

Title: INTRATUMORAL PLASMACYTOID DENDRITIC CELLS AND T CELLS ASSOCIATE WITH INCREASED SURVIVAL IN PATIENTS WITH FOLLICULAR LYMPHOMA (FL)

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Background: Gene array studies on FL have associated characteristic intratumoral macrophage and dendritic cell and/or T cell signatures with both increased and decreased survival. FL has previously been reported to depend on adequate T cell help for progression. Interferon alpha, produced by plasmacytoid dendritic cells, has been used with success in the therapy of follicular lymphoma. We wanted to test whether these features would translate into prognostic factors detectable by immunohistochemistry.

Design: A TMA was constructed with duplicate cores from 252 archival follicular lymphoma samples biopsied between 1990 and 2004. Immunohistochemistry was performed for CD123 + plasmacytoid dendritic cells (clone 3H3 from eBioscience) and CD3 + T cells (clone SP7 from Lab Vision) on a Ventana Discovery module and quantified by counting stained cells or by stained area fraction determinations. Quantifications could be correlated with survival and clinical data including FLIPI in 131 patients.

Result: High numbers of both CD3 + cells or CD123 + cells associated with increased survival. Low numbers of CD123 + cells further correlated with B symptoms and elevated LDH. Numbers of CD123 + cells correlated with CD3 + cells. In multivariate models, however, both CD123 and CD3 proved to be comparable independent prognostic factors. CD123 was more significant than CD3 in predicting B symptoms and advanced tumor stage, and CD123 was also more significant than grading, FLIPI or age in predicting survival.

Conclusion: T cells and plasmacytoid dendritic cells associate with and/or influence the clinical course of patients with follicular lymphoma. Association of CD3 + T cells and CD123 + plasmacytoid dendritic cells with survival may suggest that the preservation of the preexisting interfollicular T cell compartment associates with prognosis. The findings may, however, also suggest, that FL with numerous T cells may still be dependent on T cells for growth and may therefore carry a better prognosis. CD123 + plasmacytoid dendritic cells may associate with longer survival as they endogenously produce the interferon in situ that otherwise would need to be provided by external sources for therapy.