

Histone Deacetylase Inhibition in Cardiovascular Diseases

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ABSTRACT

Histone deacetylases (HDACs) are enzyme that removes acetyl groups from histone and nonhistone proteins. Recently, they are also called as protein lysine deacetylases (KDACs). Dysregulation of HDACs expression and enzymatic activity is associated with pathological diseases. HDAC inhibitors are small chemical compounds that inhibit HDAC. They have been studied in cancers, neurodegenerative diseases, and cardiovascular diseases. HDAC proteins are grouped into four classes (class I, II, III, and IV) and there are 18 mammalian HDAC subtypes. Each HDAC seems to have different roles in biological processes. HDAC2 has been reported to induce cardiac hypertrophy, whereas, HDAC5 and HDAC9 suppress cardiac hypertrophy. SK-7041 (HDAC1/2 inhibitors) or pan-HDAC inhibitors (trichostatin A) blocked cardiac hypertrophy. In addition, trichostatin A inhibited neointimal information after rat carotid injury. Hypertension is related to arterial remodeling and vascular smooth muscle hypertrophy. HDAC4 and HDAC5 regulate arterial hypertension. MC1568 (class II HDAC inhibitors) or LMK235 (HDAC4/5 selective inhibitors) reduced high blood pressure in hypertensive animal models. Increased HDAC6 or HDAC8 enzyme activity is associated with the chronic hypertension. However, tubastatin A (HDAC6 selective inhibitor) did not reduce hypertension.

In summary, we suggest that HDAC inhibitors may be potential therapeutics for treatment with cardiovascular diseases. To reduce side-effects of HDAC inhibitors, we need to develop a new isoform-specific HDAC inhibitor through cooperation with pharmaceutical companies or experts.

Key Words: HDAC inhibition; Cardiac Hypertrophy; Hypertension; Restenosis;