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KARCINÓM PRSNÍKA

Fridrichova I, Smolkova B, Kajabova V, Zmetakova I, Krivulcik T, Mego M, Cierna Z, Karaba M, Benca J, Pindak D, Bohac M, Repiska V, Danihel L

CXCL12 and ADAM23 hypermethylation are associated with advanced breast cancers.

Transl Res. 2015 (In press)

More than 25% of the patients with breast cancer (BC) develop metastatic disease. In the present study, we investigated the relationship between DNA methylation levels in genes regulating cell growth, invasiveness, and metastasis and advanced BCs and evaluated the clinical utility of methylation profiles for detecting metastatic potential. Pyrosequencing was used to quantify methylation levels in 11 cancer-associated genes in primary tumors (PTs), lymph node metastases (LNMs), plasma (PL), and blood cells from 206 patients with invasive BC. Protein expression was evaluated using immunohistochemistry. PTs showed hypermethylation of A isoform of the RAS-association domain family 1 (RASSF1A), adenomatous polyposis coli (APC), chemokine C-X-C motif ligand 12 (CXCL12), and disintegrin and metalloprotease domain 23 (ADAM23) (means 38.98%, 24.84%, 12.04%, and 10.01%, respectively). Positive correlations were identified between methylations in PTs and LNMs, but not between PL and PTs. The cumulative methylation of PTs and LNMs manifested similar spectrums of methylated genes that indicate the maintaining of aberrant methylation during breast tumorigenesis. Significantly increased methylation levels in RASSF1A, APC, CXCL12, and ADAM23 were found in estrogen receptor (ER) positive BCs in comparison with ER negative cases. Regarding these results, the evaluation of DNA methylation could be more informative in testing of patients with ER positive BC. The risk for LNMs development and higher proliferation of cancer cells measured through Ki-67 expression was increased by hypermethylation of CXCL12 and ADAM23, respectively. Therefore, the quantification of CXCL12 and ADAM23 methylation could be useful for the prediction of advanced stage of BC.

PODPORNÁ LIEČBA

Mego M, Chovanec J, Vochyanova-Andrezalova I, Konkolovsky P, Mikulova M, Reckova M, Miskovska V, Bystricky B, Beniak J, Medvecova L, Lagin A, Svetlovska D, Spanik S, Zajac V, Mardiak J, Drgona L.

Prevention of irinotecan induced diarrhea by probiotics. A randomized double blind, placebo controlled pilot study.

Complement Ther Med. 2015 (In press)

Purpose: Diarrhea is one of the dose limiting toxicity of irinotecan. SN-38 is main irinotecan metabolite responsible for diarrhea development, which is excreted in glucuronidated form into the intestine. This study aimed to determine the effectiveness of the probiotics in the prevention of irinotecan induced diarrhea due to reduction of intestinal beta-D-glucuronidase activity.

Methods: Between January 2011 and December 2013, 46 patients with colorectal cancer starting a new line of irinotecan based therapy were included. Patients were randomized 1:1 to probiotics (PRO) or placebo (PLA). Probiotic formula Colon DophilusTM , was administered at a dose of 10x109 CFU of bacteria tid, orally for 12 weeks of chemotherapy. The study was prematurely terminated due to slow accrual, when 46 of 220 planned patients were accrued.

Results: 23 patients were randomized to PRO and 23 patients to PLA. Administration of probiotics compared to placebo led to a reduction in the incidence of severe diarrhea of grade 3 or 4 (0% for PRO vs. 17.4% for PLA, p = 0.11), as well as reduction of the overall incidence of diarrhea (39.1% for PRO vs. 60.9% for PLA, p = 0.24) and incidence of enterocolitis (0% for PRO vs. 8.7% for PLA). Patients on PRO used less antidiarrheal drugs compared to PLA. There was no infection caused by probiotic strains recorded.

Conclusions: Administration of probiotics in patients with colorectal cancer treated with irinotecan-based chemotherapy is safe and could lead to a reduction in the incidence and severity of gastrointestinal toxicity.