Cell signaling proteomics in colorectal cancer

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To gain further insight into alterations in cellular pathways, tumor profiling and marker discovery in colorectal cancer (CRC) we have used a new antibody microarray specific for cell signaling. Soluble protein extracts were prepared from paired tumor/normal biopsies of 11 patients diagnosed of colorectal carcinoma at different stages, four liver carcinomas were used as a reference. Antibody microarray analysis identified 46 proteins that were differentially expressed between normal colorectal epithelium and adenocarcinoma. These proteins gave a specific signature for CRC, different from other tumors, as well as a panel of novel markers and potential targets for CRC. Twenty-four proteins were validated by using a specific colorectal cancer tissue microarray and immunoblotting analysis. Together with some previously well known deregulated proteins in CRC (β-catenin, c-myc, or p63), we have found new potential markers preferentially expressed in CRC tumors: cytokeratin 13, calcineurin, Chk1, clathrin light chain, MAPK3, phospho-PTK2/FAK (S910) and MDM2. Chk1 antibodies were particularly effective in discriminating between tumoral and normal mucosa in CRC. Moreover, a global picture of alterations in signaling pathways in CRC was observed, including a significant up-regulation of different components of the EGFR and Wnt/β-catenin pathways and the down-regulation of $p14^{ARF}$. The experimental approach described here should be applicable to other pathologies and neoplasic processes.

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