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INVESTIGATION OF THE EFFECTS OF NOBILETIN THROUGH TOLL-LIKE RECEPTOR-9 SIGNALLING PATHWAY IN PROSTATE CANCER

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In this study, we investigated the effect of Nobiletin (NOB) on Toll-like receptor-9 (TLR9) signaling pathway and to highlight the potential for developing a treatment for this pathway that plays an important role in prostate cancer. We investigated the effects of NOB on TLR9 in LNCaP, PC-3 as prostate cancer cells and HUVEC as a control cell. Oligodinucleotide (ODN) was used for TLR9 stimulation. Cell viability was analyzed with the WST-1 assay. TLR9 gene expression was examined by Quantitative Reverse Transcription Polymerase Chain Reaction (qPCR). Cytokines (INF-α and INF-β) were analyzed with Enzyme-Linked Immunosorbent Assay (ELISA). Gelatinase activity and protein expression were examined by zymography and western blotting, respectively. Inhibitory concentrations (IC50) of NOB were found 20 μM for LNCaP and 40 μM for PC-3 and HUVEC. It was observed that NOB increased TLR4 gene expression in PC-3 but decreased in LNCaP and HUVEC. NOB reduced the amount of INF-α and INF-β in PC-3. It was found that NOB reduced TLR9 protein levels in PC-3 and increased IRF-7 protein levels in PC-3 and LNCaP. Gelatinase activity of MMP-9 and MMP-2 was found low in PC-3 although there was high MMP-2 activity in LNCaP and MMP-9 activity was not observed in HUVEC. In conclusion, the effect of NOB is AR-dependent and shows a reducing effect on TLR9 signalling pathway. NOB may be effective on prostate cancer via TLRs and also TLR9-mediated signalling pathway with great potential may be important for new therapeutic approaches in prostate cancers.

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