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PROSTATE CANCER

Foxy-5 in prostate cancer model

A WNT5A-mimicking peptide, Foxy-5, shows promise in the treatment of prostate tumours with low or absent WNT5A levels, according to researchers in Sweden.

Previous studies have shown that a preserved high level of WNT5A protein in tumour cells of patients with localized low-grade prostate cancer is associated with increased time to biochemical recurrence after radical prostatectomy. Preserved overexpression of WNT5A protein in patients with localized prostate cancer has also been shown to predict increased relapse-free survival time and improved overall outcomes after surgery. These findings prompted Canesin and colleagues to investigate the effect of the WNT5A agonist Foxy-5 on the invasion of both DU145 prostate cancer cells (which show low endogenous expression of WNT5A) and PC3 prostate cancer cells (which show high endogenous expression of WNT5A).

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The researchers used an orthotopic mouse model to investigate the effect of Foxy-5 on the primary tumour and on metastasis *in vivo*. They injected luciferase-expressing DU145 cells or luciferase-2-expressing PC3M cells (cell types known to be highly aggressive and metastatic *in vivo*) into the prostates of 30 8-week-old NMRI (Naval Medical Research Institute) nude mice. They measured tumour growth weekly using bioluminescence optical imaging. When the imaging detected tumours in ≥50% of animals in the group, they treated the animals intraperitoneally every 2 days with either Foxy-5 or sodium chloride solution.

The researchers found that, among animals injected with DU145 cells, Foxy-5 significantly reduced the initial metastatic dissemination of tumour cells to both the regional and distal lymph nodes (by 90% and 75%, respectively). This effect was not seen in mice injected with PC3M cells. Foxy-5 had no effect on primary tumour growth, apoptosis or proliferation. The authors note that their findings are consistent with the *in vitro* data, where Foxy-5 affects invasion but has no effect on apoptosis or viability of WNT5A-low prostate cancer cells.

The authors say that their study further supports the use of Foxy-5 as a future treatment for patients with prostate cancer who lack WNT5A or show reduced endogenous expression of this protein. They note that such a treatment could stop or postpone the initial metastatic spread and could, therefore, delay the formation of local and distal metastases in these patients. The fact that Foxy-5 selectively targets metastatic dissemination could be useful in the development of combined therapies for patients with prostate cancer.

A recent phase I trial of Foxy-5 reported no toxic effects, so Canesin *et al.* postulate that it could be used in combination with currently used cytotoxic compounds as a new strategy for the treatment of patients who have prostate cancer with low expression of WNT5A protein. They say that such a combined approach might achieve a more efficient reduction in the formation and growth of metastatic foci, and consequently result in improved clinical outcomes and better quality of life in this patient group.

Rebecca Kelsey

ORIGINAL ARTICLE Canesin, G. *et al.* Treatment with the WNT5A-mimicking peptide Foxy-5 effectively reduces the metastatic spread of WNT5A-low prostate cancer cells in an orthotopic mouse model. *PLoS ONE* http://dx.doi.org/10.1371/journal.pone.0184418 (2017)

FURTHER READING Murillo-Garzón, V. A. & Kypta, R. WNT signalling in prostate cancer. *Nat. Rev. Urol.* http://dx.doi.org/10.1038/nrurol.2017.144 (2017)

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