Molecular mechanisms underlying the regulation of HAVCR2 expression in myeloid cells

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TIM-3 (T-cell immunoglobulin and mucin-domain containing-3) is a membrane protein in humans encoded by the *HAVCR2* gene. It is a member of the immunoglobulin superfamily that is expressed on differentiated T-cells and innate immunocytes. High TIM-3 expression correlates with suppression of T-cell responses during chronic viral infections and tumor development. Joint blockade of TIM-3 together with other immunological checkpoint molecules appears to be an attractive cancer treatment strategy. Besides T-cells, TIM-3 is also expressed by the cells of myeloid origin such as monocytes, macrophages, and dendritic cells where its biological role has not been studied sufficiently. In the current study, we identified the promoter and enhancer elements in the locus of human *HAVCR2* gene using bioinformatics approaches and analyzed their functional activity in activated U937 monocyte cell line using luciferase reporter assay. Potential enhancer region located in the 3 intron provided a 10-fold increase in *HAVCR2* promoter activity. We also characterized several disease-associated single nucleotide polymorphisms in *HAVCR2* gene promoter and in the enhancer region. Thus, we defined the enhancer of *HAVCR2* gene and performed functional annotation of several single nucleotide polymorphisms of its promoter. This work is supported by grant 19-14-00341 from Russian Science Foundation.