Regulation of TIM-3 expression in T cells by tumor-conditioned media

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T-cell immunoglobulin- and mucin-domain-containing molecule-3 (TIM-3) is well known as one of the immune check point molecules. TIM-3 expression is increased on exhausted T cells and senescent T cells in numerous immune diseases including cancers. However, the regulatory mechanisms of TIM-3 expression in cancers have not been well studied. Using Jurkat T cells, we examined TIM-3 regulatory mechanisms in condition similar to tumor microenvironment. TIM-3 mRNA and protein levels were increased by co-culture of Jurkat T cells with tumor cell lines and by incubation of them in tumor cell conditioned media. Given that cyclic adenosine monophosphate (cAMP) can be transferred from tumor cells to T cells, we examined the effect of cAMP signaling on TIM-3 expression. It was promoted by intracellular elevation of cAMP concentration and activation of cAMP downstream pathways. Further, inhibition of cAMP downstream pathway attenuated TIM-3 expression in Jurkat T cells cultured in tumor-CM as well as in Jurkat T cells stimulated with a cAMP elevating agent. Conclusively, this study suggests that TIM-3 expression in Jurkat T cells may be induced by tumor CM through activation of cAMP pathway.

Biography

Immune regulation has important roles in various immune diseases. The authors have studied the regulatory mechanisms and function of TIM-3 in various cells and in an in vivo tumor model. The authors revealed the involvement of MEK and c-jun in TIM-3 expression by CD4+ T cells. Additionally, they reported that the efficacy of tumor vaccine can be up-regulated by TIM-3 pathway blockade and the IL-2 production is decreased in CD4+ T cells expressing TIM-3 through NFAT dephosphorylation and AP-1 transcription.

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