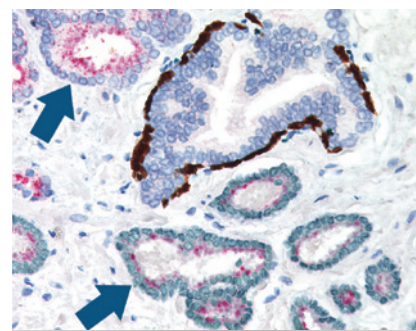
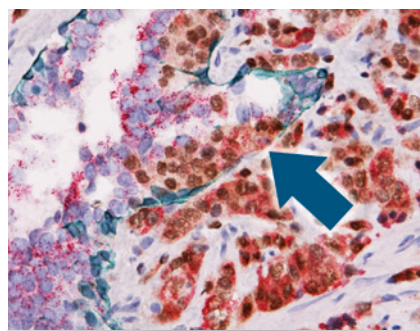
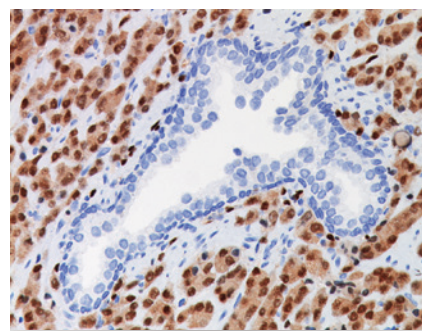


Evaluation of TMPRSS2-ERG Fusion Protein in Prostate Cancer Pathogenesis Across Continents

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Background

The incidence of prostate cancer is 30 times more prevalent in North American vs. Asian populations. Chromosomal translocations involving the ETS transcription factors, such as ERG and ETV1, are frequent events in human prostate cancer pathogenesis. In particular, the TMPRSS2-ERG fusion gene has recently been found to be the most frequent gene rearrangement in prostate cancers, occurring in 45-65% of North American patients, compared to only 15-20% of patients of Asian descent.¹ Recent reports have demonstrated a strong correlation between the presence of the TMPRSS2-ERG rearrangement and expression of the ERG protein.^{2,3} Therefore, as a hallmark of the TMPRSS2-ERG chromosomal translocation, ERG expression offers a definitive marker of adenocarcinoma of prostatic origin, and a unique opportunity to identify a potentially clinically significant subset of prostate cancer patients by IHC.

Given the ease of performing IHC vs. FISH, ERG protein expression in formalin fixed paraffin embedded tissue may be an extremely useful tool for the routine identification of the ERG gene rearrangement and diagnosis of prostate adenocarcinoma. This study evaluated the sensitivity and specificity of a mouse mAb ERG antibody [9FY] on human prostate tissues; comparing North American and Asian populations. A wide variety of normal and neoplastic tissues were tested to establish specificity.

Methods

Tissue microarrays (TMA's) of human prostate adenocarcinoma (grades 1-4 and Gleason Scores 2-10), normal prostate, and various other normal and neoplastic tissues were analyzed. TMA's were processed in the usual manner according to standard IHC protocols. Samples were incubated with mouse anti-ERG mAb [9FY] (Biocare Medical) for 30 minutes followed by visualization (DAB) using a biotin-free detection system (HRP).²

Results

Only 19% (32/169) of tissues from patients of Asian descent showed high expression of ERG, compared to 45% (15/33) of North American prostate samples that exhibited high ERG expression (Table 1). Gleason Score or tumor stage were not correlated with ERG expression (Tables 2 & 3). Of the 744 non-prostate normal and neoplastic tissues analyzed, only 0.4% (3/744) showed positive staining for ERG: one each of T-Cell Lymphoma, B-Cell Lymphoma and Melanoma; thereby demonstrating 99.6% specificity for prostate tissues, using this mouse monoclonal ERG antibody.

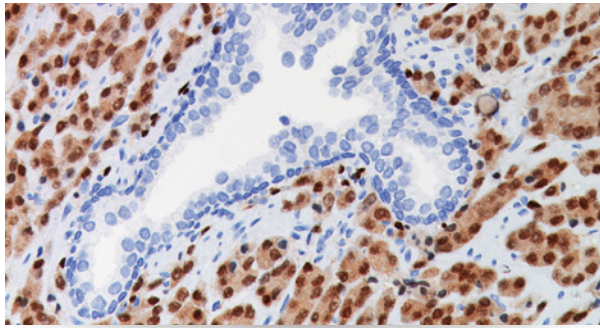
Conclusion

Evaluation of ERG expression was readily performed using a mouse mAb and routine IHC protocols. High specificity of ERG expression (99.6%) in prostate cancer tissue was demonstrated with this monoclonal antibody by examining an array of normal and neoplastic tissues. The frequency of ERG expression was higher in North American vs. Asian patients, consistent with the higher incidence of prostate cancer in North American populations. Notably, this difference is consistent with the suggestion that prostate cancer may arise from differing mechanisms in Asian and North American patients.¹

