ERG Expression in 175 Prostatic Carcinomas and 270 Carcinomas from Different Primary Sites

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BACKGROUND

ERG gene rearrangement, detected by fluorescence in situ hybridization (FISH) or reverse transcription polymerase chain reaction (RT-PCR), has been identified as a highly specific alteration, present in 40-50% of prostate carcinomas (PCa). Recent studies describe a novel anti-ERG antibody, whose positive staining by immunohistochemistry (IHC) highly correlates with the presence of TMPRSS2:ERG rearrangement. The standardization of an IHC assay would have significant clinical utility, given that the occurrence of such rearrangement has diagnostic and prognostic value. Marked variations in rates of PCa among populations in the world suggest the involvement of genetic factors. The aim of this study was to identify the incidence of this rearrangement in a Spanish population and to test the specificity of the ERG IHC assay for the evaluation of PCa.

DESIGN

Tissue microarrays (TMA's) of a wide variety of normal and neoplastic tissues were tested. For their construction, three cylindrical cores were taken from representative areas in the paraffin block of each case and transferred to recipient paraffin blocks (Beecher Microarrayer; Beecher Instruments, Sun Praire, WI, USA).

TMA's were analyzed by IHC performed by ABC immunoperoxidase staining, using a rabbit monoclonal antibody (ERG, clone EPR3864, Epitomics, San Diego, CA, USA).

The expression of ERG protein was scored as negative (-), weak (1+), moderate (2+) or strong (3+), using vascular endothelial cells, which were uniformly and strongly positive, as internal control (Figure 1). A case was judged positive if any of the evaluable cores showed a positive staining, whichever its intensity.

Three prostate TMA's were constructed using prostatectomy specimens, and their Gleason score (GS) and extent of invasion (pT) were routinely determined when it was possible. These TMA's included, besides samples of malignant cases (175), specimens with prostatic hyperplasia (25) and high grade prostatic intraepithelial neoplasia (HGPIN) (10).

In addition, TMA's of the most common tumors in Spain (breast, colon, lung and bladder) were also tested (270 samples in total).

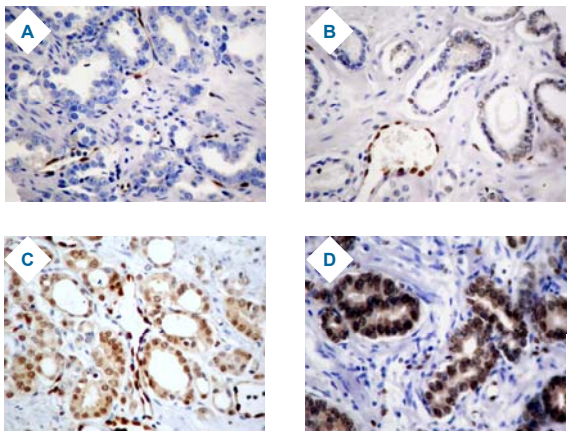

Figure 1. ERG immunostaining. (A) PCa showing negative expression (-), (B) weak expression (1+), (C) moderate expression (2+) and (D) strong expression (3+). The endothelial cells of small vessels and the lymphocytes show positive endogenous ERG expression and serve as internal control (x400).

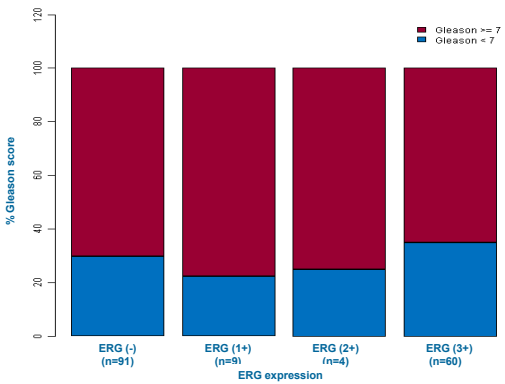

Figure 2. Distribution of percentage of cases according to their ERG vs Gleason score. Abbreviations: ERG(-), negative; ERG(1+), weak; ERG(2+), moderate; ERG(3+), strong intensity of expression.

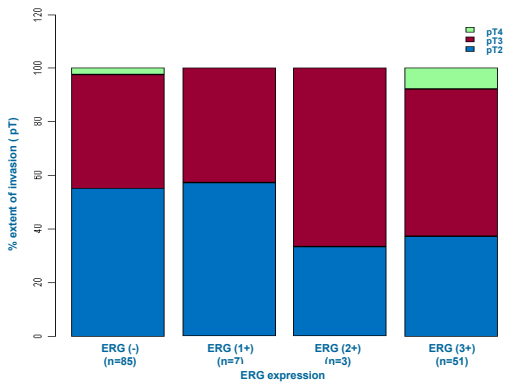

Figure 3. Distribution of percentage of cases according their ERG score vs extent of invasion (pT). Abbreviations: ERG(-), negative; ERG(1+), weak; ERG(2+), moderate; ERG(3+), strong intensity of expression.

RESULTS

In our study 44% (76/171) evaluable cases of PCa showed ERG expression, most of them presenting strong staining (61/76).

Figures 2 and 3 show the distribution of ERG IHC results according to their intensity versus the Gleason score and the extent of invasion, respectively.

No ERG expression was observed in any of the HGPIN samples, as reported by others. However, the number of cases of HGPIN included in ours TMA's was very low, and also corresponded to distant areas from the malignant lesion. ERG expression was independent of GS (p=0.735) and pT (p=0.128), determined on 164 and 146 prostate tumors, respectively (Table 1).

There was no ERG expression found in any other type of tumor, with the exception of one bladder cancer single sample which showed focal expression. The primary site of this case was confirmed by IHC (CK7+, P63+, HPAP-, PSA-).

	ERG positive	ERG negative	*p*-value
Gleason score			0.735
GS<7	24 (47.1%)	27 (52.9%)	
GS≥7	49 (43.4%)	64 (56.6%)	
Extent of invasion (pT)			0.128
pT2	24 (33.8%)	47 (66.2%)	
pT3	33 (47.8%)	36 (52.2%)	
pT4	4 (66.7%)	2 (33.3%)	

Table 1. Fisher's exact test correlating ERG expression with clinicopathological features.

CONCLUSIONS

- The frequency of ERG detected in our study correlated with that published in other Caucasian populations.
- The expression of ERG protein is exclusively detected on prostatic adenocarcinoma, corroborating the specificity of ERG rearrangement for these tumors.
- In addition to its prognostic significance, the use of ERG detection by IHC may be useful in routine practice to complement the panel of prostatic carcinoma.

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