<u>Highlights</u>

i) HDAC2 levels are increased in NPC disease models.

ii) c-Abl inhibition prevents the increase of HDAC2 in NPC disease models.

iii) Cholesterol and oxidative stress are upstream regulators of the c-Abl/HDAC2 pathway.

iv) c-Abl inhibition prevents the HDAC2-dependent gene repression in NPC models.