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

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Tcell 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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