

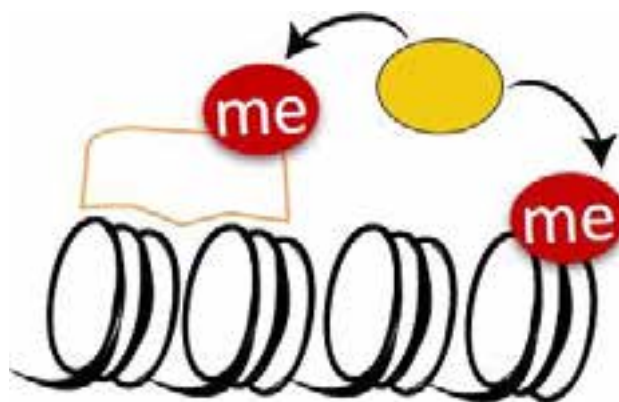
2nd International Congress on**EPIGENETICS & CHROMATIN**

November 06-08, 2017 | Frankfurt, Germany

Lysine methylation signaling at chromatin**Dan Levy**

Ben-Gurion University, Israel

Greater than fifty methyltransferases (PKMTs) are predicted to be present in the human proteome; however, the catalytic activity and substrate specificity for the majority of these enzymes is unknown. We uncovered a novel interaction between the PKMT SETD6 and the oxidative stress sensor DJ1, a protein required for Nrf2-dependent transcription of antioxidant target genes. We show that SETD6 binds DJ1 both *in-vitro* and in cells but does not methylate DJ1. Under basal conditions, SETD6 and DJ1 are associated with chromatin which leads to the repression of Nrf2-dependent transcription. In response to oxidative stress, SETD6 protein level at chromatin is reduced, leading to an elevation in Nrf2 expression level and to a weaker interaction between SETD6 and DJ1 at chromatin. Using the protoarray system, we have identified PAK4 as a new substrate for methylation by SETD6. Our data demonstrate that SETD6 methylates PAK4 both *in vitro* and at chromatin in cells. Interestingly, depletion of SETD6 in various cellular systems significantly hinders the activation of the Wnt/beta-catenin target genes. PAK4 was recently shown to regulate beta-catenin signaling, and we show that SETD6 is a key mediator of this pathway. In the presence of SETD6, the physical interaction between PAK4 and beta-catenin is dramatically increased, leading to a significant increase in the transcription of beta-catenin target genes. Taken together, these findings provide new insight into the SETD6 biology and demonstrate that SETD6 serves as a negative or a positive regulator of transcriptional signaling at chromatin through physical and catalytically dependent and independent manners.

**Recent Publications**

1. Levy D et al. (2011) Lysine methylation of the NF- κ B subunit RelA by SETD6 couples' activity of the histone methyltransferase GLP at chromatin to tonic repression of NF- κ B signaling. *Nature Immunology* 12(1):29-36.
2. Duchin S et al. (2015) A one step continuous kinetic assay for protein and DNA methyltransferase enzymatic activities; *Epigenetics & Chromatin* 8:56
3. Chen et al. (2016) SETD6 is a negative regulator of oxidative stress response 2016, *BBA Gene Regulatory Mechanisms* 859(2):420-7.
4. Vershinin et al. PAK4 methylation by SETD6 promotes the activation of the Wnt/ β -catenin pathway. *Journal of Biological Chemistry* 291(13):6786-95.
5. Cohn O et al. (2016) Chromatin associated SETD3 negatively regulates VEGF expression. *Scientific Reports* 6:37115.

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Biography

Dan Levy is the Head of the lysine methylation and epigenetics signaling lab in Ben-Gurion University in Israel. The goal of his/her research is based on the hypothesis that dynamic methylation of histone and non-histone proteins at chromatin plays a key role in the regulation cellular signal transduction pathways with fundamental effect on human health. His/her aim is to identify new methylation events and to explore how these marks are generated and under which specific physiological conditions; to investigate how these marks are sensed by other cellular factors; to elucidate the molecular mechanisms that transduce these signals; how these methylation events affect gene expression programs; what the clinical relevance of these events are; and how this knowledge can be translated into therapeutic applications in the future.

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