Forced expression of deltaN-TCF-1B in colon cancer derived cell lines is accompanied by the induction of CEACAM5/6 and mesothelin.

Abstract:
The colon cancer cell lines HT29 and SW480 were transfected with an N-terminal beta-catenin binding site-deficient high mobility group (HMG)-box T-cell factor 1 (deltaN-TCF-1) construct to identify differentially expressed genes. Oligonucleotide HG-U133A microarray expression profiling revealed increased mRNA levels of carcinoembryonic antigen-related cell adhesion molecule (CEACAM) 5, 6 and mesothelin in transfectants positive for nuclear deltaN-TCF-1B. Increased amounts of CEACAM5 (CEA) were detectable in membrane-associated compartments, particularly in cholesterol-enriched microdomains. Similarly, mesothelin was demonstrated as an uncleaved membrane-bound constituent. The identified markers were examined in specimens of 46 colorectal carcinomas (CRC) by immunohistochemistry. Patchy areas of increased CEACAM5/6 staining were seen at the tumour-host front in all samples studied. Twenty-eight (58%) of these cases showed over-expression of mesothelin in a small fraction of tumor cells displaying dedifferentiation and dissemination at the invasion front. We conclude that forced expression of deltaN-TCF-1B in HT29 and SW480 is associated with up-regulation of GPI-anchored adhesion molecules, which were assigned to the tumour-host front in CRC patients.