**The recruitment of CD8+ T cells through YBX1 stabilization abrogates tumor intrinsic oncogenic role of MIR155HG in lung adenocarcinoma**

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 **Presenter:** Liu-Chia Jung **Date/Time:** 2024/10/17, 15:10-16:00

 **Commentator:** Dr. Chang-Chih Peng **Location:** Room 601, Med College Building

**Background:** In recent years, immunotherapy, particularly, PD-1/PD-L1 immune checkpoint inhibitors has demonstrated substantial benefits for many patients with advanced cancer types. Specifically, PD-1 inhibitor immunotherapy has notably improved a 5-year survival rate in advanced lung cancer. However, the response rate to PD-1 or PD-L1 mAb therapy remains below 40% in most cases. Therefore, it is urgently needed to identify biomarkers that can predict the efficacy of immunotherapy or to explore alternative treatments such as combination therapy. The MIR155 host gene (MIR155HG), a novel member of the lncRNA family, is classified as the primary-miRNA (primiRNA) of miR-155. It has been suggested to have an oncogenic role in various cancers. With the development of research, many study reported that high expression of MIR155HG was closely related with immune checkpoint molecules expression. For all this, the specific mechanism of MIR155HG in the immune microenvironment of lung adenocarcinoma and its relationship with immunotherapy remain to be clarified.

**Objective/Hypothesis:** To provides a novel biomarker and potential combination treatment strategy for LUAD patients who received immunotherapy.

**Result:** First, they observed that MIR155HG was associated with a favorable prognosis in LUAD patients and the existence of immune system abrogated tumor intrinsic oncogenic role of MIR155HG in lung adenocarcinoma by using PBMC-transferred NCG mice. Second, they found that MIR155HG was positively associated with CD8+ T cells infiltrating in vivo and in vitro. Third, they used gene set enrichment analysis (GSEA) and conducted T cell migration assay to determine that MIR155HG promoted the recruitment of CD8+ T cells through the regulation of chemokine CCL5. Fourth, they performed an RNA pull-down assay and RNA immunoprecipitation (RIP) assays to indicate that MIR155HG interacted with YBX1 protein to increase the protein stability. Afterwards, they performed chromatin immunoprecipitation (ChIP) assay to confirm that MIR155HG promoted CCL5 transcription through YBX1 in LUAD. They then validated that MIR155HG upregulated PD-L1 transcription to hamper the activity of recruited CD8+ T cells by employing a co-culture system. Finally, they indicated that MIR155HG correlated with the efficacy of PD-L1 mAb therapy in LUAD patients and improved antitumor effect of PD-L1 blockade in vivo. Taken together, these results suggested that MIR155HG could serve as a biomarker for predicting the efficacy of immunotherapy in LUAD and had a synergistic effect with PD-L1 mAb treatment.

**Conclusion:** This study highlights the potential of MIR155HG as a biomarker of immunotherapy efficacy prediction in LUAD patients, while exploring its combination with PD-L1 mAb treatment to enhance immunotherapy efficacy. Most importantly, their work provided a new strategy and therapeutic opportunity for LUAD patients received immunotherapy.