Background While cancers arising from the colon and rectum are commonly considered colorectal cancer in clinical practice, distinct behavior and management of these two cancer types are distinctly different. Recently the consensus molecular subtyping of colorectal cancer classified CRCs into CMS1 (microsatellite instability immune), CMS2 (cancerous), CMS3 (metastatic) and CMS4 (mesenchymal). Different histologic distribution of the four classes in various anatomic regions suggests differences in pathobiology. We investigated the proteomic and genetic aberrations of a large cohort of clinical CRC samples to further delineate the molecular differences.

Results

Figure 1: Tumor characteristics. Left: Composition of the tumor cohort analyzed. Shown are the tumor origins, any cases without clear designation of a specific colon region (ascending, descending, etc.) were excluded. Right: Patient age and gender. Patients with tumors of the colon or rectum significantly older than patients with rectal tumors. Patients with primary tumors proficiency older than patients with metastatic tumors profiled for both colon and rectal tumors. Males are more prevalent in rectal tumor colon cancer.

Figure 2: Microsatellite instability is significantly higher in colon tumors than in rectal tumors, with the frequency decreasing significantly from ascending to descending colon. Stars indicate significantly higher MSI frequency than rectal tumors (p=0.05).

Figure 3: Protein expression (IHC) and Her2 amplification (CISH) differences in colon and rectal tumors. Differences in molecular profiles were observed in colon vs. rectal tumors.

Conclusions

In this large cohort of CRC patients, tumors with colon and rectal tumors showed tumors proficiency on the right and left sides, respectively, and an uneven distribution of molecular subtypes in various anatomic regions. These results hold promise in designing prospective clinical trials for personalized treatments of colorectal cancer.

References


Academic genetics analyses of colon versus rectal tumors.

Abstract 3532

Background: Colorectal cancer (CRC) is a heterogeneous disease. There is limited data on colon and rectal tumor molecular differences.

Methods: A total of 8174 CRC tumors submitted to Caris Life Sciences for IHC protein expression, ISH (gene amplification), and NGS sequencing between 2009 and 2015 were studied. Only tumors with origins that were clearly defined as ascending, transverse, or descending colon or rectum were included in this study. We excluded any cases without clear designation. Chi-square tests determined molecular differences between colon and rectal tumors.

Results: A total of 2,010 tumors met our inclusion criteria and were examined. We compared primary (1st) colon (n = 502) with 1st rectal (n = 872) tumors; the colon’s 1st had higher rates of ATM (7.5% vs. 3.2%, p = 0.01), PTEN (24% vs. 4.4%, p < 0.01), CTNNB1 (4% vs. 0.3%, p < 0.003), IDH1 (2% vs. 0%, p = 0.01), GNAS (3.3% vs. 1%, p = 0.04), HNF1A (15% vs. 9%, p = 0.01), CDKN2A (15% vs. 7.5%, p = 0.04), BRAF (24% vs. 3.4%, p < 0.01), and TS (36% vs. 28%, p < 0.01). In contrast, rectal tumors had higher MSI (17% vs. 0.7%, p < 0.01), EGFR (64% vs. 51%, p = 0.047) than rectal tumors. Frequencies in ascending, descending, and transverse descending colon are also higher than in primary colorectal cancer.