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Regulation of mitotic spindle polymerization by a novel histone deacetylase 3-linker histone H1.3 protein complex

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Histone deacetylase 3 (HDAC3) and linker histone H1 are involved in both chromatin compaction and the regulation of mitotic progression. However, the mechanisms by which HDAC3 and H1 regulate mitosis as well as the factors controlling HDAC3 and H1 activity during mitosis are unclear. Furthermore, as of now, no other association between class I, II or IV HDACs and linker histones has been reported. Here, we describe a novel HDAC3-H1.3 complex containing SMRT and N-CoR and at least four other proteins which accumulated in synchronized HeLa cells in late G_2 and mitosis. Nonetheless, the deacetylation activity by the HDAC3 in the complex was evident only in mitotic complexes. HDAC3 associated to H1.3 was highly phosphorylated on S424 only during mitosis. Isolation of inactive HDAC3-H1.3 complexes from late-G_2 cells and phosphorylation of HDAC3 in the complexes at serine 424 by protein kinase CK2 (also known as casein kinase 2), activated the HDAC3 *in vitro. In vivo,* CK2a and CK2a' double knockdown cells demonstrated a significant decrease in HDAC3 S424 phosphorylation during mitosis. HDAC3 and H1.3 co-localized in between the chromosomes with polar microtubules and spindle poles during metaphase through telophase and partially co-localized with chromatin during prophase and interphase. H1 was previously reported to associate with microtubules; thus, it could potentially function in targeting HDAC3 to the microtubules. We recently demonstrated that HDAC3, H1.3 or double knockdown cells have a lower microtubule polymerization rate in mitotic cells, thus supporting the role of the activated HDAC3-H1.3 complex in regulating mitotic microtubule growth.

Biography

Michael Bergel is currently an Associate Professor at Texas Woman's University (TWU), the largest university primarily for women in the United States. His lab has recently submitted a provisional patent application: U S Provisional Patent Application No. 62/567,089 entitled "Use of histone acetyltransferase inhibitor amidoximes as anti-proliferative agents", filed October 2, 2017. During his Postdoctoral training at the NIH, NCI with Dr. M Bustin, he specialized in the field of chromatin. Specifically, he studied the HMGN1/2 proteins and their acetylation by the histone acetyltransferases p300 and PCAF. He also demonstrated that HMGNs are involved in regulation of core histone posttranslational modifications. He obtained his Master's and PhD from the Hebrew University of Jerusalem in the field of Cancer Biology, mentored by Dr. Jacob Hochman. His research interest includes chromatin, cancer biology, DNA repair and cellular UV response.

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