Basic science

16P  Simvastatin enhances docetaxel-induced cell death in DU145 prostate cancer cells

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Aim/Background: Simvastatin downregulates cholesterol synthesis by inhibiting of hydroxymethylglutaryl-coenzyme A reductase in the mevalonate pathway and also has antitumor effects in various cancer cells. Docetaxel is a common therapeutic reagent for castration resistant prostate cancer, and the basic studies are still required for the improvement of docetaxel chemotherapy. The purpose of this study is to investigate the effect of simvastatin on the regulation of cell viability, morphology, cell death and potential network proteins by docetaxel in DU145 prostate cancer cells.

Methods: After dose- or time-dependent treatment of simvastatin and docetaxel in DU145 prostate cancer cells, the cell viability was analyzed by cell counting kit-8 (CCK-8) assay, the morphological change was visualized by phase-contrast light microscopy, the cell death was confirmed by bright field light microscopy after trypan blue staining, and the potential proteins involved in the signaling pathways of simvastatin and docetaxel were examined by Western blot analysis.

Results: DU145 cell viability was downregulated by simvastatin or docetaxel in a dose- or time dependent manner, and simvastatin enhanced downregulation of cell viability by docetaxel. DU145 cell morphology was changed similarly to a neuronal cell type by simvastatin, whereas it was changed to a round type with the nuclear fragmentation by docetaxel. DU145 cell death was induced by simvastatin or docetaxel in a dose- or time dependent manner, and simvastatin significantly enhanced docetaxel-induced DU145 cell death. Interestingly, the acetylation of α-tubulin was largely increased by docetaxel but slightly decreased by simvastatin, suggesting a different cytoskeleton structure between simvastatin and docetaxel. Moreover, the protein levels of p53 and caveolin-1 were downregulated by simvastatin or docetaxel in a dose- or time dependent manner, and simvastatin enhanced downregulation of p53 and caveolin-1 by docetaxel, suggesting a potential role of p53 and caveolin-1 in the enhancement of docetaxel-induced prostate cancer cell death by simvastatin.

Conclusions: Docetaxel-induced DU145 prostate cancer cell death was enhanced by simvastatin, and it was associated with the downregulation of p53 and caveolin-1.

Disclosure: All authors have declared no conflicts of interest.