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## PI3K/Akt/mTOR pathway dual inhibitor bez235 suppresses the growth of colon cancer stem cells through reduction of their stemness

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Colon cancer is one of the most common cancers in men and women worldwide with high mortality. The major issue in colon cancer treatment is drug-resistance and metastasis. Recent years, cancer stem cells have been recognised to be responsible for drug resistance and metastasis. In this study, we isolated colon cancer stem-like cells through sphere culture and verified with cancer stem cell markers such as CD133, CD44, and CD24. We demonstrated that the inhibition of PI3K/Akt/mTOR pathway by a dual inhibitor BEZ235 suppressed the growth of colon cancer stem cells through reducing their stemness in term of CD133 and Lgr5 expressions. Our data also showed that PI3K/Akt/mTOR pathway was highly activated in colon cancer stem cells, indicating the potential usefulness of targeted therapy against this pathway in eliminating colon cancer stem cells. In cultured colon cancer HCT-116 cells, BEZ235 also markedly decreased the cancer stem cell marker CD133 and Lgr5 levels. Signalling pathway analysis indicated that BEZ235 decreased the activation status of the pathway, evidenced by the decrease of phosphorylated Akt and mTOR after BEZ235 treatment. The role of the pathway in colon cancer stemness was further verified by the treatment of insulin, a known factor activating the PI3K/Akt pathway. We showed that insulin treatment could increase CD133 expression and decreased the effects of BEZ235 on colon cancer stemness and colon cancer cell survival. Our data collectively suggest that PI3K/Akt/mTOR pathway plays an important role in colon cancer stem cells and BEZ235 is a good drug candidate for colon cancer treatment.

### Biography

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