Oral Scientific Sessions

LBA-1

Cancer-associated Fibroblasts Transform Monocytes into Protumorigenic Macrophages via IL-22 Signaling in Head and Neck Squamous Cell Carcinoma

T.F. Olonisakin, A. Mayer, and U. Duvvuri; Medical Scientist Training Program, University of Pittsburgh, Pittsburgh, PA, Enable Medicine, Menlo Park, CA, Department of Otolaryngology, Eye & Ear Institute, University of Pittsburgh Medical Center, Pittsburgh, PA

Purpose/Objective(s): The tumor microenvironment (TME) is composed of several cell types that have been shown to play fundamental roles in tumor growth and metastasis. Uncovering landscapes and mechanisms within TME is critical for identifying new therapeutic modalities to improve outcomes in head and neck squamous cell carcinoma (HNSCC). We hypothesized that discrete cell clusters in the pathologic landscape of HNSCC drive tumor growth and result in worsened patient outcomes.

Materials/Methods: To identify motifs that define patient subsets and their clinical outcomes, a multiplexed tissue imaging platform was used to analyze 56 markers in single cells on formalin-fixed paraffin embedded (FFPE) HNSCC tissue samples. Peripheral blood mononuclear cells (PBMC) were isolated from HNSCC patients and co-cultured with normal (FFPE) HNSCC tissue samples. Peripheral blood mononuclear cells (PBMC) were isolated from HNSCC patients and co-cultured with normal (FFPE) HNSCC tissue samples. Peripheral blood mononuclear cells (PBMC) were isolated from HNSCC patients and co-cultured with normal (FFPE) HNSCC tissue samples. Peripheral blood mononuclear cells (PBMC) were isolated from HNSCC patients and co-cultured with normal (FFPE) HNSCC tissue samples. Peripheral blood mononuclear cells (PBMC) were isolated from HNSCC patients and co-cultured with normal (FFPE) HNSCC tissue samples.

Results: Using the imaging platform, we delineated the single cell pathologic landscape of HNSCC and uncovered an enrichment of macrophage-fibroblast interactions in patients that succumbed to disease (P = 0.01). In vitro, we discovered that HNSCC-associated fibroblast induced PBMC IL-22 secretion (fold change = 43.9, P = 0.004), a finding that was not observed with normal fibroblasts. Furthermore, we discovered that supernatant obtained from PBMC-fibroblast co-culture in a time- and dose-dependent manner. STAT3 activation was assayed via western blot and cell proliferation was determined using WST-1.

Conclusion: Our findings indicate that fibroblast-macrophage crosstalk within HNSCC TME induces IL-22 secretion and drives tumor growth. These findings suggest that targeting the IL-22 pathway may be beneficial in HNSCC.

Author Disclosure: T.F. Olonisakin: None. A. Mayer: None. U. Duvvuri: None.

LBA-2

Targetable Vulnerabilities of Head and Neck Cancer Cell Lines Detected by the DepMap CRISPR Screens

A.C. Cao, P. Rajagopalan, P.A. Gimotty, R. Brody, and D. Basu; Department of Otorhinolaryngology - Head and Neck Surgery, University of Pennsylvania, Philadelphia, PA, Department of Biostatistics, Epidemiology & Informatics, University of Pennsylvania, Philadelphia, PA

Purpose/Objective(s): The DepMap genome-wide loss of function CRISPR screens offer new insight into gene dependencies in HPV(-) head and neck squamous cell carcinoma (HNSSC) cell lines. We aimed to leverage this data to guide preclinical studies by cataloging targetable dependencies that are predicted to offer a therapeutic window. We also aimed to identify targets representing potential synthetic lethals by testing for associations between genetic alterations and dependency profile.

