A36 B CELL ACTIVATING FACTOR OF THE TNF FAMILY: δ4BAFF, AN ALTERNATE-SPLICE ISOFORM THAT ACTS AS A TRANSCRIPTION FACTOR AND EXAGGERATES ITS PRODUCTION IN AUTOIMMUNITY AND CANCER

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Objective Elevated serum levels of the B cell activating factor (BAFF) characterise autoimmune diseases, such as rheumatoid arthritis (RA) and Sjögren's syndrome (SS). Herein, we report the discovery of a new transcript for BAFF due to the splicing of exon 4.

Results A 3′ RACE-PCR was performed in B cells from SS patients and revealed another transcript with deletion of nucleotides 749–861 encoding the predicted exon 4. To assess the biochemical properties of the new variant of BAFF, RAMOS B cells were transiently transfected with pIRES2-EGFP-δ4BAFF. Two bands at 21 and 17 kDa prove to belong to δ4BAFF, which is very telling of a post-translational modification. Incubation with PNGase F showed that δ4BAFF was glycosylated and led to the predicted mobility of δ4BAFF at 17 kDa. Interestingly, δ4BAFF was located in the nucleus and, contrary to full-length BAFF, absent from the cytoplasm. Because BAFF was upregulated after δ4BAFF transfection in RAMOS cells, we asked the question as to whether δ4BAFF might function as a transcriptional regulator of BAFF gene. A chromatin immunoprecipitation analysis revealed that the δ4BAFF protein bound to a specific region within the BAFF promoter. Finally, we observed the presence of the δ4BAFF protein in B cells from patients with chronic lymphocytic leukaemia (CLL), in synoviocytes from patients with RA or in epithelial cells from patients with SS.

Conclusion We describe a new variant for BAFF, δ4BAFF, which acts as a transcription factor of its own gene, and could explain the overexpression of BAFF in autoimmunity and CLL.