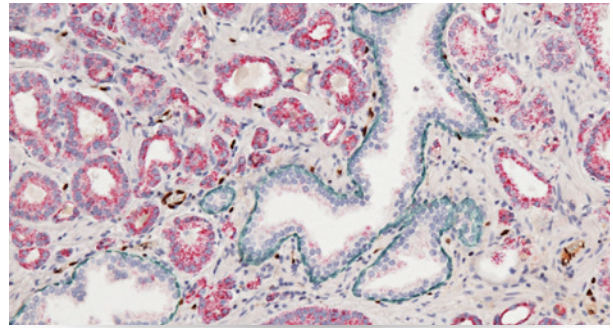
Given the prevalence of the TMPRSS2-ERG rearrangement in prostate cancer, and its exquisite specificity, this ERG mouse mAb may be a valuable tool for the clear diagnosis of adenocarcinoma in the prostate by IHC. Furthermore, the robust presence of ERG in prostatic adenocarcinoma and its absence in a wide-variety of other tissues, may make ERG an excellent tumor marker for determining prostatic origin. Finally, the strong correlation between ERG-positive PIN and ERG-positive carcinoma (96.5%) suggests that in cases of ERG-positive PIN in biopsy samples, carcinoma may be indicated and additional diagnostic follow-up may be prudent.²

References

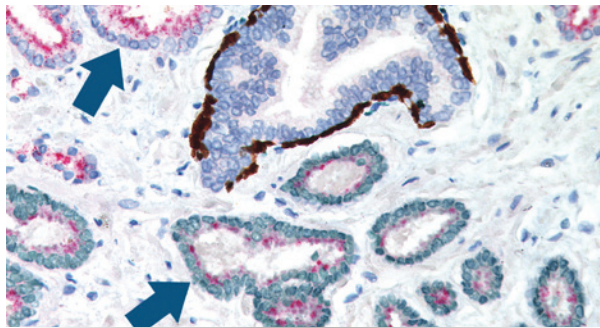
1. Mao X, Yu Y, Boyd LK, et. al. Distinct Genomic Alterations in Prostate Cancers in Chinese and Western Populations Suggest Alternative Pathways of Prostate Carcinogenesis. *Cancer Res* 2010;70: 5207-5212.
2. Furusato B, Tan SH, Young D, et. al. ERG oncoprotein expression in prostate cancer: clonal progression of ERG-positive tumor cells and potential for ERG-based stratification. *Prostate Cancer Prostatic Dis* 2010; 13:228-237.
3. Park K, Tomlins S, Mudaliar KN, et. al. Antibody-Based Detection of ERG Rearrangement-Positive Prostate Cancer. *Neoplasia* 2010;12:590-598.



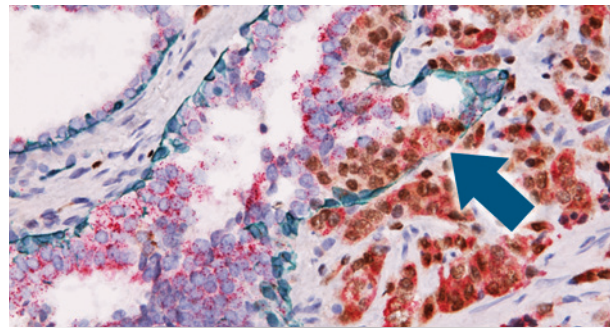
Prostate cancer stained with ERG
Note benign prostate gland is negative.



PIN-4 and ERG negative prostate cancer



PIN-4 and ERG on prostate cancer
p63 + HMWCK (DAB), p504s (Red), ERG (Green). Note areas of ERG-negative carcinoma (upper arrow) and ERG-positive carcinoma (lower arrow).



PIN-4 and ERG on prostate cancer and PIN (prostatic intraepithelial neoplasia)
p63 + HMWCK (Green), p504s (Red), ERG (Brown). Note ERG staining within the PIN gland (arrow).

Table 1: Relationship of ERG Expression with patient population

Patient Population	ERG Expression		Total	% High Expression
	Neg or Low	High		
Asian	137	32	169	19%
North American	18	15	33	45%

Table 2: Relationship of ERG Expression with Gleason sum in patients of Asian descent

Gleason Sum	ERG Expression		Total	% High Expression
	Neg or Low	High		
≤6	48	19	67	28%
7	36	6	42	14%
≥8	53	7	60	12%
Total	137	32	169	19%

Table 3: Relationship of ERG Expression with tumor stage in patients of Asian descent

pT	ERG Expression		Total	% High Expression
	Neg or Low	High		
1	3	0	3	0%
2	90	16	106	15%
3	40	11	51	22%
4	10	5	15	33%
Total	143	32	175	18%

References

1. Mao X, Yu Y, Boyd LK, et. al. Distinct Genomic Alterations in Prostate Cancers in Chinese and Western Populations Suggest Alternative Pathways of Prostate Carcinogenesis. *Cancer Res* 2010;70: 5207-5212.
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