

学位論文の要旨

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主論文の題名

Proteomics analysis of differential protein expression identifies Heat shock protein 47 as a predictive marker for lymph node metastasis in patients with colorectal cancer

主論文の要旨

The discovery of biomarkers to predict the potential for lymph node (LN) metastasis in patients with colorectal cancer (CRC) is essential for developing improved strategies for treating CRC. In the present study, we used isobaric tags for relative and absolute quantitation to conduct a proteomic analysis designed to identify novel biomarkers for predicting LN metastasis in patients with CRC. We identified 60 differentially expressed proteins specifically associated with LN metastasis in CRC patients and classified the molecular and functional characteristics of these proteins by bioinformatic approaches. A literature search led us to select heat shock protein 47 (HSP47) as the most suitable candidate biomarker for predicting LN metastasis. Validation analysis by immunohistochemistry showed that HSP47 expression in patients with CRC and the number of HSP47-positive spindle cells in the tumor stroma were significantly higher compared with those in adjacent normal colonic mucosa, and the number of the latter cells increased with tumor progression. Further, the number of HSP47-positive spindle cells in stroma was a more informative marker for identifying LN metastasis than HSP47 expression. Multivariate analysis identified spindle cells that expressed elevated levels of HSP47 as an independent predictive biomarker for CRC with LN metastasis. Moreover, these cells served as an independent marker of disease-free and overall survival of patients with CRC. Our data indicate that the number of HSP47-positive spindle cells in the stroma of CRC may serve as a novel predictive biomarker of LN metastasis, early recurrence, and poor prognosis.