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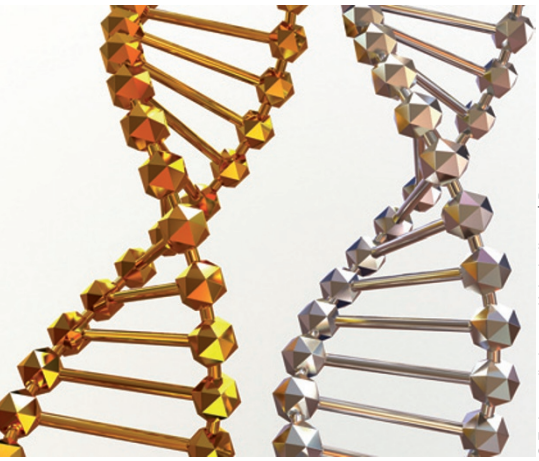
PROSTATE CANCER

Next-generation RNA sequencing identifies gene signature of neuroendocrine differentiation in prostate tumors

Neuroendocrine prostate cancer (NEPC) is a rare subtype of the disease, affecting only 0.5–2% of patients with prostate cancer. However, focal neuroendocrine differentiation is detected in between 10% and 100% of localized prostate tumors. A study published in *Cancer Discovery* has now profiled gene expression in neuroendocrine tumors and localized prostate carcinoma, reporting that NEPC has a characteristic gene signature, distinct from prostate cancer, which could provide targets for therapeutic intervention.



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Beltran *et al.* used next-generation RNA sequencing and oligonucleotide arrays to evaluate NEPC tumors, prostate cancer samples and specimens of benign tissue. They found significant differences in gene expression between NEPC and prostate cancer, with 936 of 25,932 genes being differentially expressed. In particular, the *AURKA* (Aurora-kinase A) gene was overexpressed and amplified in NEPC ($P = 1.46 \times 10^{-5}$). Aurora-kinase A is a serine/threonine kinase involved in mitotic spindle formation, previously shown to interact with the oncogene N-myc. Based on this knowledge, the team also investigated *MYCN* gene expression, and found that *MYCN* was significantly overexpressed in NEPC compared with prostate cancer ($P = 0.0005$). This study is the first to report a link between *MYCN*—which has previously been described in neuroblastoma—and prostate cancer.

Furthermore, transfection of *MYCN* into benign LNCaP cells induced expression of *AURKA*, and the N-myc protein interacted with Aurora-kinase A, enhancing its stability. When these tranfected cells were treated with Aurora kinase inhibitors, expression of neuroendocrine markers was completely suppressed.

No standard treatment currently exists for patients with NEPC. However, these data suggest that Aurora-kinase inhibitors could have an important role in this form of the disease.

Annette Fenner

Original article Beltran, H. *et al.* Molecular characterization of neuroendocrine prostate cancer and identification of new drug targets. *Cancer Discov.* **1**, 487–495 (2011)