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The dependence of expression of NF-B dependent genes: Statistics and evolutionary conservation of control sequences in the promoter and in the 3 UTR

Background: NF-B family plays a prominent role in innate (early) immune response and has impact on other processes such as cell cycle activation or cell apoptosis. Upon stimulation by pathogens such as viral RNA a kinase cascade is activated, which eventually strips the NF-B of its inhibitor IB molecule and allows it to translocate into the nucleus. Once in the nucleus, it activates transcription of approximately 90 genes, some of which trigger further stages of the immune response. NF-B-dependent genes can be categorized, based on the timing of their activation counted from NF-B translocation into the nucleus, as Early, Middle and Late genes. It is not obvious what mechanism is responsible for segregation of the genes timing of transcriptional response. Results: It is likely that the differences in timing are reflected in differences in the structure of promoter regions of genes in different categories. Specifically, this might concern differences in number and type of transcription factor binding motifs, required for NF-B itself as well as for the putative cofactors. Using this approach we analyzed if genes assignment to the Early, Middle or Late group based on expression pattern, is connected with special features in promoter structure. This connection may be one of the mechanisms underlying the different patterns of gene expression control. This issue is best considered in the evolutionary framework, first, since functional binding sites are likely to be conserved in evolution and second, since the patterns of evolutionary change of promoter regions are not very well-known and are of serious interest. Another control sequences are AU - rich elements (ARE) located in 3UTR. AREs target mRNA for rapid degradation and inflict mRNA instability. Latest studies show that genes transcribed with unstable mRNA have different transcription dynamic. We have found that there are significant differences between the Early and the Late genes promoter and 3UTR regions and many similarities are observed among the Early genes even between distant species, while the Late genes promoter regions are much more diversified. Conclusions: Wider phylogenetic analysis of NF-B dependent genes provides insight into the degree of cross species similarity found in the Early genes, opposed to many differences in promoter structure that can be found among the Late genes. This suggest that activation and expression of the Late genes is much more species specific than in the Early genes. Based on the promoter structure and ARE content Middle genes can be divided into two subgroups: Early like and Late like.