## The Angiogenic Switch of Human Colon Cancer. -It occurs Simultaneous to Initiation of Invasion

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We previously reported that vessel count, vascular endothelial growth factor (VEGF) and platelet derived endothelial cell growth factor (PD-ECGF) expression are associated with metastasis formation in human colon cancer. This study was done to determine a stage of colon cancer progression where induction of these factors occurred (i.e. the angiogenic switch). We examined vessel count, VEGF, and matrix metalloproteinase (MMP)-7 expression in cancer cells and PD-ECGF expression in infiltrating cells in 25 adenomas, 35 mucosal cancers (Tis), 29 submucosal invasive cancers (T1) and 33 muscularis propria invasive cancers (T2) by immunostaining. The intensity of staining of VEGF and MMP-7 was evaluated blindly at the invasive edge and was confirmed by image analysis. Intensity of staining for these factors was graded on a scale of 0 to 3+, with 0 representing no detectable stain and 3+ representing the strongest stain. Intensites of PD-ECGF-positive infiltrating cells were similar on a scale 0-3+, as previous studies from our laboratory have demonstrated that PD-ECGF is expressed primarily in tumor infiltrating cells.

There were significant differences in vessel densities, the intensities of VEGF, MMP-7 and PD-ECGF expression between Tis and T1. These results suggest that angiogenic switch may occur between Tis and T1, i.e. simultaneous to initiation of invasion, in the early development of colon cancer.