Abstract

T lymphomas are malignant tumors that could arise from the T cell of any type and developmental stage. Their clinical presentation could largely vary from indolent to very aggressive form. Its exact pathophysiology is still not completely understood; therefore, it is critical to uncover the main mechanism underlying T-lymphoma development and growth to guide rational treatment. T-cell receptor (TCR) is a critical sensor and major determinant of T-cell fate. Therefore, we aimed to assess the function of TCR in T-cell lymphomas.

We hypothesized that TCR might provide tumor cells with proliferative signals even in the absence of antigen stimulation. Using model human T-cell lymphoma derived cell lines expressing TCR, we investigated consequences following the knockout (KO) of TCR and CD3. We showed that TCR KO was associated with decreased cellular growth and related changes in cell cycle, however other proliferative functions seem to be uncompromised. TCR KO was also associated with a decrease of AKT kinase activity.

Our RNA sequencing-based comparison of unmodified and TCR KO cells uncovered alterations in several signaling pathways important for cell survival. Among the altered were WNT, NF-κB, Jak/STAT and others. Additionally, TCR loss was associated with defects in antigen presentation. Genetically, TCR signaling alterations are common in lymphomas and TCR is frequently completely lost. Therefore, functional consequences of altered TCR signaling or its modulation in malignant cells seems to be more complex.

We concluded that cells were dependent on signals from TCR, however they were able to stabilize and adapt to their new TCR-null phenotype. Interestingly, our results also demonstrated differences between TCR and CD3 KO, suggesting signaling differences and distinct ways of adaptations and compensations.

Key words: T lymphocytes, T-cell receptor, non-Hodgkin lymphoma, cell lines, tumor signaling