Dipeptidase 1 (DPEP1) is a marker for the transition from low-grade to high-grade intraepithelial neoplasia and an adverse prognostic factor in colorectal cancer.

Abstract:

Background: Colorectal cancer (CRC) is the second leading cause of cancer-related deaths worldwide. Improvements in the understanding of its molecular mechanism and the characterisation of CRC-specific biomarkers facilitating early detection are considered to increase overall survival. Methods: A meta-analysis of microarray and Serial Analysis of Gene Expression (SAGE) has been performed to identify differentially regulated genes in CRC. Dipeptidase 1 (DPEP1/MDP/RDP) and Syntenin-2 (SDCBP2/SITAC18) were found to be differentially expressed in tumour tissue compared with normal mucosa. Expression of DPEP1 was assessed in a validation set of 87 normal mucosa samples, 20 hyperplastic polyps, 46 CRC adenomas with low- and high-grade intraepithelial neoplasia (IEN) and 217 well-documented CRCs by immunohistochemistry and partially by immunoblotting and real-time PCR. Results: Expression of DPEP1 was specifically increased in human CRC tissue samples compared with normal mucosa (P < 0.0001, Mann-Whitney U-test), showing a striking upregulation in high-grade compared with low-grade IEN. Furthermore, high DPEP1 expression was found to strongly correlate with histological stage (P < 0.0001, chi-square test) as well as localisation (P < 0.0001, chi-square test) and has
been recognised as an independent adverse prognostic factor, showing significant prognostic values with an ROC (receiver operating characteristic)-AUC of 0.9230. Conclusion: Dipeptidase 1 has been identified as an excellent marker of high-grade IEN and CRC, and may thus be applied for screening of early neoplastic lesions and for prognostic stratification.

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