Signet-ring-cell carcinoma (SRCC) is a rare variant of adenocarcinoma, accounting for about 10% of gastric cancer (GC) and 1% of colorectal cancer (CRC). Despite a decrease in the overall incidence of GC in recent decades, the incidence of SRCC is constantly increasing, in Asia, United States and Europe [1]. Generally, SRCC is associated with female gender and young age of onset compared to non-SRCC [2]. In advanced GC, SRCCs are also associated with poor differentiation, diffuse type, distal location. More importantly, SRCCs display worse prognosis than non-SRCC counterparts [3].

Accordingly, CRC-SRCC has been shown to be associated with advanced tumor stage at presentation and worse outcomes [4]. Recently, it has been observed that 50% or less of signet-ring cell component is associated with higher mortality, independent of other clinicopathologic and molecular features (microsatellite instability, CpG island methylator phenotype, LINE-1 methylation, and KRAS, BRAF, and PIK3CA mutations) [5]. However, the molecular characteristics underlying the biology of these tumors have not been elucidated yet [6].

Herein, we aimed to comprehensively molecular characterize the features of SRCCs. Furthermore, we compared SRCCs tumors arising GC vs CRC to evaluate whether SRCC histology harbor molecular similarities, regardless of tumor location. Finally, we investigated whether SRCCs harbor different molecular characteristics compared with non-SRCC counterparts.

Methods
- Tumors submitted to Caris Life Sciences (Phoenix, AZ) for routine molecular profiling between January 2015 and January 2018 were reviewed from a de-identified database. Cases were reviewed based on available pathological notation for presence of signet ring histology. Cases with normal histologies other than signet ring carcinomas were separated.
- NGS was performed on gastric DNA isolated from FFPE tumor samples using the NextSeq 500 (Illumina, San Diego, CA). All variants were detected with greater than 99% confidence based on allele frequency results for MLH1, PMS2, MSH2, and MSH6 are reported as - IHC was performed on FFPE sections of glass slides. PD-L1 testing was performed using the SP263 (Ventana, Tucson, AZ) or 22c3 (DAKO, Santa Clara, CA) anti-PD-L1 platforms (44-gene) (Illumina, Inc., San Diego, CA).

Results

Signet-ring-cell carcinoma (SRCC) is a rare variant of adenocarcinoma, accounting for about 10% of gastric cancer (GC) and 1% of colorectal cancer (CRC). Despite a decrease in the overall incidence of GC in recent decades, the incidence of SRCC is constantly increasing, in Asia, United States and Europe [1].

Background

The table below summarizes the genomic findings of SRC-CRC:

Conclusions

Our research is the first to comprehensively characterize the molecular features of SRCC from gastric and colorectal tumors. Our data suggest that SRCCs harbor similar genomic signatures, regardless the tumor location. On the other hand, significant differences were observed between SRCCs and non-SRCC both within GC and CRC. Therefore, histology-driven tailored therapy should be provided to these patients. Further studies are warranted to elucidate molecular mechanisms accounting for the aggressive behavior of SRCCs.

References