Atorvastatin inhibits expression of programmed death ligand-1 induced by IFNγ in HepG2 cells

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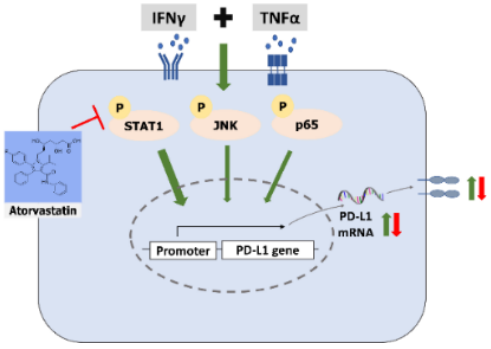
Abstract: Liver cancer is the sixth most common cancer worldwide and the most common one in Thailand. Tumour cells evade immune defense of the host by expressing programmed death ligand 1 (PD-L1), one of the negative regulatory checkpoints of immune system. PD-L1 was inducible by cytokines found in tumor microenvironment, most prominently by interferon gamma (IFNγ). This study aimed to investigate the effects of combination of tumor-related cytokines, IFNγ and tumor necrosis factor alpha (TNFα), on PD-L1 expression in human hepatocellular carcinoma cells, HepG2. Moreover, as atorvastatin, a commonly used cholesterol-lowering agent, is documented for its immunomodulatory properties, its effect on the expression of PD-L1 was investigated. In this study, PD-L1 expression in HepG2 was found to be synergistically upregulated by combination of IFNγ and TNFα in both mRNA and protein expression levels, using qRT-PCR, western blot and immunocytochemistry methods. STAT1 activation was mainly responsible for that synergism. Next, atorvastatin was shown to hamper the phosphorylation of STAT1, thereby inhibiting the expression of PD-L1 induced by IFNγ in HepG2 cells. In conclusion, in HepG2 cells, expression of PD-L1 was augmented by cytokines in tumor microenvironment; and atorvastatin inhibits induction of PD-L1 implying the effect on tumor immune response should take into consideration in cancer patients who have been prescribed atorvastatin.

Graphical abstract:



Keywords: Liver cancer, HepG2, PD-L1, IFNγ, TNFα, Atorvastatin

Funding: This research was funded by Faculty of Medicine, Chiang Mai University, Thailand. CMU Research Fund (grant number: BIO-2563-07827).

Acknowledgments: We would like to acknowledge Thailand Excellent Center for Tissue Engineering and Stem Cells, Department of Biochemistry, Faulty of Medicine, Chiang Mai University, Thailand.