

The effect of Doxycycline on NLRP3 inflammasome in Prostate Cancer**Научный руководитель – tezcан gulcin -***alsaadi m.¹, Hamza S.²*

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Background: Prostate cancer (PC) is the most common cancer in men[2]. It was shown that hypoxia can contribute to PC by priming cells for NLRP3 inflammasome activation[1]. Interestingly, some antibiotics have the tendency to affect NLRP3 activity though targeting mitochondria[3], and subsequently, influence PC development. However, our understanding of the Doxycyclin antibiotic regulation of NLRP3 inflammasome in PC remains largely unknown. Therefore, in the present study we investigated the in-vitro effect of Doxycyclin on PC cells.

Material and methods: PC3 cells, a PC cell line, were primed with LPS and treated with Doxycycline. LPS/Nigericin was used to activate NLRP3 in the positive control cells. Glybenclamide was used to inhibit NLRP3 in the negative control cells. The effect of Doxycycline on NLRP3 was analyzed using RT-qPCR of *NLRP3*, *Pro-CASP-1*, *Pro-IL1B* and *Pro-IL-18* mRNA; as well as western blot analysis of NLRP3 protein which is a key products of inflammasome activation. The effect of Doxycyclin on cytokine secretion was analyzed using a 41Plex assay for human cytokines. Data was evaluated using One Way Anova, Post Hoc Tukey test. The statistical software SPSS 20 was used.

Results: LPS/Nigericin significantly increased the mRNA expression of *NLRP3*, *pro-CASP1* and *pro-IL-1β* and protein expression of NLRP3. In contrast, Glybenclamide slightly reduced the mRNA expression of NLRP3, pro-CASP1, pro-IL-1β and pro-IL-18 ($p > 0.05$) and decreased the protein expression of NLRP3 as compared to untreated cells. Doxycycline and LPS&Doxycycline treatments decreased NLRP3 and pro-CASP1 mRNA levels in comparison with untreated and only LPS treated cells ($p < 0.05$ and $p < 0.001$, respectively). In addition, Doxycycline and LPS&Doxycycline decreased NLRP3 protein expression ($p < 0.05$) and secretion of EGF, Eotaxin and GM-CSF as compared to LPS treated cells.

Conclusion: We demonstrated that, Doxycycline decreased NLRP3 activation though reducing priming activity of LPS.

References

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