Effect of Glucocorticod-Induced Leucine Zipper (GILZ) on B cells

D. Sorcini, C. Cappelletti, V. Bardelli, O. Bereshchenko, T. Frammartino, M. Cimino, S. Bruscoli and C. Riccardi

Dept. of Medicine, Section of Pharmacology, University of Perugia, Italy.

Glucocorticoids (GC) are commonly used as anti-inflammatory/immunosuppressive drugs but also as antitumor agents in several lymphoma/leukemia, in fact therapeutic doses of GC, induce growth suppressive and cytotoxic effects on various leukocytes including B cells. Their action include induction of GC target genes, among which we found Glucocorticoid-induced leucine zipper (GILZ) that belongs to TSC22d family. Recent studies have been demonstrated that, TSC22d mutated forms are implicated in diffuse large B cell lymphoma patients, suggesting that also TSC22d family members may play a role in lymphoma development. In our study, we have used a murine model of conditional knock-out mice (cKO) for GILZ, that determine GILZ deletion specifically in B lymphocytes. We have found that GILZ deletion in B cell leads to an accumulation of B lymphocytes in the bone marrow, blood and lymphoid tissues. Gilz conditional knock out (cKO) mice develop a progressive non-lethal B lymphocytosis, with expansion of B220+ cells in bone marrow and periphery, dependent on increased B cell survival; this B expansion, mainly is due to the more differentiated B cell subpopulation. Decreased B cell apoptosis in B cell lacking GILZ is due to increased NF-kB transcriptional activity and Bcl-2 expression. These results confirmed that the defect is B cell self-intrinsic, furthermore, since lymphocytosis in cKO mice could result in increased immunoglobulins (Ig) levels we performed ELISA to measure levels of IgG, IgM and ANA sera concentration in WT and cKO mice. Results didn't show any difference between WT and cKO mice. At the end, we can consider GILZ as an important regulator of B cell survival, suggesting that the deregulation of GILZ expression could be implicated in the pathogenesis of B cell disorders.