Materials/Methods: DepMap was queried for gene probability and effect scores in cell lines from 77 tumors, including 62 HPV(-) HNSSCs plus 15 ESCCs, which have comparable etiologic and genetic profile. A probability score of ≥ 0.5 was used as the threshold for essentiality. Essential genes were selected for analysis by 3 criteria: (1) presence in ≥10% cell lines, (2) lack of common essentiality in prior CRISPR screens of normal human cell lineages, and (3) designation as druggable by the Drug-Gene Interaction Database. Gene set enrichment analysis (GSEA) was performed using the Hallmark Gene Sets. DepMap gene effect scores were used to prioritize targets likely to have a useful therapeutic window based on median scores greater than for EGF (0.66) but less than for common essential genes (1.0). The Open Targets platform was used to identify targets with inhibitors used in trials for other cancers and/or nonmalignant diseases. Associations between dependencies and genetic alterations were defined using two-sample t-tests, with filter conditions of p<0.05 and effect size ≥1.

Results: The 231 genes meeting selection criteria had a median gene effect score of 0.56. The criteria captured targets of standard therapeutic agents including TYMS (5-FU), tubulin genes (paclitaxel), EGF (cetuximab), plus known oncogenes like PIK3CA. GSEA showed enrichment of known oncogenic signaling pathways including PI3K/AKT and JAK/STAT, as well as hallmark cancer processes like DNA repair and apoptosis. 90% were not known oncogenes in the OncoKB Database. 44 genes had a median gene effect score between that of EGF and the median for common essential genes (1.0). The Open Targets platform was used to identify targets with inhibitors used in trials for other cancers and/or nonmalignant diseases. Associations between dependencies and genetic alterations were defined using two-sample t-tests, with filter conditions of p<0.05 and effect size ≥1.

Results: The 231 genes meeting selection criteria had a median gene effect score of 0.56. The criteria captured targets of standard therapeutic agents including TYMS (5-FU), tubulin genes (paclitaxel), EGF (cetuximab), plus known oncogenes like PIK3CA. GSEA showed enrichment of known oncogenic signaling pathways including PI3K/AKT and JAK/STAT, as well as hallmark cancer processes like DNA repair and apoptosis. 90% were not known oncogenes in the OncoKB Database. 44 genes had a median gene effect score between that of EGF and the median for common essential genes (1.0). The Open Targets platform was used to identify targets with inhibitors used in trials for other cancers and/or nonmalignant diseases. Associations between dependencies and genetic alterations were defined using two-sample t-tests, with filter conditions of p<0.05 and effect size ≥1.

Results: The 231 genes meeting selection criteria had a median gene effect score of 0.56. The criteria captured targets of standard therapeutic agents including TYMS (5-FU), tubulin genes (paclitaxel), EGF (cetuximab), plus known oncogenes like PIK3CA. GSEA showed enrichment of known oncogenic signaling pathways including PI3K/AKT and JAK/STAT, as well as hallmark cancer processes like DNA repair and apoptosis. 90% were not known oncogenes in the OncoKB Database. 44 genes had a median gene effect score between that of EGF and the median for common essential genes (1.0). The Open Targets platform was used to identify targets with inhibitors used in trials for other cancers and/or nonmalignant diseases. Associations between dependencies and genetic alterations were defined using two-sample t-tests, with filter conditions of p<0.05 and effect size ≥1.

Results: The 231 genes meeting selection criteria had a median gene effect score of 0.56. The criteria captured targets of standard therapeutic agents including TYMS (5-FU), tubulin genes (paclitaxel), EGF (cetuximab), plus known oncogenes like PIK3CA. GSEA showed enrichment of known oncogenic signaling pathways including PI3K/AKT and JAK/STAT, as well as hallmark cancer processes like DNA repair and apoptosis. 90% were not known oncogenes in the OncoKB Database. 44 genes had a median gene effect score between that of EGF and the median for common essential genes (1.0). The Open Targets platform was used to identify targets with inhibitors used in trials for other cancers and/or nonmalignant diseases. Associations between dependencies and genetic alterations were defined using two-sample t-tests, with filter conditions of p<0.05 and effect size ≥1.

