu
Zhanyu Wang
Yu Zhu
Jingyan Xu
Qinglong Guo
Hui Hui

Video Byte

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Abstract

Chronic myeloid leukemia (CML) is a rare, spontaneous cancer found in bone marrow. Often the causative mutation generates a fusion protein, BCR-ABL1, with abnormal tyrosine kinase activity, and that abnormal activity is the target of the current tyrosine kinase inhibitor treatments. However, these treatments are expensive if used long term and do not kill cancerous stem cells. Thus, new treatments and treatment targets are needed. One potential category of targets are transcription regulators, such as CDK9 (cyclin-dependent kinase 9). Wogonin is a naturally occurring inhibitor of CDK9, and in a recent study it showed anti-CML effects on cell lines and primary CML cells. Specifically, wogonin induced erythroid differentiation in CML cell lines and primary cells and apoptosis in the KU-812 cell line. Wogonin treatment increased binding between GATA-1 and FOG-1, key players in erythrocyte differentiation and decreased binding between GATA-1 and RUNX1, which regulate megakaryocyte differentiation. Wogonin's anti-tumor effects were also observed in immunodeficient mouse xenograft experiments. Taken together, these results suggest that wogonin inhibits CML cells via a unique mechanism and that wogonin has potential as a novel therapeutic for CML.