Background:
Recent data show that patients with left-sided colon tumors (LT) have better survival and respond differently to biologics compared to patients with right-sided tumors (RT), likely due to molecular differences. We sought to examine these differences.

Methods:
Primary colorectal tumors (n = 1730) with origins clearly defined as RT (colonoscopic biopsy; n = 273), LT (surgical resection to sigmoid colon; n = 585), or rectal (RC; n = 872) were examined by NextSeq sequencing, protein expression, and gene amplification. Tumor mutational load (TML) was calculated in 1001 of these tumors using only somatic non- synonymous missense mutations. Chi-square test was used for comparison.

Results:
When compared to LT, RT carried a significantly higher rate of BRAF (25% vs. 7%; p < 0.0001), PTEN (5.4% vs. 1.3%; p = 0.008), and ATM (4% vs. 1%; p = 0.04) mutations. RT were likely to have more MSI-high (4% vs. 1%; p = 0.04) mutations. RT were more likely to have MSS tumors compared to RC (11% vs. 24%; p = 0.04). When compared to RC, LT showed higher rates of BRAF (6.7% vs. 3.2%; p = 0.04) mutations, compared to RT (25% vs. 7%; p < 0.0001), PTEN (5.4% vs. 1.3%; p = 0.008), and ATM (4% vs. 1%; p = 0.04) mutations. PTEN (5% vs. 1%; p = 0.04), and BRCA1 mutations (4% vs. 0%; p = 0.02). However, a lower rate of TP53 (56% vs. 71%; p = 0.001) and APC (35% vs. 66%; p = 0.003) mutations were observed in RT than RC. When compared to LT, RT showed higher rates of BRAF (25% vs. 3% vs. 7%; p = 0.04), PTEN (5% vs. 1%; p = 0.04), and BRCA1 mutations (4% vs. 0%; p = 0.02). However, a lower rate of TP53 (56% vs. 71%; p = 0.001) and APC (35% vs. 66%; p = 0.003) mutations were observed in RT than RC. When compared to LT, RT showed higher rates of BRAF (25% vs. 3% vs. 7%; p = 0.04), PTEN (5% vs. 1%; p = 0.04), and BRCA1 mutations (4% vs. 0%; p = 0.02). However, a lower rate of TP53 (56% vs. 71%; p = 0.001) and APC (35% vs. 66%; p = 0.003) mutations were observed in RT than RC. When compared to LT, RT showed higher rates of BRAF (25% vs. 3% vs. 7%; p = 0.04), PTEN (5% vs. 1%; p = 0.04), and BRCA1 mutations (4% vs. 0%; p = 0.02). However, a lower rate of TP53 (56% vs. 71%; p = 0.001) and APC (35% vs. 66%; p = 0.003) mutations were observed in RT than RC. When compared to LT, RT showed higher rates of BRAF (25% vs. 3% vs. 7%; p = 0.04), PTEN (5% vs. 1%; p = 0.04), and BRCA1 mutations (4% vs. 0%; p = 0.02). However, a lower rate of TP53 (56% vs. 71%; p = 0.001) and APC (35% vs. 66%; p = 0.003) mutations were observed in RT than RC. When compared to LT, RT showed higher rates of BRAF (25% vs. 3% vs. 7%; p = 0.04), PTEN (5% vs. 1%; p = 0.04), and BRCA1 mutations (4% vs. 0%; p = 0.02). However, a lower rate of TP53 (56% vs. 71%; p = 0.001) and APC (35% vs. 66%; p = 0.003) mutations were observed in RT than RC. When compared to LT, RT showed higher rates of BRAF (25% vs. 3% vs. 7%; p = 0.04), PTEN (5% vs. 1%; p = 0.04), and BRCA1 mutations (4% vs. 0%; p = 0.02). However, a lower rate of TP53 (56% vs. 71%; p = 0.001) and APC (35% vs. 66%; p = 0.003) mutations were observed in RT than RC.