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Mass cytometry identifies loss of co-stimulatory receptor expression as a novel immune signature in follicular lymphoma

Tcells in the tumor microenvironment of Follicular Lymphoma (FL) are heterogeneous in phenotype and different subsets have differing impact on patient outcome. Using Mass Cytometry (CyTOF), we identified at least 12 subsets of CD4+ T cells in FL biopsy specimens and found that some subsets were more prevalent in FL and less prevalent in tonsil tissue. Specifically, we found that CD4+ T cells in FL more frequently had a memory phenotype, but that the number of naïve T cells, rather than memory cells, was associated with a favorable clinical outcome. To determine which memory T cell populations may negatively affect prognosis, we focused on 6 subsets of memory cells, two populations that express CD25 and four that express PD-1. In FL, one of the subsets of CD4+ CD25+ T cells had decreased expression of CD27 and CD28 and this subpopulation was expanded when compared to controls. Similarly, in the PD-1 expressing T-cell subsets, two subsets had decreased expression of CD27 and CD28 when compared to controls. While the total number of PD-1-expressing T cells was not associated with FL patient outcome, we found that increased numbers of PD-1+ T cells exhibiting decreased CD27 and CD28 expression was associated with poorer patient survival. We found that T cells with decreased CD27 and CD28 expression tended to lose expression of other functional T cell markers, failed to proliferate when stimulated and appeared terminally differentiated. Furthermore, we found that CD70+ lymphoma cells play an important role in down-regulating expression of CD27 and CD28 on T cells. Taken together, our mass cytometry results have identified novel CD4+ memory T cell populations that are poorly functional and are associated with an inferior survival in FL.

Biography

Zhi-Zhang Yang is an Assistant Professor at Mayo Clinic, USA. He has published more than 30 papers in reputed journals such as *Journal of Clinical Investigation, Blood, Cancer Research* and *Leukemia*. He has been serving as reviewer for journals and funding grants.

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