Results

CMS4 Transverse unclear Right Rectal

• Original data from Lenz lab show that single nucleotide
  polymorphisms in the dopamine pathways are associated
  with outcome in mCRC patients receiving frontline
treatment.

• Notably, when compared to primary tumors, all 7 gene sets were significantly enriched in brain metastases (mets; ES ratio 1.14-1.55), while abdomen, liver, and peritoneal mets displayed significant decreases in most NT gene sets. DA was enriched in ovarian and lung mets (ES ratio: 1.18 and 1.09, respectively), the latter also showing increased neurotrophins ES (1.06) (all

• When investigating primary tumors grouped according to overall ES by unsupervised clustering,
  a higher prevalence of TMB-
  low ES clusters in primary tumors (including CMS subtypes, TMB,
  MSI and PD-L1 rates), and differential immune cell infiltration.

• In addition, neurotransmitters can affect endothelial cells
  and immune cells in the tumor microenvironment to
  promote tumor progression.

• Notably, this is the first and most extensive molecular profiling study to
  investigate NT signaling pathway alterations in CRC.

• Our data show a distinct distribution of pathway enrichment
  according to metastatic site, distinct molecular features in high vs
  low ES clusters in primary tumors (including CMS subtypes, TMB,
  MSI and PD-L1 rates), and different immune cell infiltration.

• These findings support the role of NT signaling in the metastatic
  spread of CRC and modulation of tumor immune microenvironment.

Conclusions

Methods

• A total of 7,595 CRC tumors tested at Caris Life Sciences
  Phoenix, AZ; 2. Caris Life Sciences, Phoenix, AZ; 3. Departments of Neurosurgery, Physiology & Neuroscience, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA; 4. West Virginia University Cancer Institute, Morgantown, WV; 5. University of Miami Sylvester Comprehensive Cancer Center, Miami, Florida; 6. Levine Cancer Institute, Carolinas HealthCare System, Charlotte, NC; 7. Department of Hematology and Oncology, Comprehensive Cancer Center Institute, Instituto Molecular de Investigación y Formación, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA; 8. Lawrence J. Ellison Institute for Transformative Medicine, USC Norris Comprehensive Cancer Center, Keck School of Medicine, Los Angeles, CA; 9. Department of Oncology, Karmanos Cancer Institute, Wayne State University, Detroit, MI; 10. Ruesch Center for The Cure of Gastrointestinal Cancers, Lombard Comprehensive Cancer Center, Georgetown University Medical Center, Washington, DC.

• Introduction

• Table 1. Enrichment Score (ES) According to Metastatic Sites.

• Figure 1. Sample Distribution and Patient Demographic.

• Figure 2. Clustering of Primary Tumors According to ES.

• Figure 3. Tumor Characteristics According to Enrichment Cluster.

• Figure 4. Molecular Characteristics According to Enrichment Cluster.

• Figure 5. Immune Cell Infiltration According to Enrichment Cluster

• Table 1. Enrichment Score (ES) According to Metastatic Sites.

• Summary

• ES based on sample sites showed a substantial heterogeneity in NT enrichment.

• Notably, when compared to primary tumors, all 7 gene sets were significantly enriched in brain metastases (meta; ES ratio: 1.14-1.55), while abdomen, liver, and peritoneal mets displayed significant decreases in most NT gene sets. DA was enriched in ovarian and lung mets (ES ratio: 1.18 and 1.09, respectively), the latter also showing increased neurotrophins ES (1.06) (all

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  spread of CRC and modulation of tumor immune microenvironment.

• All effects remain significant after multiple correction.

• Conclusions

• This is the first and most extensive molecular profiling study to
  investigate NT signaling pathway alterations in CRC.

• Our data show a distinct distribution of pathway enrichment
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