A Subtle Difference in Histone H2A Isoforms Brings Changes in Expression Profile and Phenotype in Cancer

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Epigenetic mechanisms help to coordinate changes in gene expression that accompany the transition from undifferentiated embryonic cells to terminally differentiated tissue to ensure cellular homeostasis. This precise stage-specific gene expression patterns are strongly influenced by the nucleosome organization and chromatin structures. Recently, we have performed a detailed study investigating the association between histone isoforms/variants abundance and histone modification enrichments on a global genome-wide level correlating with aberrant gene expression in cancer. The data in animal model suggests increase in expression of histone isoform, H2A.1 in hepatocellular carcinoma, and also in various human cancer cell lines compared to normal counterpart having H2A.2. Further, biophysical and biochemical experiments along with in silico molecular simulation studies have shown that H2A.1 containing nucleosomes are more stable and are associated with increase in cellular proliferation. Also, the cancer epigenome has condensed chromatin organization with the decrease in euchromatic and increase of heterochromatic histone modification ‘marks’. These alterations are directly associated with nucleosome reorganization and decrease in the rate of global transcription. In humans, sixteen H2A genes code for eleven different H2A proteins and they differ among themselves by one to three residues. These genes have a complex arrangement and high sequence similarity among each other. In the presentation, we will discuss our recent advances inunderstanding of differential expression profile of H2A isoforms in human cancers and their normal counterparts and their potential relevance in differentiation and dedifferentiation processes.