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Molecular profiles and clinical outcome of stage UICC II colon cancer patients.

Gröne J, Lenze D, Jurinovic V, Hummel M, Seidel H, Leder G, Beckmann G, Sommer A, Grützmann R, Pilarsky C, Mansmann U, Buhr HJ, Stein H, Hummel M.

Source

Department of General, Vascular and Thoracic Surgery, Charité University Medicine Berlin, Campus Benjamin Franklin, Hindenburgdamm 30, 12200, Berlin, Germany. joern.groene@charite.de

Abstract

PURPOSE:
Published multigene classifiers suggesting outcome prediction for patients with stage UICC II colon cancer have not been translated into a clinical application so far. Therefore, we aimed at validating own and published gene expression signatures employing methods which enable their reconstruction in routine diagnostic specimens.

METHODS:
Immunohistochemistry was applied to 68 stage UICC II colon cancers to determine the protein expression of previously published prognostic classifier genes (CDH17, LAT, CA2, EMR3, and TNFRSF11A). RNA from macrodissected tumor samples from 53 of these 68 patients was profiled on Affymetrix GeneChips (HG-U133 Plus 2.0). Prognostic signatures were generated by "nearest shrunken centroids" with cross-validation. Previously published gene signatures were applied to our data set using "global tests" and leave-one-out cross-validation

RESULTS:
Correlation of protein expression with clinical outcome failed to separate patients with disease-free follow-up (group DF) and relapse (group R). Although gene expression profiling allowed the identification of differentially expressed genes ("DF" vs. "R"), a stable classification/prognosis signature was not discernable. Furthermore, the application of previously published gene signatures to our data was unable to predict clinical outcome (prediction rate 75.5% and 64.2%; n.s.). T-stage was the only independent prognostic factor for relapse with established clinical and pathological parameters including microsatellite status (multivariate analysis).

CONCLUSIONS:
Our protein and gene expression analyses do not support application of molecular classifiers for prediction of clinical outcome in current routine diagnostic as a basis for patient-orientated therapy in stage UICC II colon cancer. Further studies are needed to develop prognosis signatures applicable in patient care.

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