Regulation of Tissue-Specific Gene Expression by Coordinated Changes in DNA Methylation and Histone Modifications in the Coding Region

Jeung-Whan Han

Department of Biochemistry and Molecular Biology, College of Pharmacy, Sungkyunkwan University

Various cell types in a higher multicellular organism are genetically homogenous, but are functionally and morphologically heterogeneous due to the differential expression of genes during development, which appears to be controlled by epigenetic mechanisms. However, the exact molecular mechanisms that govern the tissue-specific gene expression during development are poorly understood. We herein show that dynamic change of histone modifications and DNA methylation in the coding region containing transcription site determines the tissue-specific gene expression pattern during development of cloned mammal. The tissue-specific expression of transgene coincides with DNA unmethylation at specific CpG sites and drastic change of histone modification from low ratio of methylated H3-lysine 4 or acetylated H3-lysine 9, 14 over acetylated H4 in each tissue to high ratio, but does not with the level of methylated H3-lysine 4 between transgene-expressing and -nonexpressing tissues. Based on the programmed status of transgene silenced in cloned mammalian ear-derived fibroblasts, the transgene could be reprogrammed by change of histone modification and DNA methylation with inhibition of both histone deacetylase and DNA methylation or by re-nuclear-transfer, resulting in high expression of the transgene. These findings indicate that dynamic change of histone modifications and DNA methylation during mammalian development is potentially important in the establishment and maintenance of tissue-specific gene expression.