Microarray-based prediction of tumor response to neoadjuvant radiochemotherapy of patients with locally advanced rectal cancer.

BACKGROUND & AIMS: Neoadjuvant chemoradiotherapy has become a standard treatment of locally advanced rectal carcinomas, even though the responsiveness varies from complete response to resistance. The aim of the study was to evaluate the capacity of gene expression signatures to identify responders and nonresponders pretherapeutically. METHODS: By using microarray technology we generated gene expression profiles of 43 biopsy specimens of locally advanced rectal carcinomas. The transcription profile then was compared with histopathologic response and used to identify a set of genes discriminating responders from nonresponders. RESULTS: We identified a gene expression signature of 42 genes, mostly encoding proteins that either play a role in the nucleus, such as the transcription factor ETS2, or are associated with transport function, such as the solute carrier SLC35E1, or the regulation of apoptosis, such as caspase-1. In leave-one-out cross-validation the correct classification of a responder was 71%, the specificity of the analysis for a correct classification of a nonresponder was 86%. By applying an additional statistical method of 200 successive splittings into training and test data sets we generated an individual prediction accuracy measure for each predicted response. CONCLUSIONS: Our study shows
that pretherapeutic prediction of response of rectal carcinomas to neoadjuvant chemoradiotherapy is feasible, and may represent a new valuable and practical tool of therapeutic stratification.

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