

Genetic variability of alpha chain of high-affinity IgE receptor gene and its expression

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Introduction and aims of the study

High-affinity IgE receptor (Fc RI) present on mast cells or basophils surface plays a crucial role in the pathogenesis of allergic disorders [1,2]. The α chain (Fc RI) forms the only extracellular part of the Fc RI and is responsible for antigen binding [1,2]. Recent work by Nishiyama et al. [3–8], provided some new insights into the structure and function of the gene encoding for Fc RI (*FCER1A*). However, till the previous year only 2 papers were published on *FCER1A* genetic variability [9,10]. Shikanai et al. [9] described –344 C>T polymorphism indirectly associated with total serum IgE levels in asthmatics, whereas Hasegawa et al. [10] reported on –95 T>C polymorphism associated with alterations in gene proximal promoter activity due to changes in transcription factor GATA-1 binding. Recently, an association between –344 TT genotype and total serum IgE levels in allergic subjects was reported [11,12].

We, therefore, decided to study joint –344 C>T/–95 T>C *FCER1A* polymorphisms influence on proximal promoter transcriptional activity with subsequent search for eventual –344 C>T-associated changes in transcription factors binding [Fig. 1.].

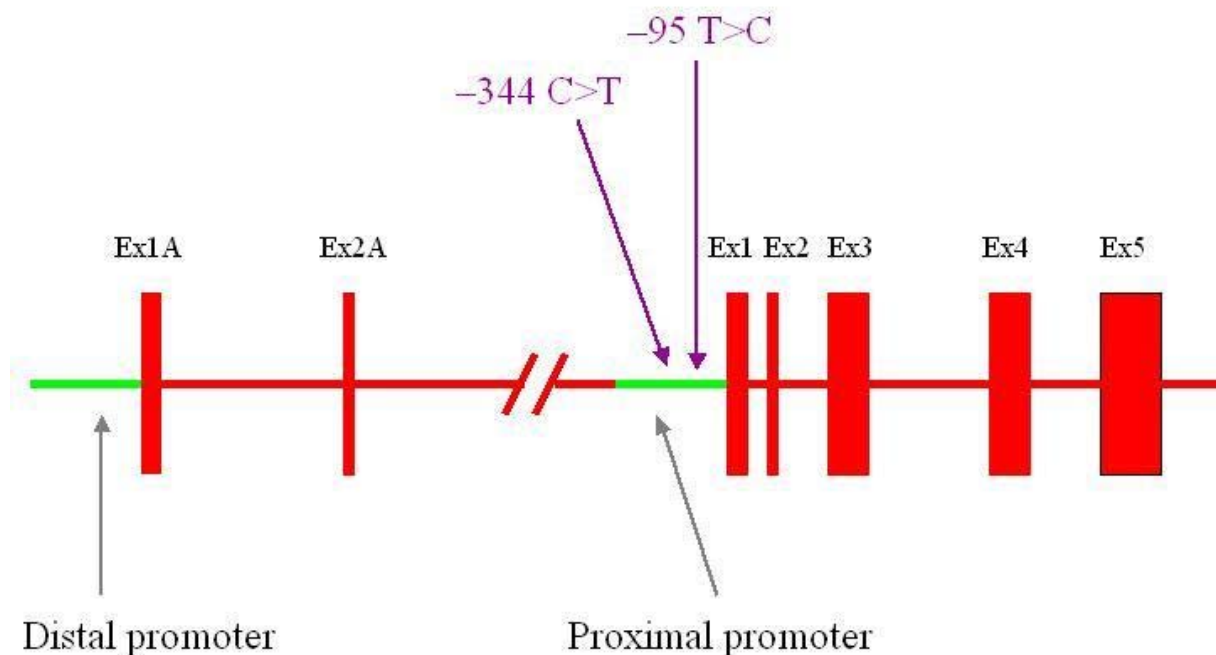


Fig. 1. Schematic representation of the *FCER1A* gene and two promoter polymorphisms we studied.

Material and Methods

During the Fellowship period 3 luciferase assays (in PT18 or RBL-2H3 cells) and 6 electrophoretic mobility shift assays (EMSA) (using extract from PT18 or RBL-2H3 cells) were performed.

Results

Luciferase assay in both cell lines showed interesting transcriptional activity pattern [Fig. 2.]. The proximal promoter relative transcription activity was the lowest for constructs carrying –344 C/–95 C variants, while that for –344 T/–95 T constructs were the highest [Fig. 2.]. The proximal promoter relative transcriptional activity observed for –344 C/–95 T and –344 T/–95 C constructs was intermediate [Fig. 2.]. These results were further confirmed in experiments conducted after the termination of the Fellowship (data not included).

