The Journal of Immunology, 2007, 178: 42.12.

42.12

Polymorphisms in *Paan-AG* promoter influences NF-κB binding and transcription activity in HEK293 cells

Daudi K Langat[1], Pedro J Morales[1], Charles O Omwandho[2], Asgerally T Fazleabas[3] and Joan S Hunt[1]

[1] Department of Anatomy and Cell Biology, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS, 66160-7400, [2] Department of Biochemistry, University of Nairobi, P . O . Box 30197, Nairobi, Kenya, [3] Department of Obstetrics and Gynecology, University of Illinois at Chicago, 820 S. Wood Street (m/c 808), Chicago, IL, 60612-7313

Abstract

HLA-G is a protein highly expressed at the human maternal-fetal interface during pregnancy. It is thought to be critical for the survival of the semi-allogenic fetus. The baboon (*Papio anubis*) expresses an HLA-G-like protein termed Paan-AG in the placenta, and may serve as a model for HLA-G studies. Paan-AG shares many characteristics with HLA-G, including alternative splicing of the mRNA and restricted tissue expression of the protein. Our hypothesis is that the two genes share similar regulatory mechanisms. The objective of the current study was to assess binding of the transcription factor NF-κB to *Paan-AG* κB elements and determine the effects of binding on *Paan-AG* promoter activity. We assessed two *Paan-AG* alleles each containing two κB elements, κB1 and κB2. NF-κB bound both κB1 and κB2 elements in the AG1 allele. In contrast, only κB1 of the AG-2 allele bound to NF-κB; κB2 did not bind. Mutagenesis studies showed that the difference in binding was due to two nucleotide differences in the 3' end of κB1. The functional activity of the two alleles also differed; AG2 consistently showed higher luciferase activity compared to AG1. Mutating the last two nucleotides in the 3' end of κB1 resulted in an increase of luciferase activity to levels comparable to that of AG2. Overall, these results suggest that variations in the proximal promoter may influence transcription rates of *Paan-AG* as reported recently for *HLA-G*, and provide further evidence of the potential usefulness of the baboon as a model for in *vivo* HLA-G studies.

Supported by NIH grant HD39878 (JSH).