Prognostic Role of MMPs in Colorectal Cancer

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While most matrix metalloproteinases (MMPs) are produced in stromal cells, MMP-7 is produced in cancer cells and is known to affect the invasion and the metastasis of cancer cells by destroying the basement membrane [1]. MMP-7 is expressed mainly in the epithelial cells of the large intestine [2], and the over-expression of MMP-7 is known to influence early carcinogenesis of colorectal cancer from a normal colorectal mucosa to an adenoma [3]. Due to this mechanism, MMP-7 was reported to be an independent prognostic factor upon which to base a prognosis for colorectal cancer patients [4]. In this study, no correlation between the expression of MMP-7 and the prognosis for colorectal cancer patients was found. However, by using immunohistochemistry, this study confirmed a finding of a previous study by showing that MMP-7 was expressed mainly in cancer cells rather than in interstitial cells.

MMP-2 is one of the zinc-dependant matrix metalloproteinases working as main extracellular matrix remodelling enzymes, and it is called gelatinase. MMP-2 is regulated positively or negatively at the gene transcription level by various oncogenes, cytokines or growth factors [5]. The up-regulation of MMP-2 provokes the loss of basement membrane type IV collagen to destroy the extracellular matrix and promote the progression and the local invasion by a tumor [6]. As mentioned in many reports, over-expression of MMP-2 is expected for a higher-stage tumor [7]. However, unlike MMP-7, the down-regulation of MMP-2 was also reported at a higher stage [8], so the role of MMP-2 in colorectal cancer has not been clearly determined. Considering that tissue inhibitor of metalloproteinase (TIMP)-1, (or an inhibitor of MMP-2) is significantly up-regulated at higher stages, such as stage III or IV, than stage I or II

[9], the action of MMP-2 is thought to be determined by the interaction with TIMP1.

According to the results of this study, no correlations of the expression of MMP-2 with factors related with the tumor's stage, differentiation, lymphovascular invasion, distant metastasis and recurrence were found, so drawing a conclusion in this study about the prognostic role of MMPs was difficult. This study aimed to investigate the expressions of MMP-2 and -7 in patients with colorectal cancer and to determine their meaning as prognostic factors by examining the characteristics of the expressions, the correlations with other pathologic findings and the correlation with prognosis, but it did not fulfill that aim. However, the study did include an in-depth morphologic study on the ways in which MMP-2 and MMP-7 are expressed in colorectal cancer tissues, so it should help in understanding the mechanisms for the expressions of the two MMPs.

Future studies to investigate whether the expression of MMP-7 actually has a negative influence on the prognosis for colorectal cancer and how it is related with other substances such as β catenin, survivin or PRL-3 will be meaningful. For MMP-2, continuous studies to examine its correlation with its inhibitor TIMP-1, as mentioned above, at a molecular biological level are recommended.

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