ImmunoTools *special* Award 2015

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Influence of posttranslational regulation of histone deacetylase 2 (HDAC2) by acetylation on gene expression patterns and cell survival

Histone acetyltransferases (HATs) and histone deacetylases (HDACs) are enzymes involved in chromatin remodeling and transcriptional regulation. They play important roles in numerous biological processes. In the past decades, acetylation was found also on thousands of non-histone protein targets and emerged as a modification comparable in importance to phosphorylation. There are two distinct subfamilies of deacetylases, differing in their catalytic mechanism. The so-called “classical family” of proteins related to *S. cerevisiae* Rpd3 and Hda1 harbor a Zinc-ion for the catalytic mechanism while the sirtuins (proteins related to yeast Sir2 protein) utilize NAD^+ for catalysis. Deacetylases are further subdivided into four classes based on evolutionary conservation. In humans, class I comprises HDAC1, HDAC2, HDAC3 and HDAC8.

During embryonic development HDAC2 has crucial functions in hematopoiesis, neuronal development, and heart functions. Furthermore, HDAC2 is often overexpressed in tumor cells and involved in tumorigenesic processes. Interestingly, HDAC2 can be used as prognostic marker for clinical cancer treatment e.g. with HDAC inhibitors (HDACi). Overexpressed HDAC2 in cancer cells affects several pathways including the tumor suppressor p53, STAT proteins, the NF-κB pathway and pro-apoptotic protein expression. Referring to non-histone proteins as targets for HDACs, HDAC2 can deacetylate a variety of transcription factors, coactivators, corepressors and tumorigensis-relevant proteins. A large number of transcription factors are described to be a target for acetylation or deacetylation and also the tumor suppressor p53 is found to be deacetylated by HDAC2 and its functions in vivo is thus influenced by the activity of HDAC2.

The activity of HDAC2 and its interaction with transcription factors is modulated by posttranslational modifications (PTMs), e.g. phosphorylation, sumoylation, nitrosylation, and the recently discovered acetylation of HDAC2. The acetylation of HDAC2 is a pivotal factor in the regulation of heart muscle specific gene expression and the development of cardiac hypertrophy.

To check which role the acetylation of HDAC2 plays in different cellular settings I will focus my work on colon carcinoma cells, murine embryonic fibroblasts (MEFs) and leukemic cells from human and mouse origin. The impact of HDAC2 acetylation on enzymatic activity or interaction partner binding of HDAC2 will be monitored by resulting changes in gene expression, cell survival and cell cycle distribution. To expand my previous findings and to get a closer look on molecular mechanisms, I first want use the ImmunoTools anti-human antibodies for flow cytometry to check for abnormal cell cycle distribution and aberrant expression patterns of surface molecules on cells differing in their HDAC2 acetylation status with flow cytometry. Cells treated with various HDACi will also be analysed. Also, I plan to monitor cytokine production from different sources by ELISA techniques. Further, for investigating the gene expression of several pathways regarding the HDAC2 acetylation, I like to use recombinant cytokines from ImmunoTools to stimulate the cells and check for changed gene expression patterns depending on HDAC2 acetylation status.

With the reagents from ImmunoTools I can extend my knowledge about the cellular regulation and take further steps in researching and understanding the role of HDAC2 and its posttranslational regulation.

ImmunoTools *special* AWARD for **Peter Bohm** includes 25 reagents

FITC - conjugated anti-human CD44, CD95, Control-IgG2b, Annexin V

PE - conjugated anti-human Annexin V

APC - conjugated anti-human CD44, Control-IgG2a

recombinant human cytokines: rh EGF, rh Flt3L /CD135, rh IL-3, rh IL-6, rh TGF-beta3, rh TNFα

recombinant human soluble receptors: rh FAS-Ligand / CD178, rh Flt3L /CD135

human ELISA-set for 96 wells, human IL-6, human TNF-a (each 3 reagents)

recombinant mouse cytokines: rm IL-3, rm TNFa DETAILS more AWARDS