T CELL RECONSTITUTION STUDIES IN ZAP-70 DEFICIENT MICE

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The ZAP-70 kinase (70kDa Zeta-Chain Associated Protein) plays a central role in signal transduction through the antigen receptor during T cell activation. The importance of the molecule is clearly demostrated when it is absent: several signaling pathways are inhibited, and severe T-cell immunodeficiency appears both in humans and mice. The reason of the latter is that ZAP-70 is indispensable in T cell differentiation: in its absence the maturation of T cells in the thymus is blocked in the double positive (CD4+CD8+) stage, and, as a consequence no mature T-cells can be found in the peripheral lymphoid organs.

In our work we studied the possibilities of T cell reconstitution in ZAP-70 deficient mice. We performed adoptive transfer experiments, where ZAP-70-/- mice were reconstituted with bone marrow or thymus cells from their wild type (ZAP-70 expressing) siblings intrahepatically or intraperitoneally.

According to our results both transfer techniques were effective in restoring T cells. After the cell transfers, blood was taken every 2 weeks to detect the presence of T cells in the blood. The survival of those animals which had T cells reconstituted exceeded significantly those which were immunodeficient. Both flow cytometric measurements and immunohistochemistrical staining performed after the experiments (following the transfers) proved that T cells appeared in the spleen, lymph nodes and gut associated lymphoid tissues of the animals. Furthermore, during the investigation of cell constitution of the thymus, we have found that the ratio of CD4+ or CD8+ single positive cells increased significantly, which indicated the normalisation of T-cell maturation.

Thus, we managed to establish stable chimerism in ZAP-70 deficient mice with two methods. We proved that both thymus and bone marrow originated cells were able to restore the development of T-cells.

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