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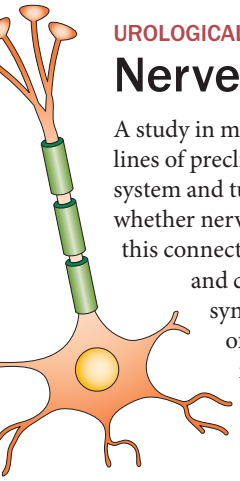


UROLOGICAL CANCER

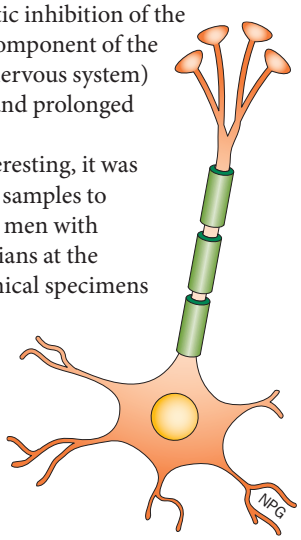
Nerves linked to prostate cancer

A study in murine models of prostate cancer has confirmed several lines of preclinical evidence that pointed to a link between the nervous system and tumour growth and metastasis. It was not previously known whether nerve fibres infiltrate tumours and alter their behaviour; now this connection has been established by Claire Magnon, Paul Frenette and colleagues."We published back in 2006 that signals from the sympathetic nervous system had played a role in the migration of haematopoietic stem cells, and hypothesized that there might be some similarities between healthy and cancer stem cells," says Frenette.

The researchers established a xenograft mouse model of prostate cancer to monitor the growth and dissemination of cancer. They observed that there were tumour-infiltrating sympathetic nerve fibres that had arisen from the normal prostate tissue, as well as intratumour parasympathetic fibres. Furthermore, using chemical or surgical sympathectomy (destroying the nerves) they were able to prevent tumorigenesis. The importance of these nerves was confirmed using a genetically modified mouse model with deficient adrenergic signalling, in which tumour development in the prostate was severely compromised.

In a total-penetrance prostate tumour genetically modified mouse model, the incidence of prostatic intraepithelial neoplasia (PIN) was reduced by 83% in mice treated with chemical sympathectomy at 2 days old. However, the timing of this treatment was important: if the mice reached 2 months old before sympathectomy was performed, there was no effect on the incidence of PIN.

The researchers then turned their attention to the parasympathetic nervous system. Pharmacological and genetic inhibition of the stromal type 1 muscarinic receptor (a key component of the parasympathetic branch of the autonomic nervous system) inhibited tumour invasion and metastasis, and prolonged survival of the mice.



Although these data are undoubtedly interesting, it was important that the researchers used clinical samples to determine the relevance of their research to men with prostate cancer. In collaboration with clinicians at the VA Medical Center, they showed that in clinical specimens from 43 patients with low-risk prostate cancer who had not received treatment for their disease, high density of sympathetic and parasympathetic nerve fibres was associated with poor survival. Although the statistical significance of nerve density was not sustained in multivariable analyses that included clinical variables, such as prostate-specific antigen, it is possible that nerve fibre density could provide clinically useful prognostic information.

As Magnon points out, "both branches of the autonomic nervous system have distinct, but complementary functions. This brings new insights into how tumours initiate and disseminate. These are potential new markers for tumour aggressiveness and new targets for cancer therapy."

Rebecca Kirk

Original article Magnon, C. *et al.* Autonomic nerve development contributes to prostate cancer progression. *Science* doi:10.1126/science.1236361