

HDAC11 Enzyme: Multifaceted Roles and New Avenues in Cancer Therapy

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Histone deacetylases (HDACs) are enzymatically super-active in various malignancies, deacetylating lysine (K) moieties of amino acids, and altering the functional properties of a plethora of histone and non-histone proteins. Histone deacetylase 11 (HDAC11), a novel class IV HDAC, is a newly discovered HDAC, regulating multiple physiological programs in a wide variety of normal tissues and cancer cells. Enzymatically, it is a modest deacetylase as well as a deacylase of target proteins. Functionally, genetic ablation of HDAC11 is not lethal in murine models with no major implications on immune cell maturation or steady state hematopoiesis making it a potential therapeutic target in malignancies of hematopoietic stem and progenitor cells (HSPCs). Within various immune cell compartments, the regulatory role of HDAC11 is most prominent in antigen presenting cells (APCs) as a negative regulator of Interleukin 10 (IL-10) at transcriptional level. Also, the loss of HDAC11 is associated to increase in immunosuppressive properties of myeloid derived stem cells (MDSCs) suggestibly due to increase in expression of immunosuppressive molecules via increased transcription of C/EBP β . Current studies designate HDAC11 as a sentinel molecule to maintain immunological homeostasis in naive immune cells and also pose as a therapeutic target in context of stress activated immunity. Interestingly, rapidly increasing evidences show HDAC11 as a potential target in metabolic disorders too. Depletion of HDAC11 is shown to improve the metabolic health of murine models through transcriptional control of genes of thermogenesis. Also, in context of tumorigenic cells, a direct regulation of metabolic pathways like glycolysis and fatty acid utilization

is amongst the top targets of HDAC11. Altogether, HDAC11 is an identified vulnerability with various physiological roles involved in multiple aspects of tumor biology. Further investigations at mechanistic level are needed to know long term therapeutic potentials of HDAC11.

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