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Transcriptional directionality of the human insulin-degrading enzyme promoter

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Abstract Unidirectional promoters dominate among mammalian genomes. However, the mechanism through which the transcriptional directionality of promoters is accomplished remains to be clarified. Insulin-degrading enzyme (IDE) is a ubiquitously expressed zinc metalloprotease, whose promoter contains a CpG island. We previously showed that the basal promoter region of mouse *IDE* has bidirectional transcriptional activity, but an upstream promoter element blocks its antisense transcription. Therefore, we wonder whether the human *IDE* promoter contains an analogous element. Similarly, the basal promoter region of human *IDE* ($-102 \sim +173$ and $-196 \sim +173$ relative to the transcription start site) showed bidirectional transcriptional activity. However, the region from -348 to $+173$ could only be transcribed from the normal orientation, implying that an upstream promoter element between -348 and -196 blocks the antisense transcription of the human *IDE* promoter. Through promoter deletion and mutagenesis analysis, we mapped this element precisely and found that the upstream promoter element locates between -318 and -304. Furthermore, the transcription-blocking elements in the mouse and human *IDE* promoters inhibited the transcription of the SV40 promoter when put downstream of it. In conclusion, we identify an upstream promoter element which blocks the antisense transcription of the human *IDE* promoter. Our studies are helpful to clarify the transcriptional directionality of promoters.

Keywords Transcriptional directionality · Insulin-degrading enzyme · CpG island · Unidirectional promoter · Bidirectional promoter

Introduction

Bidirectional promoters can be transcribed from both normal and opposite orientations, while unidirectional promoters can only be transcribed from one orientation. In the human genome, approximately 11 % of genes are arranged in a divergent fashion regulated by a bidirectional promoter, whose transcription start sites are less than 1 kb away [1, 2]. Bidirectional promoters are generally TATA-less [3–6] and are frequently found among CpG islands [1, 2, 7]. Binding sites of several transcription factors, including nuclear respiratory factor 1 (NRF-1), myelocytomatosis oncogene (Myc), GA-binding protein α subunit (GABPA), nuclear factor Y (NF-Y), Ying Yang 1 (YY1), E2F1, and E2F4, are over-represented in bidirectional promoters and, therefore, may play important roles during their transcriptional regulation [8].

Interestingly, most unidirectional promoters have bidirectional transcriptional potential in *Saccharomyces cerevisiae*, while the Rpd3S deacetylation complex represses upstream antisense transcription through deacetylating the

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