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PROSTATE CANCER

A role for neoneurogenesis in tumour progression?

Development of new nerve fibres (neoneurogenesis) might serve a similar purpose to neoangiogenesis in prostate cancer, according to new research published in *Science*. "We have described, for the first time, neonerves growing around and inside the tumour and shown that these nerves affect the behaviour of prostate cancer," explains Paul Frenette, of the Albert Einstein College of Medicine, New York.

The researchers used several experimental approaches, in both mouse models and patients with prostate cancer, to study the neural landscape of prostate tumours. Mice bearing PC3 xenografts were monitored for tumour growth after chemical or surgical ablation of sympathetic adrenergic nerves and were found to show markedly less tumour growth than control animals. Similar sympathectomy experiments were performed in a genetic model of prostate cancer (Hi-Myc mice). A strong inhibitory effect on tumorigenesis was demonstrated in Hi-Myc mice ablated at 2 days old, with no effect in mice that were 2 months of age or older, leading the investigators to propose that sympathetic adrenergic signalling drives the early stages of tumorigenesis. By contrast, modulation of parasympathetic signalling revealed a role for cholinergic fibres in the promotion of tumour cell dissemination (invasion and metastasis). "Thus, both branches of the autonomic nervous system have distinct but complementary functions," Clare Magnon, first author of the study, told *Nature Reviews Urology*. "This discovery brings new insight into how prostate tumours initiate and disseminate."

Following on from these findings, researchers assessed adrenergic and cholinergic nerve densities in a cohort of 43 men with untreated prostate cancer. They found that adrenergic fibres densely innervated normal prostate tissue surrounding the tumour, whereas cholinergic fibres infiltrated the tumour itself. Moreover, nerve fibre density was found to correlate positively with preoperative PSA, time to biochemical recurrence and extraprostatic extension in preliminary analyses.

Frenette and Magnon intend to continue their studies in order to understand exactly how sympathetic and parasympathetic signals exert their effects on prostate cancer, as well as investigate whether there is any crosstalk between neurogenesis and angiogenesis in this context. In the meantime, it is tempting to suggest that targeting both branches of the autonomic nervous system will provide therapeutic benefit for patients with prostate cancer and we await further data with interest.

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