

# Unveiling surface Tumor-Associated Antigens across Diverse Immune Scenarios for Osteosarcoma

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**INTRODUCTION:** Tumor development and drug resistance are intricately influenced by the tumor immune microenvironment and tumor-associated antigens (TAAs). However, the identification of universally applicable TAAs across diverse immune scenarios, named uTAAs, is a challenge, attributed to immune-related biases in the cancer transcriptome.

**METHODS:** To address this challenge, we introduce a Cell-Surface Antigen Targeting (CSAT) system that integrates machine learning techniques to identify TAAs. Applied to osteosarcoma (OS), a tumor thriving within an immune-rich bone marrow microenvironment, we employed the CSAT system on 73 human primary OS transcriptomes. Clinical information and RNA-seq counts of 73 primary osteosarcoma patients were obtained from the Therapeutically Applicable Research to Generate Effective Treatments (TARGET) database.

**RESULTS SECTION:** This approach yielded 153 potential surface uTAAs universally relevant across varying immune infiltration levels. Bioinformatics analysis highlighted their association with immune systems and G-protein-coupled receptors. Literature scrutiny revealed that these CSAT findings were predominantly assessed in cancer studies, with a subset evaluated in OS contexts. From these, 26 surface uTAAs (CD34, CXCR4, KDR, GGT1, PTPRC, CD68, FOLH1, CSF3R, CD86, ITGAM, CSF1R, CD163, TNFRSF9, HAVCR2, CSF2RA, IL21R, CDH5, SPN, IFNAR2, CX3CL1, PTAFR, FLT4, CASR, CXADR, LPL, and ITGB4) emerged as high-priority therapeutic targets, with 23% (KDR, CSF3R, CSF1R, CSF2RA, IFNAR2, and FLT4) currently under investigation in ongoing OS clinical trials, underscoring CSAT's accuracy and adaptability. Moreover, external datasets confirmed the heightened expression of selected uTAAs in OS patients and cell lines. Notably, multivariate analysis showcased a significant correlation of all 153 uTAAs with OS.

**DISCUSSION:** These discoveries hold implications for enhancing comprehension and treatment strategies in OS and potentially other malignancies.

**SIGNIFICANCE/CLINICAL RELEVANCE:** Our CSAT system effectively identifies potential surface uTAAs, offering prospects as OS diagnostic markers and for immunotherapeutic interventions.

**REFERENCES:** NA

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## IMAGES AND TABLES:

