Mcl-1 Interacts with AKT to Promote Lung Cancer Progression

Chen et al. Published Online First October 29, 2019; DOI: 10.1158/0008-5472.CAN-19-0950

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Commentator: Nan-Shan Chang, PhD **Location**: Room 601, Med college building

Abstract

Mcl-1 is a member of anti-apoptotic Bcl2 family, which function as regulating apoptosis and survival in cancer cells. AKT is known as an oncogenic kinase which participates in many cellular function and expression much higher in human cancers tissues than in normal tissues. In this article, the authors discover that Mcl-1 can use its own PEST domain to interact with AKT PH domain. By this strategy, Mcl-1 can block PH and KD domain of AKT interaction with each other and then activate AKT. They ensure that this mechanism directly related with cancer progression and survival rate. Also, they discover a new small molecule named PH-687 that can directly bind with AKT PH domain and block the interaction between AKT and Mcl-1. By targeting the Mcl-1/AKT interaction, this mechanism-driven agent provides a highly attractive strategy for the treatment of lung cancer.

Objective/Hypothesis

The authors` purpose in this article is validating the interaction between Mcl-1 and AKT. Also, they try to figure out an effective agent can treat this problem in lung cancer patients.

Results

At beginning, the authors discover that Mcl-1 is positively related with lung cancer progression. They try to figure out the whole mechanism of Mcl-1`s effect on cancer. They finally find that Mcl-1 can utilize its PEST domain to interact with AKT PH domain. In previous study, AKT is known that it can perform self-inhibition by its PH and KD domain interaction. However, Mcl-1 can block this interaction by its PEST domain and then activate AKT, which can further activate the downstream signaling pathway and finally cause tumor progression elevated. They also find a small molecule named PH-687 can directly interact with PH domain to block the binding between AKT and Mcl-1. Their data validate the effect of PH-687 in human lung cancer tissues.

Conclusion

From the authors` results in this article, Mcl-1 and AKT interaction can be validated. They also find some related evidences to indicate the effect of this interaction in human lung cancer tissues. As result, they confirm that Mcl-1 can become a treatment target in lung cancer patients. Besides, the authors discover a small molecule called PH-687 to solve this problem. Finally, from the authors` works in the article, they do provide an effective treatment target and agent for lung cancers.

References

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