High Density of Tumor-Associated Macrophage Staining Correlates with Poor Clinicopathologic Markers in Head and Neck Squamous Cell Carcinoma: A Meta-Analysis

Alexander Knops, BA  
*Thomas Jefferson University, alexander.knops@jefferson.edu*

Ayan Kumar, BS  
*Thomas Jefferson University, ayan.kumar@jefferson.edu*

Brian Swendseid, MD  
*Thomas Jefferson University, brian.swendseid@jefferson.edu*

Ubaldo E. Martinez-Outshoorn, MD  
*Thomas Jefferson University, Ubaldo.Martinez-Outschoorn@jefferson.edu*

Larry Harshyne, PhD  
*Thomas Jefferson University, larry.harshynejr@jefferson.edu*

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Authors
Alexander Knops, BA; Ayan Kumar, BS; Brian Swendseid, MD; Ubaldo E. Martinez-Outshoorn, MD; Larry Harshyne, PhD; Nancy Philp, PhD; Ulrich Rodeck, MD, PhD; Christopher Snyder; Adam Luginbuhl, MD; David Cognetti, MD; Jennifer Johnson, MD; and Joseph Curry, MD

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High density of tumor-associated macrophage staining correlates with poor clinicopathologic markers in head and neck squamous cell carcinoma: A Meta-Analysis

Authors: Ayan T. Kumar, Alexander M. Knops, Brian Swendseid, Ubaldo Martinez-Outschoorn, Larry Harshyne, Nancy Philp, Ulrich Rodeck, Chris Snyder, Adam Luginbuhl, David Cognetti, Jennifer Johnson, Joseph M. Curry

Background: Head and neck squamous cell carcinoma (HNSCC) develops within a complex cellular microenvironment that promotes tumor growth, but also represents many potential therapeutic targets. Macrophage presence within that environment has been implicated in the growth, aggression, and persistence of HNSCC. Current literature reports variable degrees of association between tumor-associated macrophage (TAMs) density and clinicopathologic markers of disease. Inconsistent findings may result from grouping of TAM subtypes, which include both M1 (pro-inflammatory) and M2 (immunosuppressive). Our aim is to define the prognostic significance of the phenotypes of tumor-associated macrophages in HNSCC.

Methods: We conducted a meta-analysis of the existing publications investigating the relationship between TAMs (total and M2 subtype) and T stage, nodal involvement, vascular invasion, lymphatic invasion, and tumor differentiation. Forest plots and risk ratios were generated to report overall effect.

Results: Higher density of both total and M2 subtype of TAMs in the tumor microenvironment is associated with advanced T stage, increased rates of nodal positivity, presence of vascular invasion, and presence of lymphatic invasion (p < 0.0001). There is no significant association between either total or M2 TAM density and tumor differentiation.

Conclusion: Increased density of TAMs, including those of the M2 phenotype, correlates with poor clinicopathologic markers in HNSCC, and therefore poor clinical prognosis. It is unknown whether
this relationship is causative or correlative. Additional investigation into the mechanisms behind TAM recruitment and differentiation, and effect of TAM population manipulation on tumor behavior will help define the feasibility of TAM-targeted therapies.