CpG Island Region Outside the Putative Promoter Controls CXCL12 Expression in Breast Cancer Cell Lines

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Metastasis contributes to 90% of all breast cancer death. Several studies have highlighted the role of epigenetic events such as DNA methylation in promoter regions of genes as an important event in the process of metastasis in breast cancer. The promoter of the CXCL12 gene, encoding a chemokine, is silenced by methylation in gastric, colon as well as in the breast cancer. The promoter region of CXCL12 gene has five CpG islands regions and the forth region is hypermethylated in breast tumors from patients with metastasis. The aim of this work was to map methylated regions flanking the promoter of CXCL12 by cloning bisulfite treated DNA containing the distinct CpG regions and also correlate methylation pattern with the gene expression in different breast tumor cell lines. The results showed that the CpG islands 1, 3, 5 as well as the final third of CpG 2 were more than 80% methylated in the cell lines that expressed the gene CXCL12 (HB4a, PMC42 and MCF7). Expression analysis indicates strongly that these regions do not regulate this gene. However CpG island 4, located approximately 1550 bp away from the transcription start region and outside of the putative promoter region, was differentially methylated and it seems to promote CXCL12 gene silencing in breast cancer cell lines.

Word keys: CXCL12, chemokine, DNA methylation, epigenetics, breast cancer.

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