Immune Microenvironment of Vestibular Schwannomas

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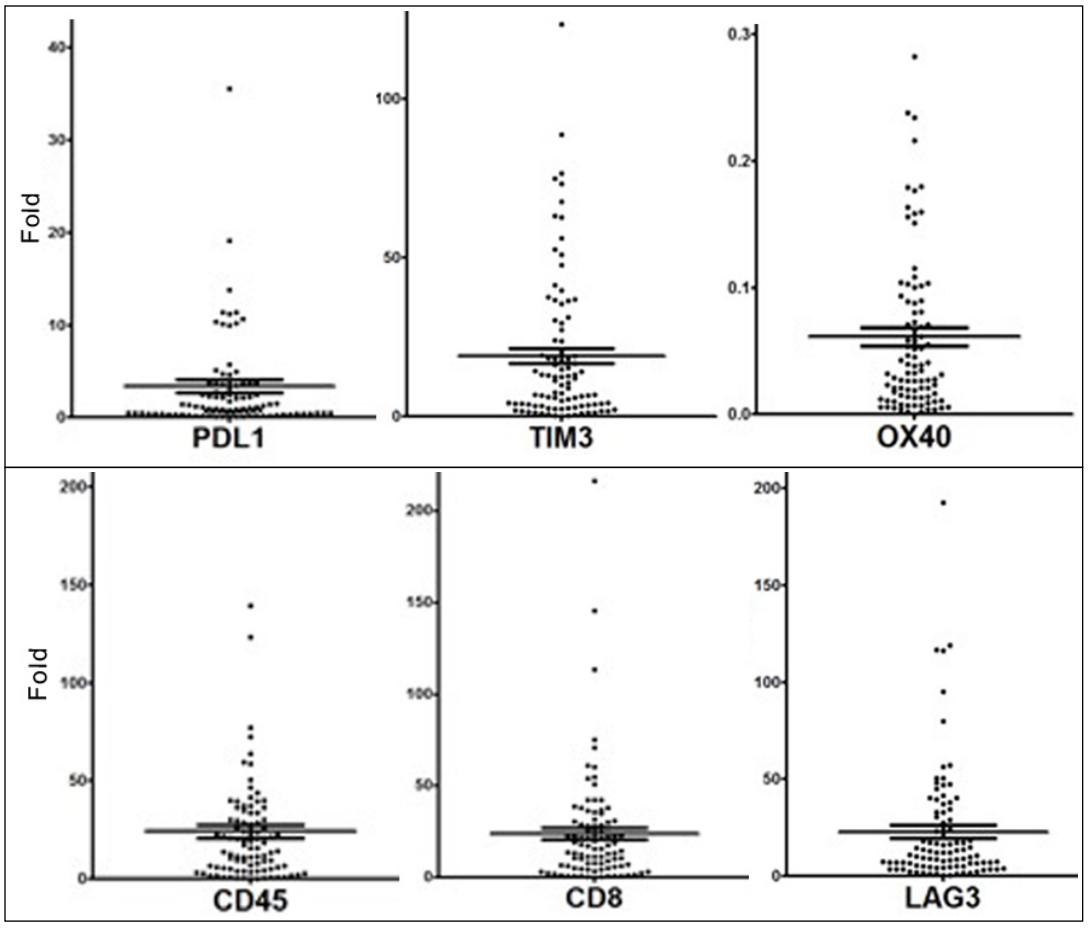
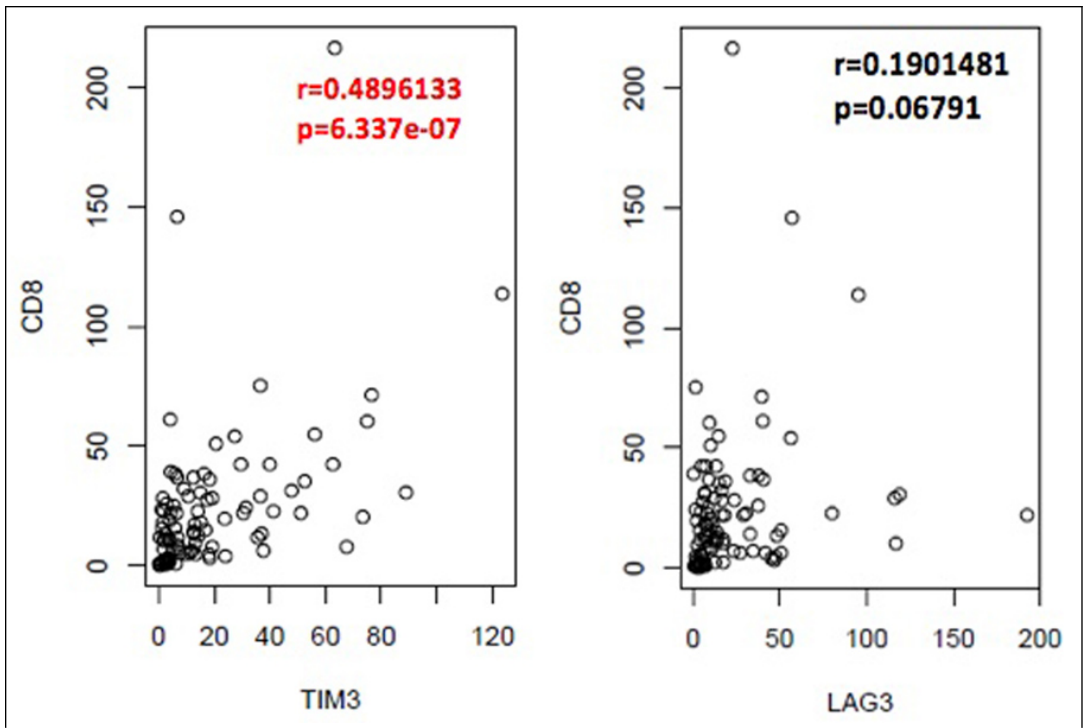
Introduction

Vestibular schwannomas exhibit a variable natural history, with one-third demonstrating growth on extended observation and two-thirds maintaining a stable size or exhibiting spontaneous regression. Elucidation of the biological basis for this difference in natural history may open potential therapeutic avenues for control of tumor growth. We hypothesized that schwannomas attract a variable immune profile which may influence their behavior, and sought to characterize this immune microenvironment.

Methods

90 vestibular schwannomas were evaluated for immunohistochemical expression of the immune regulators PD-L1, TIM-3, OX40, and LAG3, as well as for the T cell markers CD45 and CD8. Expression levels in vestibular schwannomas were normalized to that of normal brain tissue.





Correlation between TIM3 and LAG3 with CD8 expression levels in vestibular schwannomas.

Results

Negative regulators of the immune response, including PD-L1 and TIM-3, were elevated across vestibular schwannomas, compared to normal brain. In contrast, OX40, a T cell activator was lower in vestibular schwannomas compared to normal brain. Notably, although CD8 expressing cells were higher across vestibular schwannomas compared to controls, LAG3, a marker of T cell exhaustion was also markedly elevated. These results suggest a role for altered immune response in vestibular schwannomas.

Conclusions

Vestibular schwannomas demonstrate variable expression of immune regulatory markers as well as immune infiltrates. Elevated expression of negative regulators of the immune response as well as markers of T cell exhaustion suggests that tumor-associated inflammation orchestrated with local immunosuppression may critical role in these tumors. A role for immunotherapy modulation in select schwannomas may merit further exploration.