deficiency. Whether this protein can only be used as a "surrogate" marker, or is functionally involved in the progression of tumors through this pathway remains to be elucidated.

Corresponding author
PD Inti Zlobec, PhD
Murtenstr. 31
CH-3010 Bern, Switzerland
Phone: 0041-31-6328755
Fax: 0041-31-6324995
inti.zlobec@pathology.unibe.ch

FP10
ZEB2 CpG promoter methylation in colorectal cancer is associated with lymph node metastases and invasion in KRAS wild-type patients

I. Zlobec[1], M. Helbling[1], H. Dawson[1,2], V. H. Koelzer[1,2], E. Karamitopoulou[1,2], A. Lugli[1,2]

[1]Translational Research Unit (TRU) and [2]Clinical Pathology Division, Institute of Pathology, University of Bern, Bern, Switzerland

Background. ZEB2 is thought to be involved in epithelial-mesenchymal transition (EMT) through transcriptional repression of E-cadherin and up-regulation of genes including anoikis-resistance factor neurotrophic tyrosine kinase receptor, TrkB. The aim of this study is to determine the clinical relevance of ZEB2 protein expression and ZEB2 promoter methylation in patients with colorectal cancer and their relationship to E-cadherin, TrkB and molecular features KRAS/BRAF mutation and CpG Island Methylator Phenotype (CIMP).
Methods. ZEB2, E-cadherin and TrkB immunohistochemistry was evaluated in 160 colorectal cancer patients using a multi-punch (4–5 tumour punches/patient) tissue microarray. ZEB2 promoter methylation, CIMP, KRAS (codon 12/13) and BRAF (V600E) mutation were determined in 95 patients using pyrosequencing.
Results. High ZEB2 expression was associated with advanced pT (p=0.0308), high-grade tumour budding (i.e., detached tumor cell clusters representing an EMT-like process; p=0.0376) and KRAS mutation (p=0.0141), whereas hypermethylation was frequent in KRAS wild-type cases (p=0.0233). In KRAS wild-type cancers, ZEB2 hypermethylation showed marked relationships with lymph node metastasis (p=0.0004), venous invasion (p=0.0247), lymphatic vessel invasion (p=0.0001), unfavourable survival (p=0.0417; 5-year survival: 27 vs. 74 months) and a positive correlation with TrkB (r=0.40). In KRAS mutated cancers, there were no associations of ZEB2 methylation with clinicopathological features, although a strong inverse correlation between methylation and expression (r=−0.45) was observed. Only weak associations with E-cadherin were noted.
Conclusions. ZEB2 over-expression and CpG methylation occur frequently in colorectal cancers, but may cause their effects in a KRAS-dependent manner. Among KRAS wild-type patients, methylation of ZEB2 may represent a novel route to tumour cell dissemination.

Corresponding author
PD I. Zlobec, PhD
Head Translational Research Unit (TRU)
Institute of Pathology, University of Bern
Murtenstrasse 31, Room L414
CH-3010 Bern, Switzerland
Phone: +41 31 632 8755
Fax: +41 31 632 4995
inti.zlobec@pathology.unibe.ch

FP11
Influence of KRAS mutations on outcome in patients with curatively resected stage III colon cancer treated with adjuvant chemotherapy

M. Nucifora[1], S. De Dosso[2], A. Spitale[3], N. Sahnane[1], M.E. Riveiro[4], V. Bertolini[5], E. Bucci[5], S. Crippa[1], P. Saletti[2], L. Mazzucchelli[1], M. Frattini[1]

[1]Institute of Pathology, Locarno, Switzerland, [2]Oncology Institute of Southern Switzerland, Switzerland, [3]Ticino Cancer Registry, Institute of Pathology, Locarno, Switzerland, [4]Beaujon University Hospital, Clichy, France, [5]Istituto Ospedaliero MultiMedica, Castellanza, Italy

Background. Postoperative chemotherapy improves survival in curatively resected stage III colon cancer (CC) patients and oxaliplatin in combination with fluoropyrimidine-based regimens has been established as a standard treatment. There is no clear evidence for a predictive marker regarding the effect of adjuvant chemotherapy. KRAS mutations could predict oxaliplatin sensitivity in in vitro experiments, as recently demonstrated. Here, we profiled KRAS and correlated it with outcome in stage III CC patients who underwent adjuvant chemotherapy.
Methods. Eligible patients were those with resected stage III CC who underwent 6-months adjuvant chemotherapy, either with single-agent fluoropyrimidine (FP: modulated 5FU or capecitabine) or with oxaliplatin-based regimens (O-FP: FOLFOX or XELOX). DNA extraction was performed on formalin-fixed paraffin-embedded sections, and KRAS mutations were analyzed by direct sequencing. Disease-free survival (DFS) and overall survival (OS) analyses were computed using the Kaplan-Meier method and the Log-rank test.
Results. The study population included 261 patients: 115 treated with FP, 146 O-FP. We identified KRAS mutations in 71/261 (27.4%) cases, of which 33 (46.5%) received FP, and 38 (53.5%) O-FP. In wild-type (wt) KRAS cases, DFS and OS group did not significantly differ between the two treatment modalities [in months, FP vs O-FP—median OS: 62.0 vs 49.6, HR: 1.12 (95% CI: 0.65; 1.92); median DFS: 57.1 vs 44.4, HR: 0.93 (95% CI: 0.55; 1.56)]. In patients treated with FP, a worse DFS [in months, mutant vs wt—median DFS: 46.0 vs 57.1, p=0.04; HR: 1.86 (95% CI: 1.01; 3.41)] and a trend toward a worse OS in months, mutant vs wt—median OS: 56.1 vs 62.0, p=0.08; HR: 1.71 (95% CI: 0.94; 3.10)] were observed in KRAS mutated patients. On the contrary, DFS and OS were not statistically different for mutated and wt KRAS patients treated with O-FP [in months, mutant vs wt—median DFS: 43.7 vs 44.4, p=0.62; HR: 1.17 (95% CI: 0.63; 2.18); median OS: 48.9 vs 49.6, p=0.77; HR: 1.11 (95% CI: 0.55; 2.23).
Conclusions. Our results suggest that curatively resected stage III CC patients exhibiting wt KRAS status might benefit from FP alone thus avoiding oxaliplatin-adverse effects. On the contrary, an oxaliplatin-containing regimen should be recommended in KRAS mutated patients.

Corresponding author
Martina Nucifora, PhD Student
Laboratory of Molecular Pathology, Institute of Pathology
Via In Selva, 24
6600 Locarno, Switzerland
Phone: 0041918160803
Fax: 0041918160719
martinanucifora85@hotmail.it

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