Research Highlights

Highlights from the latest articles on epigenetics in tumorigenesis

Differential epigenetic regulation of *GATA4* in gastric adenocarcinomas

Evaluation of: Yamamura N, Kishimoto T. Epigenetic regulation of *GATA4* expression by histone modification in AFP-producing gastric adenocarcinoma. *Exp. Mol. Pathol.* 93(1), 35–39 (2012).

AFP-producing gastric adenocarcinoma (AFP-GC) is a highly malignant subtype of adenocarcinoma [1]. *GATA4*, a member of the GATA-binding transcription factors, is expressed in the endoderm and has a crucial role in differentiation [2]. Frequent methylation of promoter CpG islands in the *GATA4* gene has been reported previously in various types of cancer [3]. Epigenetic regulation of *GATA4* in AFP-GC has not been looked into yet. Yamamura and Kishimoto studied the expression and epigenetic regulation of the *GATA4* gene in AFP-GC [4]. Immunohistochemical analysis of a small number of tumors revealed that *GATA4* expression is less common in AFP-GC compared with common type gastric adenocarcinomas (C-GC). Furthermore, no correlation was found between *GATA4* expression and promoter DNA methylation in AFP-GC. By contrast, *GATA4*-negative C-GC cells exhibit promoter methylation whereas the *GATA4* promoter in *GATA4* positive cells is hypomethylated. Further experiments revealed that histone

lysine hypoacetylation and methylation seemed to be the dominant mechanism to repress *GATA4* expression in AFP-GCs. These results therefore reveal different epigenetic mechanisms to silence *GATA4* between AFP-GC and C-GC. Further studies to deduce the specific acetylation marks involved in regulating *GATA4* expression and also studying a larger number of AFP-GC cancers can shed more light on the specificity of epigenetic deregulation of gene expression in AFP-GC and C-GC.

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Epigenetics and the prognosis of hepatocellular carcinoma

Evaluation of: He C, Xu J, Zhang J *et al.* High expression of trimethylated histone H3 lysine 4 is associated with poor prognosis in hepatocellular carcinoma. *Hum. Pathol.* doi:10.1016/j.humpath.2011.11.003 (2012) (Epub ahead of print).

In recent years, epigenetic modifications have been linked to the molecular pathogenesis of several cancers [1]. For example, H3K4me3, a mark associated with active transcription, has been demonstrated to be of prognostic importance in prostate and lung cancer [2]. One of several kinds of cancers that lead to deaths worldwide despite advances in surgical strategies and chemotherapy is hepatocellular carcinoma (HCC) [3]. Wang and colleagues

studied the cellular expression pattern of H3K4me3 in HCC tumor tissues and looked into its association with clinical outcomes [4]. They also analyzed the status of the H3K4me ‘writer’, SMYD3 and found that expression of H3K4me3 and SMYD3 correlated positively and were enhanced in HCC. Based on several analyses the authors found that the level of H3K4me3 serves as a significant and independent predictor of poor survival of HCC patients, especially at tumor node metastasis I/II stage. These studies indicate that H3K4me3 could be included as a biomarker at early clinical screening stages. As a follow-up it would be interesting to look into the roles of other H3K4 methylases and also demethylases in regulating the levels of H3K4me3 in HCC and other types of cancer. A comprehensive investigation of the epigenetic deregulations in

HCC will provide novel opportunities for therapy.

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