Transcriptional Regulation by Epigenetics Modulators Induced during Hepatocarcinogenesis

○ Shigehiro Osada
(Dept. of Mol. Biol., Grad. Sch. of Pharm. Sci., Nagoya City Univ.)

Eukaryotic DNA is condensed into chromatin, the basic unit, nucleosome, of which consists of 146 base pairs of DNA and two copies of histones H2A, H2B, H3 and H4. This highly organized structure contributes to the regulation of gene function including transcription, DNA replication and DNA repair. The fundamental chromatin state is controlled by three mechanisms: histone modification (acetylation, methylation, etc.) enzymes, ATP-dependent chromatin remodeling complexes, and incorporation of histone variants. These epigenetics modulators are essential for proper cell growth and differentiation. This means that aberrant epigenetical regulation leads to disease including cancer.

Cancer epigenetics has focused mainly on changes in DNA methylation. Observations revealed that CpG island hypermethylation and global genomic hypomethylation are commonly detected in cancer cells. Other epigenetics features have not been studied well. To elucidate epigenetic changes, which affect gene expression and cell transformation, in tumor marker-positive cells, hyperplasic nodules were chemically induced by Solt-Farber procedure in rat, and expression levels of epigenetics modulators were observed. We revealed that expression levels of histone acetyltransferases, histone methyltransferases, and histone variant were induced in hyperplasic nodules. Glutathione *S*-transferase placental form is a well-known tumor marker that is specifically elevated during hepatocarcinogenesis, and expression of this tumor maker is regulated by the transcription step. I will discuss our recent progresses on the aberrantly expressed epigenetics modulators and tumor maker gene expression.