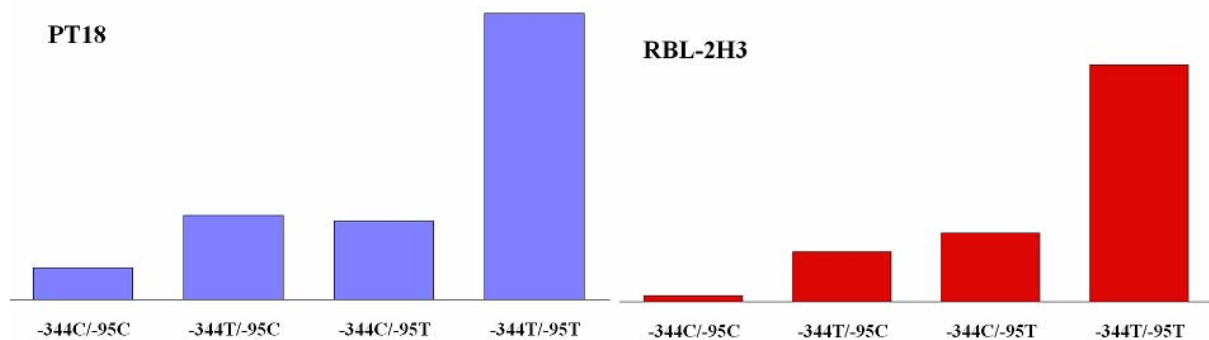


Fig. 2. Results of luciferase assay performed in PT18 or RBL-2H3 cells.

Initial EMSA results (obtained during the Fellowship period) suggested the presence of differences in transcription factors between –344 T and –344 C variants [Fig. 3.]. This issue is, however, still under investigation and the final results are expected to be obtained in the nearest future.

Conclusions

The results we obtained suggest that both –344 C>T and –95 T>C polymorphisms influence *FCERIA* gene proximal promoter activity. This is in line with the previous findings by Hasegawa et al. (–95 T>C) [10] and very recent report by Bae et al. (–344 C>T) [13]. The originality of our study is that we analyzed the influence of both mutations on *FCERIA* proximal promoter activity together. This enabled us to find an interesting stepwise –344 C>T/–95 T>C-dependent proximal promoter activity pattern, in which the highest activity is reached for –344 T/–95 T promoter version while the lowest for –344 C/–95 C one. Also our initial EMSA results suggest some genotype-related differences in transcription factors binding. Further investigation on transcription factors binding profile is currently ongoing.

The differences in total serum IgE levels together with varying proximal promoter activity associated with *FCER1A* genetic variability might possibly suggest the presence of *FCER1A* polymorphisms-dependent total serum IgE levels regulation.

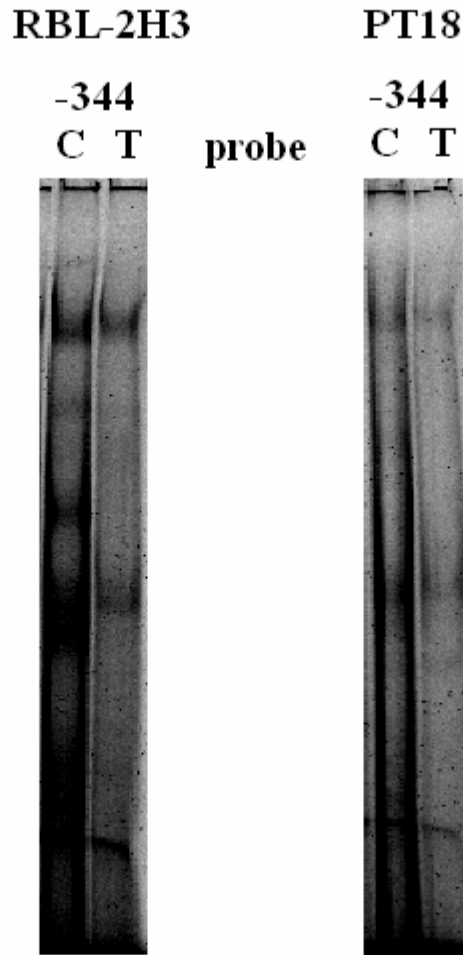


Fig. 3. Initial results from EMSA performed in RBL-2H3 and PT18 cells.

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