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Functional Analysis of the Human FCGRT Promoter Polymorphisms

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FUNCTIONAL ANALYSIS OF THE HUMAN FCGRT PROMOTER POLYMORPHISMS

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Recent studies have indicated that the neonatal Fc Receptor may play a role in autoimmune diseases such as Systemic Lupus Erythematosus (SLE). The neonatal Fc receptor (FCGRT, also called FcRn) mediates transmission of immunoglobulin G (IgG) from mother to fetus perinatally and also plays a central role in the protection of serum IgG from catabolism. The expression levels of FCGRT directly correlate with serum IgG concentrations. FCGRT deficient mice were protected against SLE because serum IgG level is not at the concentration necessary to produce autoantibodies leading to the disease. Therefore, understanding the transcriptional regulation of the human FCGRT gene and how genetic polymorphisms in the promoter affect the receptor expression will help identify alleles that contribute to autoimmune diseases. In this study, we sequenced 20 individuals and identified a 37 base pair deletion in the promoter region. Promoter reporter analyses in both monocytic U937 cells and epithelial MDA468 cells demonstrated that the proximal 1 kb promoter of human FCGRT confers the greatest promoter activity and the 1 kb promoter with the 37 nucleotide deletion leads to decreased promoter activity. Our data suggests that the transcriptional control of the human FCGRT gene may reside within 1 kb proximal promoter and the deletion polymorphism decreases the promoter activity. These results provide insights for the regulation of the endogenous FCGRT receptor expression and predict that individuals with the deletion polymorphism express lower levels of FCGRT. Lower levels of FCGRT may indicate that the deletion polymorphism acts as a protection against autoimmune disease.