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Title: KDM5 is a Novel Therapeutic Target for Colorectal Cancer

Colorectal cancer is one of the deadliest malignant tumors worldwide. And it is a very challenging disease to manage due to the lack of effective drugs. Studies have demonstrated that over 90% of colorectal cancer cases are caused by abnormal activation of a cell signaling pathway called Wnt/ β-catenin signaling by stimulating the expression of crucial oncogenes that promote cancer cell growth and expansion. Thus, inhibition of Wnt/ β-catenin signaling is an effective way to cure colorectal cancer, which many research studies have demonstrated.
Despite immense efforts in developing drugs that specifically inhibit Wnt/ β-catenin signaling, only a few of them have progressed to clinical trials, and there are still no FDA-approved drugs available to hit Wnt/ β-catenin signaling, indicating an urgent need for more effective remedies. Identifying critical regulators of this pathway may provide drug targets for developing more effective therapeutics to meet the current clinical needs. Our preliminary studies identified that two similar proteins, KDM5C and KDM5D, are required to maintain Wnt/ β-catenin signaling in colorectal cancer. We demonstrated that KDM5C and KDM5D positively control Wnt/ β-catenin signaling and stimulate colorectal cancer cell growth in a mouse model. This proposed study will explore how KDM5C/D control key oncogene expression through Wnt/ β-catenin signaling in colorectal cancer. And we will also validate whether the elimination of KDM5C/D is a practical way to inhibit colorectal cancer growth using mouse models. In summary, this study will unravel novel key regulators that control Wnt/ β-catenin signaling in colorectal cancer. The knowledge obtained will lead to the developing of more effective drugs to suppress Wnt/ β-catenin signaling to cure colorectal cancer.