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Editorial

Epigenetics of Transcription Factor Twist1 and Cancer

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EDITORIAL

The concept of 'epigenetics' is comparatively newer and less known section in 'biomolecular science. However, this has gained immense interest among modern molecular biologists. This is a field of study, which deals with the changes of genetic expression affecting the cellular phenotypes caused by the modifications of DNA materials other than change of nucleotide sequence. Literally, 'Epigenetics' means 'over/outer/above genetics'. While genetic changes mean modifications in nucleotide sequence (base substitution, deletion, insertion, dimerization, etc.), in epigenetic changes, the nucleotide sequences are unchanged, but there are specific type of base base modifications. The major patterns of epigenetic changes leading to cancer are DNA methylation, chromatin remodeling, histone modification (histone acetylation and deacetylation), genomic imprinting, non-coding RNA, etc. These epigenetic changes in certain genes have been implicated in several diseases including cancers, as well as the genetic changes are.

The basic helix-loop-helix transcription factor Twist1 is one of the master regulators of Epithelial to mesenchymal transitions (EMT) process, which plays a vital role in cancer metastasis [1-2]. In recent years, Twist1 has become an important diagnostic and prognostic marker for cancer, and became an interesting target for cancer therapeutics. Twist has been indicated as 'oncoprotein' and up-regulation of Twist1 expression has been reported in several cancers [2-3]. More interestingly, in addition to overexpression, methylation of *TWIST1* (the gene which encodes for Twist1 protein) has also been found to be associated with cancer [4]. Thus, epigenetic changes in Twist1 transcription factor are a very interesting topic to explore for cancer researchers.

DNA methylation is the epigenetic change, which has been mostly reported to be associated with *TWIST1* and interfere with Twist1 expression. Usually, hypermethylation of the promoter region of *TWIST1* gene has been known in certain cancers of breast, uterine cervix, ovary, bladder, colorectam, gastric, lung, bone and brain [2]. For the detection of cancer cells and cancer typing in biological samples, the tumor specific promoter hypermethylation of *TWIST1* is becoming a promising tool. However, it is not very clear how the *TWIST1* promoter hypermethylation is responsible for carcinogenesis. Evidences showed that the increased frequency of hypermethylated genes in distant metastasis might be an important event in cancer progression. It has been reported that the hypermethylated *TWIST1* gene is more frequently found in the local and distant metastasis than in primary breast carcinomas [5]. To clarify the epigenetic mechanism of Twist1, Gort [6] proposed two possibilities: (1) the proximal part of the *TWIST1* promoter is not related to *TWIST1* expression, rather it interferes with other genes in genomic proximity like *HDAC9* and *FERD3L*], (2) hypermethylation of *TWIST1* promoter might be an early event that precedes compensatory *TWIST1* over-expression [7]. Chromatin remodeling is another important epigenetic change of Twist1 responsible for cancer. Evidence showed that a protein complex formed by Twist1 with the Mi2/nucleosome remodeling and deacetylase, termed as Twist/Mi2/NuRD plays an essential role in invasive and metastatic cancer cells [8]. miR-10b has also been reported to target Twist1 but change of miR-10b expression alone can't induce breast cancer cell into EMT [9], and other factors might be associated. However, these mechanisms are not enough to understand the epigenetics of Twist1 in cancer clearly, and a vast things to know.

In cancer therapeutics, controlling metastasis remains one of the mainstream focuses, and targeting Twist1 might be the new dimension in controlling metastatic cancers. Several attempts have been taken to manipulate Twist1 function in cancer cells, including epigenetic approaches. Particularly, in hormone resistant breast cancer, epigenetic modification of Twist1 is able to restore hormone sensitivity, as Twist can serves as a potential target for converting estrogen receptor (ER)-α-negative breast cancers to ER-α-positive breast cancers [10-11]. Exploring Twist1 epigenetics might be a very interesting topic for the cancer researchers for the invention of new therapeutic approach for cancer treatment

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