The class III histone deacetylase SIRT1-mediated post-translational modification of Ca^{2+}-activated K^+ channel $K_{Ca}3.1$ in cancer cells

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The intermediate-conductance Ca^{2+}-activated K^+ channel $K_{Ca}3.1$ is involved in the promotion of tumor growth and metastasis, and is a potential therapeutic target for cancer. Higher $K_{Ca}3.1$ gene expression correlates with the shorter overall survival in cancer patients. Histone deacetylases (HDACs) post-translationally regulate the expression and activity of a number of proteins that play a crucial role in cancer development and progeression. We have showed that the $K_{Ca}3.1$ expression and activity are potentially reduced by the treatment with class I HDACs, HDAC2 and HDAC3 in prostate and breast cancer cell lines. Hypoxic tumor microenvironment is a common characteristic of solid cancers, and is associated with cancer metastasis and poor cancer prognosis. Hypoxia up-regulates the class III HDAC, SIRT1. Here we investigated the effect of the SIRT1 inhibitor on the $K_{Ca}3.1$ expression and activity in several types of cancer cells using real-time PCR, western blotting, flow cytometry, and voltage-sensitive fluorescence dye imaging assays. Pharmacological and siRNA-mediated inhibition of SIRT1 down-regulated $K_{Ca}3.1$ transcription and reduced its activity. These results suggest that SIRT1 may be a potential therapeutic target for $K_{Ca}3.1$-overexpressing cancers.