Glucocorticoid-Induced Leucine Zipper (GILZ) and the new isoform L-GILZ mediate the anti-inflammatory effects of glucocorticoids

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Glucocorticoids (GC) hormones have been widely used to treat many inflammatory and autoimmune diseases as well certain neoplastic diseases, including haematological malignancies. Physiological production of GC plays a role in many aspects of immune system function and anti-inflammatory activity of GC has been described as one of the mechanisms underlying their pharmacological and physiological effects. Their therapeutic activity is due to regulatory effects on cell growth and differentiation on a number of tissues, including the immune/inflammatory system.

To characterize the molecular mechanisms of GC action, we have identified a number of GC-induced genes including GILZ (Glucocorticoid-Induced Leucine Zipper), a protein rapidly induced by GC treatment. GILZ mediates most of GC effects including regulation of NF-kB and MAPK pathway that is part of the GC-mediated anti-inflammatory activity. Moreover, we identified a new GILZ isoform, L-GILZ, involved in mediating the effects of GC on inflammation and on cell differentiation. Furthermore, our study demonstrates that both GILZ and L-GILZ are crucial mediators of GC-induced effects in that mediate the anti-inflammatory/immunosuppressive activity. In particular, GILZ regulates T cell activation and differentiation, cytokines, including pro-inflammatory cytokines, production and inflammatory process development. Our results indicate that GILZ is an important player of GC-induced effects, mediate the anti-inflammatory/immunosuppressive activity of GC and regulate cell differentiation.