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Oxytocin in prostate pathology. Is there a sinister side to the hormone of love?

Oxytocin has been dubbed the hormone of love for its physiological and psychosocial roles. Indeed, it is used to pharmacologically manage a number of disorders, including autism spectrum disorder. But are there unconsidered contraindications for such use? Our work has shown oxytocin to be implicated in both benign prostatic hyperplasia and prostate cancer. In both diseases oxytocin stimulates local steroidogenesis, whilst ithas been shown to have different effects on the proliferation of normal prostate stromal, epithelial and prostate cancer cell lines. Towards understanding the reasons for the differential effectswe used a transcriptomeanalysis of PC-3 and DU145 prostate cancer cell lines treated with or without oxytocin. Both cell lines displayed increased expression of genes for enzymes involved in the cholesterol biosynthetic pathway. This was unexpected, as we have previously hypothesised that the response to oxytocin is determined by the localisation of the oxytocin receptor to caveolae. It is known that DU145 form caveolae whereas PC-3s do not due to their lack of the protein PTRF (cavin-1). This was further investigated by determining the effect of oxytocin on the transcriptomeof PC-3 cells in which PTRF is re-expressed (PC-3/PTRF). In these cells oxytocin also increased the expression of genes involved in cholesterol biosynthesis. In PC-3, PC-3/PTRF and DU145 oxytocin was shown to increasegenes expression of DHCR7 (7-dehydrocholesterol reductase), ACAT (acetyl-CoA acetyltransferase 2) and HSD17B7 (hydroxysteroid 17-beta dehydrogenase 7), key enzymes in cholesterol synthesis and metabolism. A flow cytometric assay for esterified cholesterol demonstrates increased cholesterol following oxytocin treatment. In conclusion, oxytocin appears to up-regulate expression of genes involved in cholesterol biosynthesis irrespective of the presence of PTRF.

Biography

Steve Assinder completed his Doctorate studies at the University of Bristol, UK in 1996. He now leads the Bosch Institute's Andrology Research Group, at the University of Sydney. Research interests include: the roles of structural proteins in cancer development; signaling pathway integration and dysregulation in cancers; the actions of oxytocin in both benign and malignant prostate disease; identification of prognostic markers of prostate disease and treatment. He is also a founding member of the Copper Biology Research Group which is focused on chemotherapeutic implications of copper transproters.

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