Conclusions

Through this novel co-culture model (figure 5), we demonstrate that patient-derived NSCLC cells reproducibly induce three major macrophage phenotypes in an oncotype-independent manner. Furthermore, cytokine release from NSCLC cells and CAFs is implicated in this process. This co-culture model provides a physiologically consistent experimental platform to identify tumor cell and CAF features that drive macrophage phenotype which may be suitable for targeted therapy.

Acknowledgements

We thank the McDermott Center Next-Generation Sequencing Core at UT Southwestern. Figure 5 was created with Biorender.com

REFERENCES


http://dx.doi.org/10.1136/jitc-2020-SITC2020.0746

EVALUATION OF IMMUNE MICROENVIRONMENT OF PRIMARY LUNG CANCER AND SYNCHRONOUS LIVER METASTASIS WITH MULTISPECTRAL IMAGING SYSTEM

Hyeonbin Cho*, 1Jae-Hwan Kim, 2Ji-Hyun Kim. 1Iolani School, Honolulu, HI, USA; 2Yonsei University College of Medicine, Seoul, Korea, Republic of

Background Cancer immunotherapy (CIT) has substantially improved the survival of cancer patients. However, according to recent studies, liver metastasis was reported to predict worse outcomes for CIT. The main objective of the study is to evaluate the differences in the immune microenvironment (IME) between the primary lung cancer (PL) and synchronous liver metastasis (LM) using a multispectral imaging system.

Methods Six immune markers (CD4, CD8, CTLA-4, granzyme B (GZB), Foxp3 and PD-L1) were analyzed using a multiplex IHC system and inForm program (Akoya) on paired lung-liver samples of 10 patients. Cells were categorized into tumor nest and stroma, and cell counts per unit area were measured for comparison.

Results The number of tumor-infiltrating cytotoxic T cells (TIL) in PL (262.5 cells/mm2) was higher than that of LM (113.3 cells/mm2). Additionally, the ratio between the number of TIL and non-TIL was greater in PL (0.31) compared to that of LM (0.26). A similar trend appeared for Helper T
cells and regulatory T cells (Treg), as PL consisted of higher numbers of T cells (791.8 Helper T cells/mm², 195.7 Treg/mm²) than LM (626.3 Helper T cells/mm², 121.3 Treg/mm²). However, cytotoxic T cells expressing GZB+ and CTLA-4- were fewer in PL (140.2 cells/mm²) than in LM (203.3 cells/mm²), and the ratio is 0.69. The mean number of GZB+ TIL in PL (32.5 cells/mm²) was lower than in LM (35.3 cells/mm²), and their proportions among total TIL counts were 0.12 and 0.31, respectively. In PL, GZB+: GZB- ratio is 0.16 while the ratio is 1.91 for LM. A fewer number of TILs exhibiting GZB suggests that PL has lower efficiency in immune response than LM. Another crucial checkpoint receptor that inhibits immune response, CTLA-4, was more prevalent in PL, with CTLA-4+: CTLA-4- ratio in Treg being 0.36 in PL, compared to 0.11 in LM. The tumor proportion score (TPS) of PD-L1 was higher in PL than LM (40.0 vs. 6.6).

Conclusions In our study, we showed the differences in the numbers of TIL or regulatory T cells and expressions of immune checkpoint receptors (PD-L1, CTLA-4), which significantly influence outcomes for CIT. The study is ongoing to confirm different IME between the PL and LM groups in a larger tumor cohort.

REFERENCES


http://dx.doi.org/10.1136/jitc-2020-SITC2020.0747

Abstract 748 Figure 1 Mesothelin expression by primary tumor location
A+C Representative low Mesothelin expression at low (X10) (A) and higher power (X20) (C). B+D Representative high Mesothelin expression at low (X10)(B) and higher power (X20)(D). E) Log(x+1) transformed Mesothelin Expression as determined by automated cell counting, median and IQR, all data points shown. Median: 5.5, 79.5, 146.0 for ICC, H-ECC, D-ECC, respective, p-value = 0.025. F-H) Mesothelin Expression determined by visual inspection and scoring for ICC (F), H-ICC (G), and D-ECC (D).

MYELOID CELL INFILTRATION CORRELATES WITH PROGNOSIS AND VARIES BASED ON TUMOR LOCATION IN CHOLANGIOCARCINOMA

Paul Kunk, Sean Dougherty*. University of Virginia, Charlottesville, VA, USA

Background Cholangiocarcinoma (CC) is a rare malignancy with an increasing incidence and poor prognosis. Immunotherapy represents one potential treatment for CC, however identification of immunotherapeutic targets requires a thorough characterization of the tumor immune microenvironment (TIME). Mesothelin, a tumor associated antigen, is abundantly expressed in CC tumors (1+ in 68% of tumors, while PD-L1 was expressed (≥1+) in 68% of tumors (figure 1), while PD-L1 was expressed (≥1%) in only 16% of tumors. Higher densities of M1 macrophages (CD68+) were present in D-ECC relative to ICC and H-ECC (figure 2). M1 macrophages were also found in higher densities in metastatic tumors. Mesothelin and granzyme-B expression was significantly higher in D-ECC. Increasing density of myeloid cells (CD14+) and M2 macrophages (CD163+) was associated with worse survival (p = 0.02, 0.03, respectively) (figure 3). Intraepithelial and intratumoral T cell infiltration did not correlate with OS.