Correlations of androgen receptor (AR) and transforming growth factor beta receptor type 2 (TGFbR2) expression in prostate cancer (PCa)

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MOLECULAR ANALYSIS FOR PRECISION ONCOLOGY VIRTUAL CONGRESS MAP
7-9 OCTOBER 2021
Molecular Analysis for Precision Oncology Virtual Congress

Background

Transforming growth factor beta (TGFb) is a potent inducer of epithelial-mesenchymal transition. Of all members of TGFb receptors family only TGFbR2 is capable of direct binding to ligand. In experimental conditions interactions were shown between TGFbR2 and AR signaling pathways, often leading to negative feedback loops. However, data on expression levels of both receptors in clinical cancer samples are scarce.

Aim

To assess expression and possible coexpression of AR and TGFbR2 in PCa clinical samples.

Material and methods

- 31 radical prostatectomy specimens
- FFPE slides, 4 µm thick
- double immunofluorescence staining
- primary mouse monoclonal anti-AR (BioGenex, 1:100) and rabbit polyclonal anti-TGFbR2 (elabscience, 1:100) antibodies (Ab)
- secondary goat Ab (ThermoFischer, 1:200) labelled with Alexa Fluor 488 and 555
- 3-12 random high power fields (HPF) (x400) per case (total of 277 HPFs) studied
- staining characteristics assessed semiquantitatively separately for different subcellular compartments

Conclusions

In clinical PCa samples AR staining intensity directly correlated to that of TGFbR2 in nuclei. The biological mechanisms and clinical significance of that and of TGFbR2 nuclear staining need further investigation.

Results

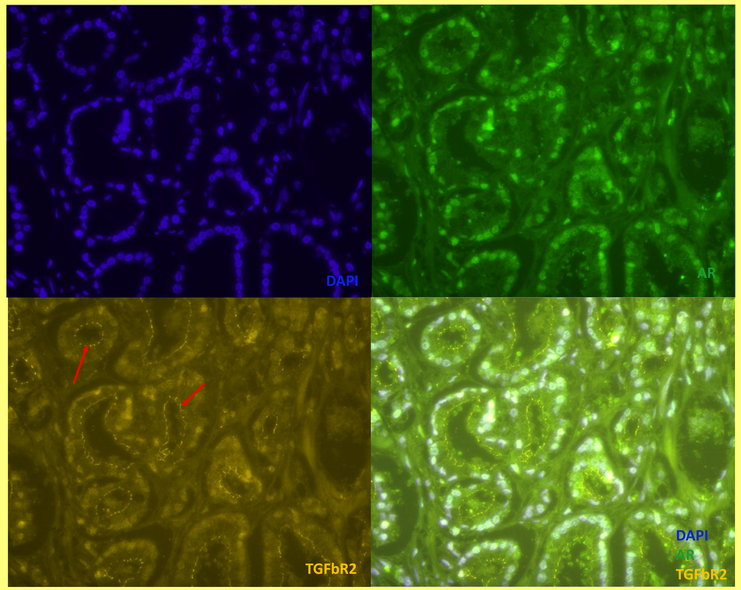

Fig. 1. Staining of a representative HPF. Nuclear AR and TGFbRII with coexpression, TGFbRII on apical membrane (arrows)

Table 1. Criteria of semiquantitative staining assessment

	0	1	2	3
Proportion of stained cells	Absent	<1/3	1/3-2/3	>2/3
Intensity	Absent	Weak	Moderate	Strong

Table 2. Results of semiquantitative assessment of AR and TGFbR2 staining in PCa (number of HPFs)

Score	AR, nuclear, cancer cells		TGFbR2, cancer cells			
			Nuclear		Membranous	
	Int	Prop	Int	Prop	Int	Prop
0	12	12	37	39	197	197
1	179	70	183	119	65	57
2	63	66	46	67	15	10
3	23	129	9	52	0	13

- AR nuclear expression was seen mostly in PCa cells, but was reduced relatively to non-cancerous epithelium
- AR staining intensity was mostly weak (64,6% of HPFs), but present in most cells (46,6%)
- staining of AR in stroma was weak and present in up to 1/3 of cells in almost all HPFs
- TGFbR2 was expressed mostly in nuclei using this Ab, but staining was mostly weak (66,1%)
- TGFbR2 membranous expression was present in 20 (64.5%) cases (in 80 (28,9%) HPFs), but was mostly low and seen in single glands
- statistically significant correlation was seen between staining intensity of AR and TGFbR2 in the same cell, but TGFbR2 was usually weaker ($p<0,05$)
- no significant correlations were found in this sample cohort between presence of TGFbR2 membranous staining and AR expression
- no correlation was seen of both markers expression with PCa stage or Gleason score

The work was funded by Belarusian Republican Foundation for Fundamental Research, Grant No. M19M-123.
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