第 306 回つくば分子生命科学セミナー

TSUKUBA MOLECULAR LIFE SCIENCE SEMINAR

演題：Acetylation of Chromatin and Histone Chaperones in Transcription Regulation: Implications in Cancer Manifestation and Therapeutics

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日時：2010 年 1 月 22 日（金）　17:00-18:30

会場：医学学群棟 1 階　4A103

要旨：

Eukaryotic genome is organized into a dynamic chromatin structure composed of nucleosomes as the basic structural unit. There are different cellular factors that confer chromatin fluidity and precise organization. We have found that Nucleophosmin (NPM1/B23), a ubiquitously expressed, highly dynamic multifunctional nuclear protein is a histone chaperone. NPM1 enhances transcription from the chromatin template in an acetylaiton dependent manner. Acetylation of NPM1 is a prerequisite for its transcriptional activation potential. We have found that indeed NPM1 gets acetylated by p300/KAT3B in vivo. Significantly, acetylated NPM1 is localized in the active transcription foci and gets deacetylated by SIRT1, which is a Class III histone deacetylase. Furthermore, our studies carried out on oral cancer suggest that NPM1 could play a role in transcriptional activation during cellular transformation and as a consequence may influence the cancer manifestation. The combination of siRNA mediated knockdown of NPM1 followed by microarray analysis and chromatin immunoprecipitation experiments revealed that some of the genes involved in oral cancer malignancy are regulated by NPM1 and have acetylated NPM1 localized on their promoters along with active RNA polymerase II. These observations suggest that manifestation of oral cancer could be related to NPM1 mediated transcription regulation, conferred by the enhanced acetylated status of the chaperone. We have further found that histones are also hyperacetylated in oral cancer patient samples. Presumably, hyperacetylation of both histone and histone chaperone induces the expression of genes involved in oral cancer manifestation. In agreement with this view, it was found that in a nude mice model, the treatment of a water soluble small molecule inhibitor of p300 acetyltransferase activity could control tumor progression.

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