P34 Androgen receptor (AR) suppresses prostate cancer metastasis yet promotes bladder cancer metastasis via differential altering the miRNA525-5p/SLPI-mediated vasculogenic mimicry (VM) formation

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Introduction & Objectives: Early studies suggested that androgen receptor (AR) may play differential roles to influence the prostate cancer (PCa) and bladder cancer (BCa) metastasis, but the underline mechanisms remains unclear. Here we found that AR might function via differential altering the vasculogenic mimicry (VM) formation to either decrease PCa metastasis or increase BCa metastasis. Mechanism dissection showed AR could differential alter the VM marker SLPI expression through miR-525-5p to the 3'UTR of SLPI, and AR can either increase miR-525-5p transcription in PCa or decrease it in BCa via binding different androgen-response-elements (AREs) located on the different position of miR-525-5p 5' promoter. Further, results from LC-MS showed that the co-factors of AR in PCa and BCa are NFIX and HDAC2, respectively. Together, these results provide the first detailed mechanism how AR can differentially alter the PCa vs BCa metastasis and targeting these newly identified AR-miR-525-5p-SLPI axis may help us to better suppress the metastasis in BCa and PCa.

Conclusions: We identified AR as a key player to suppress prostate cancer cell VM yet promotes bladder cancer VM via differentially modulating the miRNA525-5p/SLPI signals, and different co-factor in BCa interact with AR may cause opposite influence to PCa. Thus could be a novel therapeutic modality to enhance ADT while also to reduce its negative side effects such as PCa metastasis.