Bidirectional promoters with asymmetric expression profiles of the target genes induce differential transcription levels in different human cell lines

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Coordinated gene expression and it`s spatiotemporal changes to both individual genes and groups of genes in response to different stimuli, comprises the basis of the life. The primary step of this multistage process is the initiation of transcription on the gene promoter. In the past decades, using different RNA-seq approaches, it has been revealed, that the vast majority of the gene promoters are capable to initiate transcription in both directions, producing mostly short and unstable antisense transcripts. However, there is a special group of bidirectional promoters, driving the processive and stable expression of protein-coding gene pairs. In human genome, they comprise about 10% of the all protein-coding genes, and often include genes involved in the same cellular processes. Generally, these gene pairs show similar expression levels, but of particular interest are the pairs with significant asymmetry of expression. To date, the mechanisms, that provide such an imbalance in transcription of gene pairs remains mostly unclear. To test the ability of such bidirectional promoter regions to initiate differential expression levels of the reporter gene in different human cell lines, we cloned 5 different promoter regions in both orientations into a vector, containing the firefly luciferase gene and transfected these constructs in HEK293T, HeLa, and K562 human cell lines. After measuring the activity of the reporter gene, we determined the expression levels in both directions. Interestingly, some constructions in different cell lines exhibited a different expression levels. The obtained data suggest that, outside of the preformed native chromatin context, bidirectional promoters are able to induce asymmetric expression by themselves, and the expression levels depend, apparently, on the influence of cell-specific transcription factors and different distal regulatory elements. The study was supported by the Russian Science Foundation (grant no. 21-14-00035).