AroCell TK 210 ELISA May Complement Pro PSA and the Prostate Health Index in Differentiating Non-Cancerous from Cancerous Conditions in Prostate Disease

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ABSTRACT

- Thymidine kinase 1 (TK1) is a pyrimidine salvage pathway enzyme involved in DNA precursor synthesis and its expression is S-phase dependent.
- During uncontrolled cell proliferation, high levels of TK1 leak into the blood and form stable aggregates which, in turn, indicate cell turnover[1].
- TK1 enzyme activity is an established biomarker for haematological malignancies. However, activity based assays may under-estimate TK1 levels particularly in sera from patients with solid tumours due to presence of inactive TK1[2,3].
- AroCell AB has developed an ELISA using antibodies against a specific TK1 antigenic site (TK 210) and a recent study demonstrated that TK 210 ELISA had significantly better sensitivity in differentiating healthy from breast cancer patients compared to TK1 activity assays[4].
- Combinational ROC analysis demonstrated that the AroCell TK 210 ELISA kit can complement both pro PSA and PHI in differentiating Prostate Cancer patients from subjects with non-cancerous prostate conditions.

OBJECTIVES

- The main objective of this study is to determine if TK 210 ELISA can complement the PSA-related biomarkers leading to a higher specificity and sensitivity in the diagnosis of prostate cancer.

METHODS

- Serum samples from 130 male patients with PSA values ranging from 2 to 10 µg/L were collected between 2013 to 2015 at the University Medical Centres in Ljubljana and Maribor, Slovenia.
- 68% of patients were in a non-cancerous group that included benign prostate hyperplasia, prostatitis and high grade prostatic intraepithelial neoplasia. 32% were from the patients with confirmed prostate cancer.
- The age range of this group was 48 to 86 years (mean and median = 68).
- 60 serum samples from male blood donors were collected from the Blood Transfusion Centre, Ljubljana. The age range of the blood donors was 22 to 64 years (mean = 41 and median = 40).
- TK1 protein levels were determined with the AroCell TK 210 ELISA kit in both patients and blood donors using the procedure as described (www.e-labeling.eu/ARO1001-15-3).
- PSA, free PSA and pro PSA levels were analyzed with commercial assays (Hybritech PSA, Hybritech Free PSA and Access p2PSA - Beckman Coulter USA) on the Access 2 Beckman Coulter analyzer. PHI was calculated using the formula PHI = (p2PSA/fPSA) x √tPSA

CONCLUSIONS

- These results indicate that the AroCell TK 210 ELISA kit can aid in differentiating the non-cancerous group from the confirmed PCa group in urology patients with PSA values between 2 to 10 µg/L.
- Combinational ROC analysis demonstrated that the AroCell TK 210 ELISA kit can complement both pro PSA and PHI in differentiating PCa patients from the other groups.
- Further clinical studies are needed to establish the role of TK 210 ELISA as a complement to pro PSA and PHI, which could be a valuable tool in prostate cancer diagnosis.

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**The AroCell TK 210 ELISA kit is for research use only in the USA.
Not for use in diagnostic procedures.**

RESULTS

- Serum TK1 protein levels in male blood donors were in the range of 0.07 to 0.35 µg/L (mean±SD = 0.20±0.08). 0.36 µg/L was used as a cut-off for elevated serum TK1 values.
- The cut-off value for each parameter, and the no. of samples from each group are shown in Table 1. Neither PSA nor free-PSA values showed significant differences between the non-cancerous and PCa groups.
- TK1 protein values in the PCa group (mean±SD = 0.42±0.21; median = 0.36) differed significantly from those with non-cancerous conditions (mean±SD = 0.31±0.18; median = 0.28).

		Non-cancerous	Confirmed PCa	
Parameter	**Cut-off value**	**N = 88 (% above cut-off)**	**N = 42 (% above cut-off)**	**P value**
Pro PSA (ng/L)	8.6	50 (56.8%)	34 (81%)	0.0092
PHI	37	37 (35.2%)	27 (64.2%)	<0.0001
TK 210 ELISA (µg/L)	0.36	17 (19.3%)	21 (50%)	0.007

Table 1: Summary of parameters in different groups

- Out of the PSA-related biomarkers, only pro PSA and PHI could significantly differentiate PCa from non-cancerous conditions.
- Significant correlations were found between TK 210 ELISA and PHI (*rs* = 0.28; p = 0.0014) and between pro PSA and PHI (*rs* = 0.58; p <0.0001).

- To determine if combining biomarkers would increase diagnostic accuracy, combinational analyses of ROC curves were performed. TK 210 ELISA plus pro PSA gave an increased AUC compared to each alone (Fig 1A) .
- Similarly, combination ROC curves for TK 210 ELISA and PHI showed increased AUC and sensitivity compared to either alone (Fig 1B).

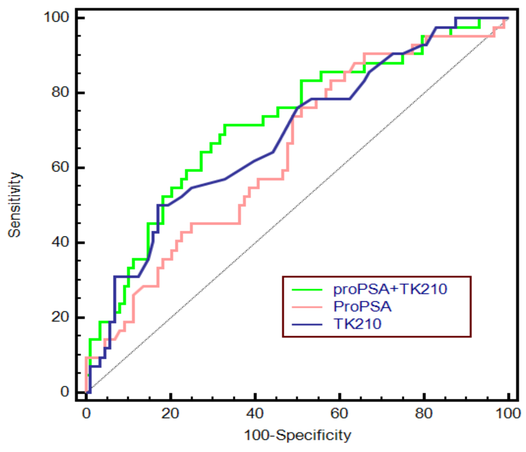

Fig 1A

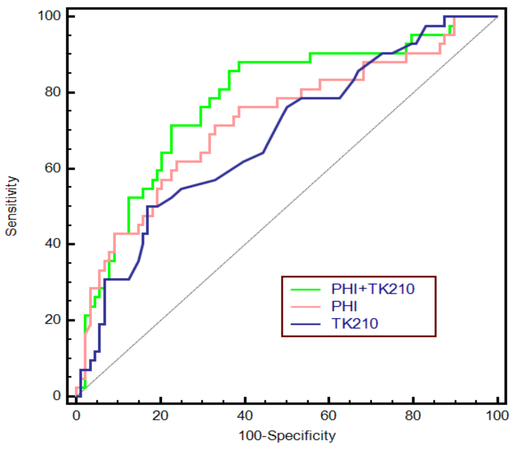

Fig 1B

- ROC curve analysis of pro PSA, TK 210 ELISA and PHI demonstrated similar AUC values for differentiating PCa from controls (Table 2).

Parameter	Cut-off value	Sensitivity	Specificity	AUC
Pro PSA (ng/L)	>8.6	83.3	42	0.64
PHI	>37	71	67	0.72
TK 210 ELISA (µg/L)	>0.36	50	83	0.68
Pro PSA+ TK 210	0.298	71.4	67	0.72
PHI+ TK 210	0.252	88.1	61.4	0.78

Table 2: ROC curve analysis for various parameters comparing the PCa and the control groups

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