Elevated levels of anti-tumor immunity related markers and cells are the best correlates of long-term survival in SCLC

Farhad Kosari
Mayo Clinic, USA

Introduction: While most small cell lung cancer (SCLC) patients die within a few months, a sub-group of patients survive for many years. Factors determining long-term survivorship remain largely unknown. We present the first comprehensive comparative genomic and tumor microenvironment analyses of small cell lung cancer (SCLC) between patients with long term (LTS) and expected (EXS) survival times.

Methods: We compared surgically resected tumors of 23 LTS (survival>4 years) and 18 EXS (survival≤2 years). There were no differences in clinical variables including TNM staging and curative versus non-curative intend surgery between the groups. Gene expression profiling was performed by microarrays and tumor microenvironment analyses were by IHC of prominent immune related markers.

Results: Immune related genes and pathways represented the majority of the differentially overexpressed genes in LTS compared to the EXS. The differences in the immunological tumor-microenvironment were confirmed by quantitative immuno-staining. Increased numbers of tumor infiltrating and associated lymphocytes were present throughout tumors of LTS. Several differentiating patterns of enhanced anti-tumor immunity were identified. While some areas of LTS tumors also harbored higher numbers of suppressive immune cells (monocytes, regulatory lymphocytes, and macrophages), ratios of these suppressive cells to CD3+ lymphocytes were generally lower in LTS tumors indicating a more tumor suppressive microenvironment.

Conclusions: Our data demonstrate that long-term survivorship of SCLC patients is strongly influenced by the presence of anti-tumor immune cells in the tumor microenvironment. Characterization of the anti-tumor immune responses may identify opportunities for individualized immunotherapies for SCLC.

e: kosari.farhad@mayo.edu

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