

Histone H4 acetyllysine coordination by ATAD2 bromodomain

Margaret Phillips¹

¹ACPHS

margaret.phillips@med.uvm.edu

The ATPase family, AAA domain-containing protein 2 (ATAD2, or ANCCA) is an AAA nuclear co-regulator protein containing two ATPase domains and a bromodomain. Bromodomains are protein-interaction modules that specifically recognize acetylation on histones. Growing evidence suggest that ATAD2 is upregulated and correlated with poor prognosis in various cancers specially breast cancer. Since ATAD2 bromodomains are known to recognize post-translationally modified histones, the inhibition of the acetyllysine recognition offers an innovative target for cancer therapeutics. Despite being an important drug target there is limited information on how the bromodomain interacts with the chromatin to perform its functions. We investigate the structure and function of ATAD2 BRD in-vitro, using NMR spectroscopy and X-ray crystallography to study how this chromatin reader domain is targeted to the post-translational modifications on the histones.