**ABSTRACT**

Follicle-stimulating hormone receptor (FSHR) is attributed to testicular Sertoli and ovarian granulosa cells. Recently found extragonadal FSHR in prostate cancer cells suggested FSH-FSHR involvement in the pathogenesis of prostate cancer. FSHR was also localized in the tumor vessel endothelial cells. Primary prostate cancer and tumor vessel endothelial cells FSHR has opened up an oputrunity to image tumor foci as well as to target selectively the FSHR possessing cancer cells. The aim of the study was to investigate the functional role of FSHR in primary prostate cancer and androgen-dependent (LNCaP) and androgen-independent (PC-3, DU 145) prostate cancer cell lines, in primary umbilical cord vein endothelial cells (HUVEC) and the immortalized HUVEC line (HUV-ST). We also determined the therapeutic potential of a lytic peptide Phor21 conjugated to the fragment of FSHβ subunit (Phor21-FSHRβ33-53C/S) to kill selectively FSHR-expressing cancer cells. Therapeutic effects of Phor21-FSHRβ33-53C/S conjugate drugs were studied in 3 xenograft models with: 1) LNCaP cells to kill the FSHR-expressing tumor endothelial cells; 2) HEK293-FSHR tumor cells with FSHR membrane expression to test the cytotoxicity of Phor21-FSHβ33-53C/S conjugate and 3) HEK-293 cells without FSHR as negative control. On the contrary to earlier reports, FSHR expression could not be confirmed in prostate cancer cells or LNCaP, PC-3 and DU 145 cell lines. qPCR analysis, *in situ* hybridization and functional studies like cAMP production or AKT phosphorylation, angiogenesis or proliferation of HUVEC and HUV-ST cells, all failed to confirm the presence of FSHR in endothelial cells. The Phor21-FSHβ33-53C/S conjugate inhibited the growth of HEK293-FSHR xenografts possessing FSHR proving the specificity and selectivity of action, but had no effect on LNCaP and HEK-293 cells without FSHR. Taken together, no FSHR expression was found in primary prostate cancer, tested prostate cancer cell lines or xenograft tumor vessel cells. Therefore a revisit to the FSHR expression in extragonadal tissues and a caution before claiming their functional relevance in human prostate cancer or endothelial cells is needed. Phor21-FSHβ33-53C/S could be highly effective in targeted cancer therapy of FSHR-possitive cancer cells.