**Abstracts**

**479** EXPRESSION OF LEUCINE-RICH REPEATS AND IMMUNOGLOBULIN-LIKE DOMAINS PROTEIN 1 (LRIG1) ON CD4+/CD8+ T CELLS MAY ASSOCIATE WITH PATHOLOGICAL CHARACTERISTICS OF DIFFERENT TYPES OF CANCER

Dia Roy*, Hieu Ta, Cassandra Gilmour, Timothy Chan, Kemian Zhang, Li Wang, Sarah Stone. Lerner Research Institute, Cleveland, OH, United States

**Background** The tumor microenvironment (TME) gets infiltrated with numerous components of adaptive and innate immune system. However, the immune surveillance imparted by these components are often suppressed by numerous mechanisms in the TME in a context dependent manner. The tumor cells can mediate the signaling suppression of the immune cells which is reflected by the reduction in the activity of stimulatory immune-receptors and the concomitant activation of the inhibitory immune-receptors. In case of T cells, for instance, tumor cells facilitate the inhibition of the TCR-mediated activation signaling. Alongside, the tumor cells can also facilitate the up tuning of numerous inhibitory checkpoint receptors (ICRs). Several ICRs like CTLA-4, PD-1, and LAG3 have been studied in context of cancer immunotherapy in past decades. However, a great many drawbacks have begun to come to light with the gradual increase in accumulation of clinical data-the most obvious gridlock being its low response rate in most cancers thereby urging the need for the discovery of novel immune checkpoint molecules.

**Methods** Multi panel flow cytometry and Western blot analysis was done to check LRIG1 expression. Bioinformatics analysis was done on the RNA seq data from the study by Feldman et al.

**Results** The current study manifested the expression of Leucine-rich repeats and immunoglobulin-like domains protein 1 (LRIG1) on both CD4+ and CD8+T cells. Expression of LRIG1 can be detected in the tumor infiltrating lymphocytes (TILs) and also on the in-vitro activated T cells from both human and murine cancer models. Within the CD4 compartment, expression of this molecule on the immunosuppressive regulatory T cell was highly upregulated.

Further, the single cell RNA seq data from melanoma patients reanalyzed from the study obtained by Feldman et al. revealed the exclusive expression of LRIG1 among other exhausted markers such as TIM3, LAG3 and TIGIT.

**Conclusions** LRIG1 has been identified as a potent immune suppressor molecule in numerous tissue but its role remains widely unexplored in context of the immune cells.

Detection of LRIG1 in different subsets of CD4+ and CD8+ might lead to interesting findings about its role in context of mounting anti-tumor immune response.

**Acknowledgements** The Wang lab is funded by American Cancer Society RSG-18-045-01-LIB, NIH/NCI (7 R01CA223804, 5 R01CA164225, 1 R21CA258618-01), Department of Defense (W81XWH-21-LCRP-IITRA and W81XWH-21-MRP-MCAA).

**REFERENCES**

1. Y Wang, EJ Poulin, RJ Coffey, LRIG1 is a triple threat: ERBB negative regulator, intestinal stem cell marker and tumour suppressor. 2013 May 14;108(9):1765–70.

**Ethics Approval** The human samples were obtained from Cleveland clinic after ethical approval.