

# Proteomic analysis shows down-regulations of cytoplasmic carbonic anhydrases, CAI and CAII, are early events of colorectal carcinogenesis but are not correlated with lymph node metastasis

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## ABSTRACT

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**Aim.** The aim of the study was to screen the markedly down-regulated proteins in colorectal cancer and analyze their relationship to carcinogenesis, cancer progression and pathological aspects.

**Methods.** Proteomic analysis was performed on six fresh colorectal cancer tissues and paired normal colorectal mucosa by two-dimensional differential gel electrophoresis and matrix-assisted laser desorption/ionization-time of flight mass spectrometry. Two markedly down-regulated proteins among the proteins, of which the expressions were significantly decreased in colorectal cancer compared to normal mucosa, were confirmed by Western Blot in 12 colorectal cancers. Their relationship to carcinogenesis, cancer progression and pathological aspects of colorectal cancer were analyzed in 64 colorectal cancer and paired normal mucosa, 27 benign polyps, and 20 lymph node metastases by immunohistochemistry.

**Results.** Two-dimensional differential gel electrophoresis analysis showed there were 2 protein spots, of which the average abundances decreased 3.62 and 3.76 fold in colorectal cancer compared to normal mucosa, respectively. They were identified by matrix-assisted laser desorption/ionization-time of flight mass spectrometry as carbonic anhydrase I and II (CAI and CAII). Validation by Western Blot in 12 colorectal cancers showed there were significantly different expressions of CAI and CAII between colorectal cancer and normal mucosa ( $P = 0.002$  and  $0.027$ , respectively). Immunohistochemistry analysis indicated the expression of CAI and CAII was decreased from normal mucosa to benign polyps, and to colorectal cancer stepwise significantly ( $P < 0.05$ ). However, there were no differences in their expressions between lymph node metastasis and colorectal cancer ( $P > 0.05$ ). There were decreasing trends of CAI and CAII expressions from well to poor differentiation and from stage I or II to stage III or IV, but they were not statistically significant ( $P > 0.05$ ).

**Conclusions.** CAI and CAII are necessary enzymes of the colorectum for their normal function. Down-regulations of CAI and CAII are early events of colorectum carcinogenesis. They have no correlations with lymph node metastasis.

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**Key words:** carbonic anhydrase I, carbonic anhydrase II, colorectal cancer, proteomics.

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