

## Alternative transcription start sites contribute to acute-stress-induced transcriptome response in human skeletal muscle

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More than half of human protein-coding genes have an alternative transcription start site (TSS). We aimed to investigate the contribution of alternative TSSs to the acute-stress-induced transcriptome response in human tissue (skeletal muscle) using the cap analysis of gene expression approach. TSSs were examined at baseline and during recovery after acute stress (a cycling exercise). We identified 44,680 CAGE TSS clusters (including 3,764 first defined) belonging to 12,268 genes and annotated for the first time 290 TSSs belonging to 163 genes. The transcriptome dynamically changes during the first hours after acute stress; the change in the expression of 10 % of genes was associated with the activation of alternative TSSs, indicating differential TSSs usage. The majority of the alternative TSSs do not increase proteome complexity suggesting that the function of thousands of alternative TSSs is associated with the fine regulation of mRNA isoform expression from a gene due to the transcription factor-specific activation of various alternative TSSs. We identified individual muscle promoter regions for each TSS using muscle open chromatin data. Then, using the positional weight matrix approach we predicted time course activation of “classic” transcription factors involved in response of skeletal muscle to contractile activity, as well as diversity of less/un-investigated factors. In conclusion, transcriptome response induced by acute stress strongly related to activation of the alternative TSSs indicates that differential TSSs usage is an essential mechanism of fine regulation of gene response to stress stimulus.

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