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EFFECTS OF GENISTEIN ON REGULATION OF DIHYDROTESTOSTERONE-INDUCED CELL PROLIFERATION IN ENDOTHELIAL AND PROSTATE CANCER CELLS

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Objectives There is currently no cure therapy available once prostate cancer is metastasised, and androgen deprivation is one of the standard therapies. However, the long-term use of oestrogens in treatment of prostate cancer is limited due to their cardiovascular side effects, such as thrombosis and cardiovascular events. This study was to examine the effect of genistein comparing to 17b-oestradiol on modulation of androgen actions in human aortic endothelial cells (HAECs) and prostate cancer LAPC-4 and LNCaP cells.

Methods MTS, RT-PCR, and Western blot were used to detect cell proliferation, mRNA and protein expression of oestrogen receptor (ER) gene, and cyclin A genes, respectively. Specific ERb siRNA was synthesised and transfected to knockdown ERb expression in prostate cancer cells.

Results Dihydrotestosterone (DHT) produced a time and dose-dependent induction of cell proliferation in HAEC, LAPC-4 and LNCaP cells. These DHT actions were inhibited by genistein in a dose-dependent way in LAPC-4 and LNCaP cells but not in HAEC cells. While bE2 only attenuated the DHT-induced cell proliferation in HAEC and LAPC-4 cells without any inhibition of DHT-induced cell proliferation in LNCaP cells. Moreover, treatment with bE2 alone in LNCaP cells significantly increased cell proliferation. In LAPC-4 cells, knockdown of ERβ expression partially eliminated the blockade of DHT-induced cell proliferation.

Conclusions This study demonstrates that genistein may be a potential agent for prostate cancer therapy since genistein inhibits DHT-induced LAPC-4 and LNCaP prostate cancer cell proliferation but not HAEC cell growth. 17b-oestradiol completely blocked DHT-induced cell growth in HAECs while inhibiting LAPC-4 cell proliferation, accounting for the side-effect of cardiovascular in Androgen deprivation therapy of prostate cancer with 17b-oestradiol. DHT-induced LNCaP prostate cancer cell proliferation cannot be attenuated by 17b-oestradiol instead 17b-oestradiol induced LNCaP cell growth dose-dependently, suggesting 17b-oestradiol is inactive in treating metastasized prostate cancer. ERβ played an important role in the modulation of androgen receptor actions.