Author's response to reviews

Title: Androgen receptor and chemokine receptors 4 and 7 form a signaling axis to regulate CXCL12-dependent cellular motility

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Author's response to reviews: see over
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Dear BMC Cancer Editorial Board,

Please find enclosed our manuscript “Androgen receptor and chemokine receptors 4 and 7 form a signaling axis to regulate CXCL12-dependent cellular motility,” which we are submitting for your consideration as a research article in BMC Cancer.

CXCR4 overexpression increases the metastatic potential of organ-confined prostate tumor cells, and is implicated in the bone metastasis of prostate tumor cells to bone marrow-derived CXCL12. Androgens also increase CXCR4 expression to increase the motility of prostate tumor cells to CXCL12. Metastatic disease is normally detected in patients with hormone-naïve prostate cancer to suggest that androgens increase the metastatic potential of human prostate tumor cells. CXCR7 is a key regulator of CXCR4-mediated motility and how androgens regulate the CXCL12/CXCR4/CXCR7 motility axis is incomplete. Our manuscript demonstrates a novel function for CXCR7 in regulating androgen-mediated motility of prostate-cancer cells through the CXCR4/CXCL12 axis. We provide the first experimental evidence that androgens inversely regulate the expression of CXCR7 and CXCR4 to coordinate the motility of prostate tumor cells to CXCL12. We also report that CXCR7 is a novel coregulator of AR-mediated transcription, and that CXCR7 acts as a rheostat to balance the motility of prostate tumor cells to androgens. We believe that these novel findings are significant to those researchers studying androgen-regulated disease processes, but will also be of broader interest to the readership of BMC Cancer, especially those studying the CXCL12/CXCR4/CXCR7 axis in the development and progression of human cancers. Clinical researchers, in particular, will be interested since our findings suggest that CXCR7 is a key regulator of prostate-cancer metastasis, and that pharmacological attenuation of CXCR7 might decrease the metastatic potential of organ-confined prostate cancers to CXCL12.

We look forward to hearing from you regarding this manuscript.

Sincerely,

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