Expression of gamma-aminobutyric acid receptor (subtype A) in prostate cancer.

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Abstract

BACKGROUND:
In prostate cancer, gamma-aminobutyric acid (GABA) has been previously reported to increase cellular proliferation via the ionotropic GABAa receptor (GABAar) and to promote cellular invasiveness via the metabotropic GABAb receptor.

METHODS:
In this study, we have investigated, by immunohistochemistry, GABAar levels in 12 normal human prostate, 13 benign prostatic hyperplasia (BPH) and 148 human prostate cancer specimens. We have also examined the effect of several GABA agonists and antagonists on the in vitro proliferation of four human prostate cancer cell lines: LNCaP, MDA-PCA-2b, DU145 and PC3.

RESULTS:
GABAar immunoreactivity was present in the stroma of ~75% of the normal and BPH specimens, and in 95% of the prostate cancer specimens. Also, low to moderate GABAar staining was observed in the acinar epithelium of 50 (33%) prostate cancer specimens. No correlation was observed between GABAar staining and patient age, Gleason Sum or TNM stage. A GABAa agonist isoguvacine, at doses between 5-50 microg/ml (31-310 microM), stimulated the proliferation of all four human prostate cancer cell lines, tested. Baclofen, a GABAb agonist (up to 50 microg/ml, 234 microM) had no effect on growth. Also, at concentrations up to 100 microg/ml, GABA antagonists, bicuculline (223 microM), picrotoxin (166 microM) and saclofen (400 microM), did not have significant growth-inhibitory effects. However, dihydroergotoxine, which binds the GABAar chloride ion-channel, inhibited cellular proliferation (IC(50) 18-38 microM).

CONCLUSIONS:
These data indicate frequent expression of GABAar in prostate cancer and support a role for GABAar in the proliferation of prostate cancer cells.

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