ORAL PRESENTATION Turkish Journal of Immunology, 14(Suppl 1):15

The Importance of Antigen Presentation Mechanisms and HLA Expression in Cancer Stem Cells' Immune Evasion Strategies of Pancreatic Cancer

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Abstract

Objective: HLA molecules and antigen presentation pathways are critical for interactions between tumor cells and T cells. Defects in these mechanisms during carcinogenesis enable immune evasion. Cancer stem cells (CSCs) contribute to recurrence and treatment resistance due to their tumorigenic capacity and resistance to conventional therapies. Targeting CSCs and restoring HLA expression may improve outcomes. This study aimed to evaluate antigen presentation components and HLA expression in pancreatic cancer and CSCs.

Materials and Methods: In silico analyses assessed expression of 40 antigen presentation genes according to high and low levels of 10 CSC markers across two pancreatic cancer datasets. Survival analyses compared patients with mutated and unmutated antigen presentation genes. In vitro studies were performed using BxPC3 and CFPAC1 cell lines. CSC presence was determined using specific markers. Tumor spheres were generated, and CSC proportions, along with HLA-ABC and B2M expression, were analyzed in spheres and parental cells by flow cytometry. This study was supported by the Hacettepe University Scientific Research Projects Coordination Unit (No: 19477).

Results: Differential expression of antigen presentation molecules was observed across CSC marker groups. NLRC5 expression was significantly reduced in groups with high CSC marker expression, including PROM1 (CD133), SOX2, CD24, and CD44 ($p<0.05$). Survival was higher in patients without mutations in antigen presentation genes, although not statistically significant ($p=0.564$; $p=0.128$). In vitro findings showed increased CSC proportions in spheroids, while B2M and HLA-ABC expression was significantly decreased ($p<0.05$).

Conclusion: These findings indicate that impaired antigen presentation and reduced HLA expression contribute to immune evasion in pancreatic cancer and CSCs. Targeting key molecules in this pathway may improve treatment strategies and warrants further investigation.

Keywords: Antigen presentation mechanism, HLA expression, cancer stem cell, pancreatic cancer

OP-10

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Published
July 13, 2026

DOI
10.36519/tji.2026.op10