세미나 초록

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발표 주제	**Intrinsic glucocorticoid signaling in refractory gastric cancer & tumor microenvironment**
발표 내용	**BACKGROUND & AIMS**: Cancer immunotherapy is an emerging treatment, particularly for malignant tumors; however, resistance poses a significant challenge. Using the gastric cancer stem-like subtype, known for its poor clinical outcomes, this study explores how glucocorticoid receptor (GR) signaling via the target gene RASD1 promotes tumor progression and immune evasion, positioning RASD1 as a potential target for immunotherapy. **METHODS:** We investigated the transcriptomic features of 497 patients with gastric cancer. Syngeneic mouse models were generated using cancer cells with modulated RASD1 expression, a gene that is highly upregulated in the stem-like subtypes. These models were treated with immunotherapy and analyzed using single-cell RNA sequencing. To overcome immunotherapy resistance, GM-CSF was co-administered with anti-PD1 to improve the efficacy of RASD1-overexpressed tumors. **RESULTS:** Elevated RASD1 promotes tumor growth and resistance to anti-PD1 therapy. Immune profiling of RASD1-overexpressing tumors revealed an increase in the number of myeloid derived suppressor cells (MDSCs) and a decrease in the number of cytotoxic CD8+T cells. GM-CSF treatment reduced tumor growth and MDSC levels, which were upregulated by the downregulation of RASD1. Combined GM-CSF and anti-PD1 treatment suppressed tumor growth by increasing the number of cytotoxic CD8+GZMB+ T cells. **CONCLUSIONS:** Tumor progression driven by RASD1-induced immunosuppression highlights the need for additional treatments beyond anti-PD1 treatment. RASD1 promotes immune evasion by facilitating MDSC accumulation and skewing the tumor microenvironment toward an immunotherapy-resistant state. GM-CSF reverses the immunosuppressive effects and restores effective anti-tumor immune response.