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Differing deregulation of EGFR and downstream proteins in primary colorectal cancer and related metastatic sites may be clinically relevant.

Molinari F, **Martin V**, **Saletti P**, **De Dosso S**, **Spitale A**, **Camponovo A**, **Bordoni A**, **Crippa S**, **Mazzucchelli L**, **Frattini M**.

Institute of Pathology, Locarno, Switzerland.

Cetuximab and panitumumab efficacy in metastatic colorectal cancer (mCRC) may be influenced by EGFR gene status and/or deregulation of its downstream signalling proteins detected in primary tumour. However, metastasis might have different molecular patterns with respect to primary tumour, possibly affecting the prediction of EGFR-targeted therapy efficacy. We analysed primary tumour and metastasis in 38 mCRC patients. Twelve cases were cetuximab/panitumumab treated. EGFR gene status and protein expression were investigated through fluorescent in situ hybridisation and immunohistochemistry (IHC), K-Ras/BRAF mutations by sequencing and PTEN expression by IHC. We observed EGFR gene deregulation in 25 out of 36 primary tumours and 29 out of 36 metastases, K-Ras mutations in 16 out of 37 cancers and in 15 out of 37 metastases, BRAF mutations in 2 out of 36 cancers and 2 out of 36 metastases and PTEN loss in 8 out of 38 cancers and 12 out of 38 metastases. For the first time in literature, we show that primary colorectal cancer and paired metastasis may exhibit difference with respect to EGFR pathway deregulation mechanisms possibly implying a different response to cetuximab or panitumumab treatment. The investigation of treated patients confirms this hypothesis. We therefore suggest that the analysis of metastatic lesion should be considered in patient management as well as in designing future clinical trials aimed to investigate the effect of anti-EGFR monoclonal antibodies in the treatment of mCRC.