The therapeutic activity of the epidermal growth factor receptor (EGFR)-directed monoclonal antibody cetuximab in gastric cancer is currently being investigated. Reliable biomarkers for the identification of patients who are likely to benefit from the treatment are not available. The aim of the study was to examine the drug sensitivity of five gastric cancer cell lines towards cetuximab as a single agent and to establish predictive markers for chemosensitivity in this cell culture model. The effect of a combination of cetuximab with chemotherapy was compared between a sensitive and a nonsensitive cell line. EGFR expression, activation and localisation, the presence and subcellular localisation of the cell adhesion molecule E-cadherin as well as MET activation were examined by Western blot analysis, flow cytometry and immunofluorescence staining. Cells were treated with varying concentrations of cetuximab and cisplatin and 5-fluorouracil in tumour-relevant concentrations. The biological endpoint was cell viability, which was measured by XTT cell proliferation assay. Response to treatment was evaluated using statistical methods. We assessed the activity of cetuximab in five gastric cancer cell lines (AGS, KATOIII, MKN1, MKN28 and MKN45). The viability of two cell lines, MKN1 and...
MKN28, was significantly reduced by cetuximab treatment. High EGFR expression and low levels of receptor activation were associated with cetuximab responsiveness. MET activation as well as mutations of KRAS and CDH1 (gene encoding E-cadherin) was associated with cetuximab resistance. These data indicate that our examinations may be clinically relevant, and the candidate markers should therefore be tested in clinical studies.