Background: Differences in molecular profiles of males and females with colorectal cancer (CRC) have been reported. Here, we investigated differences in the molecular profile of CRC as an explanation for the differences in the outcomes.

Methods: CRC cases submitted to Caris Life Sciences from 2015 to 2017 were analyzed. The cases were tumors with next generation sequencing (NGS) of 592 genes and a panel of IHC and copy number variation assessment. Microsatellite instability (MSI) was evaluated with NGS for known MSI loci in the target regions. High Tumor mutational load (TML-H) was defined as ≥17 mutations/megabase.

Results: Data from a total of 1768 CRC tumors (F: 819; M: 949) was available for analysis. The comparison of selected biomarker prevalence in male vs. all male CRC (Bottom) showed higher rates of right sided tumors, MSI, loss of expression of MLH1, Her2/Neu, PD-L1, and BRAF in older females is most likely due to methylation as a mechanism for sporadic MSI-high tumors. A star and connective lines indicate statistical significance using Chi Square test.

Conclusions: There are significant differences in the tumor location and molecular profile between females and males with colorectal cancer. Higher rates of right sided tumors, MSI, loss of expression of MLH1, and BRAF in older females is most likely due to methylation as a mechanism for sporadic MSI-high tumors. Given that PDX models are used as a benchmark to assess the preclinical efficacy of new treatments, differences in the gender and age of the primary tumor should be considered in the selection of these models.

Abstract

Differences in Molecular Profiles of Males and Females with Colorectal Cancer (CRC)

Afsaneh Barzi, Mohamed E. Salem, Joanne Xiu, W. Michael Korn, John Marshall, Anthony Frank Shields, Heinz-Josef Lenz

Division of Medical Oncology, University of Southern California Norris Comprehensive Cancer Center, Los Angeles, CA; Georgetown Lombardi Comprehensive Cancer Center, Washington, DC; Caris Life Sciences, Phoenix, AZ; University of California, San Francisco, San Francisco, CA; Georgetown University Medical Center, Washington, DC; Wayne State University, Karmanos Cancer Institute, Detroit, MI; Division of Medical Oncology, Norris Comprehensive Cancer Center, Keck School of Medicine, University of Southern California, Los Angeles, CA

Background: Males (M) and females (F) with colorectal cancer (CRC) present different clinical characteristics. Understanding the differences in the molecular profile of CRC as an explanation for the differences in the outcomes.

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