Results: The 231 genes meeting selection criteria had a median gene effect score of 0.56. The criteria captured targets of standard therapeutic agents including TYMS (5-FU), tubulin genes (paclitaxel), EGF (cetuximab), plus known oncogenes like PIK3CA. GSEA showed enrichment of known oncogenic signaling pathways including PI3K/AKT and JAK/STAT, as well as hallmark cancer processes like DNA repair and apoptosis. 90% were not known oncogenes in the OncoKB Database. 44 genes had a median gene effect score between that of EGF and the median for common essential genes (1.0). The Open Targets platform was used to identify targets with inhibitors used in trials for other cancers and/or nonmalignant diseases. Associations between dependencies and genetic alterations were defined using two-sample t-tests, with filter conditions of p<0.05 and effect size ≥1.

Results: The 231 genes meeting selection criteria had a median gene effect score of 0.56. The criteria captured targets of standard therapeutic agents including TYMS (5-FU), tubulin genes (paclitaxel), EGF (cetuximab), plus known oncogenes like PIK3CA. GSEA showed enrichment of known oncogenic signaling pathways including PI3K/AKT and JAK/STAT, as well as hallmark cancer processes like DNA repair and apoptosis. 90% were not known oncogenes in the OncoKB Database. 44 genes had a median gene effect score between that of EGF and the median for common essential genes (1.0). The Open Targets platform was used to identify targets with inhibitors used in trials for other cancers and/or nonmalignant diseases. Associations between dependencies and genetic alterations were defined using two-sample t-tests, with filter conditions of p<0.05 and effect size ≥1.
Conclusion: We catalog numerous targetable dependencies in cell line models of HNSCC. While well-studied targets were captured, many genes lacked known roles in malignancy. Targets of inhibitors tested in other diseases provide further resources to guide preclinical studies. Association of some dependencies with known molecular subgroups in HNSCC may enhance use of cell line models to personalize therapy.


LBA-3

Patient-reported Outcomes in Oropharyngeal Cancer Treated With Definitive Chemoradiation vs. Surgery With Postoperative Radiation With or Without Chemotherapy

M.W. McDonald,1 J.E. Bates,1 M.R. Patel,1 B.J. Boyce,2 S. Rudra,1 A.S. Kaka,3 C. Steuer,3 D.M. Shin,1 S. Tian,1 M.R. Nathan,2 J.M. Waller,2 S.E. Thomas,3 J.S. Remick,1 T. Barrett,1 L. Ottenstein,1 N.F. Saba,1 and W.A. Stokes1; 1Department of Radiation Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; 2Department of Otolaryngology, Winship Cancer Institute of Emory University, Atlanta, GA; 3Department of Hematology and Medical Oncology, Winship Cancer Institute of Emory University, Atlanta, GA; 4Winship Cancer Institute of Emory University, Atlanta, GA

Purpose/Objective(s): There are limited data comparing patient-reported outcomes (PROs) for pts treated with definitive CRT versus TOS and postop IMRT with or without chemotherapy.

Materials/Methods: We included patients with clinical T0-T2 N0-3 oropharyngeal cancer treated from 08/2019 − 08/2021 with CRT to 70 Gy IMRT or TOS with pathology-directed adjuvant IMRT (60 − 66 Gy) with or without chemotherapy. All received bilateral neck radiation. Patients completed MDADI and MDASI-HN questionaries prior to, weekly during, or without chemotherapy. All received bilateral neck radiation. Patients treated with CRT had fewer average days of hospitalization per reason (0.5) compared to those treated with T+aCRT (3.1, p<0.001) or T+aRT (6, p<0.001).

Conclusion: Despite smaller average tumor volumes, lower dose RT, omission of chemo in 42% and omission of the primary site in 21%, TOS pts reported worse MDADI scores 3 mos after RT (6 mos after TOS) compared to those treated with proton-based CRT.