Neuropeptide Y in prostate cancer biology

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Introduction:

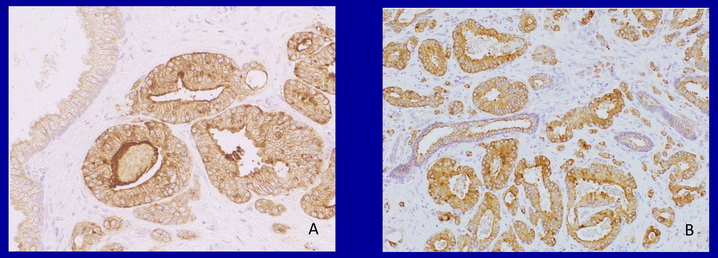
- The involvement of the nervous system in cancer development and progression has been identified as one of the hallmarks of cancer. The role of neural signalling is complex and multifaceted, involving effects on carcinogenesis, cancer spread and interactions between tumoral cells and microenvironment
- Neuropeptide Y (NPY) is a neurotransmitter, which regulates the important biological mechanisms of cell growth and survival.
- The aim of this study was a comprehensive analysis of the NPY system in prostate pathology.

Methods:

- The study was based on immunohistochemical analysis of NPY and its receptors, (Y1R, Y2R and Y5R), in tissue samples from benign prostate (BP), primary prostate cancer (PCa, n=51) and PCa bone metastases (n=11).
- The specimens were examined using tissue microarray technique. Intensity of the immunoreactivity, expression index (EI), and distribution of the immunostaining in tumoral cells and stromal elements were evaluated.
- Perineural invasion and extraprostatic extension areas were assessed separately.
- In addition, chemotactic activity of NPY in PCa cells w as measured using a transwell migration assay.

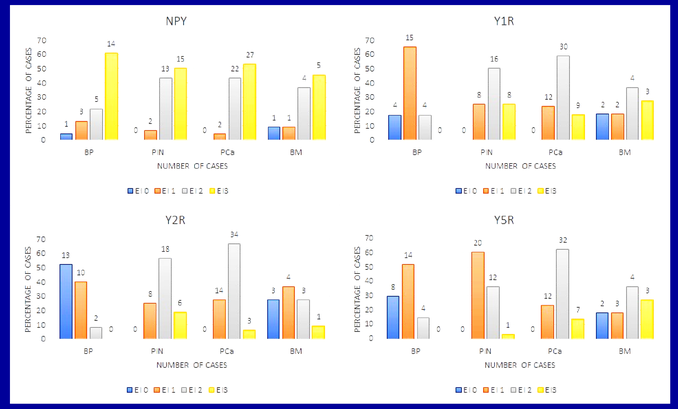
Results

- Morphological analysis revealed homogeneous membrane -cytoplasm pattern of NPY immunostaining in cancer cells, while immunoreactivity in BP glands concentrated on the cell membrane.



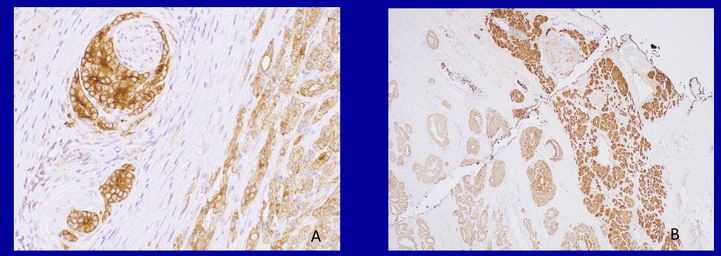
A. Membranous staining with apical accentuation within the normal prostate glands (400x).
B. Strong, mainly cytoplasmic NPY-immunoreactivity in malignant glands and luminal excretion (200x).

- All elements of the NPY system were upregulated in prostate intraepithelial neoplasia, PCa and metastases, as compared to BP.

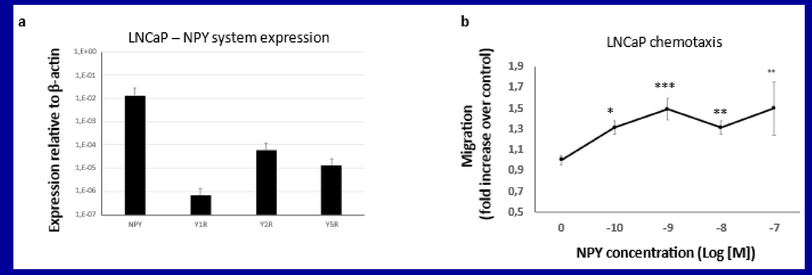


The NPY system expression scores in the study group. Abbreviations: BP- benign prostate, EI- expression index, PIN- prostate intraepithelial neoplasia, PCa- prostate cancer, BM- bone metastases.

- There was a positive correlation between Y2R and Y5R expression.
- The levels of NPY system expression were elevated in perineural invasion and extraprostatic extension areas.
- In bone metastases, the Y1R and Y5R presented high expression scores.



A. Strongly enhanced NPY expression in perineural invasion(200x).
B. Increasing NPY staining gradient towards extraprostatic invasion (100x)



Chemotactic effects of NPY: A. The expression of NPY and its receptors in LNCaP cells B: NPY acts as chemoattractant for LNCaP cells ($p<0.05$)

Conclusions:

Results of our study suggest that the NPY system is involved in PCa biology starting from early stages of its development to metastatic stadium of the disease

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