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PROSTATE AND BREAST CANCER;
A COMPARISON OF CK2 MODULATION OF C-MYC IN PROSTATE AND BREAST CANCER

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ABSTRACT... Background: CK2, a serine/threonine, protein kinase, targets over and above 300 substrates including c-Myc. CK2 expression is elevated in human cancers including breast cancer and prostate cancer. c-Myc protooncogene expression is also up-regulated in these cancers. **Objectives:** To evaluate the co expression and correlation of CK2 and c-Myc in prostate cancer as compared to their correlation in breast cancer. **Study Design:** Cross sectional analytical study. **Setting:** Army Medical College and AFIP, **Duration:** Two years. **Methods:** A retrospective study of immunohistochemical analysis, approved by Armed Forces Institute of Pathology Ethical Committee. Paraffin embedded tissues of diagnosed prostate cancer, 30 in number, 30 cases of Benign Prostatic Hypertrophy (BPH) and 30 cases of breast adenocarcinoma, were included in the study. We stained tissue sections for CK2 and c-Myc and measured staining intensity for each protein expression. Data analysis was done by SPSS version 20. Pearson correlation coefficient was used for correlating the expression of both proteins. P-value was calculated. **Results:** A strong correlation of CK2 with c-Myc was seen in prostate cancer tissue, in comparison to BPH. There was a very significant correlation present between CK2 and c-Myc, especially in invasive cases of breast cancer. **Conclusion:** CK2 and c-Myc expressions are highly and significantly correlated in prostate cancer and breast cancer especially in invasive cases. CK2 has influence over c-Myc and both can be used for forecasting the cancer phenotype and aggression of disease.

Key words: c-Myc, Ck2, Ca Breast, Ca Prostate, Correlation.

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INTRODUCTION

Cancer is the well-known basis of death worldwide killing 7.4 million people in 2004.[1] Among the males at elder stage, two commonly occurring diseases are prostate cancer (PCa) & benign prostatic hyperplasia (BPH).[2] A limited number of prognostic biomarkers are accessible for clinical use e.g., serum Prostate Specific Antigen (PSA).[3] Researches kept focusing on finding the prognostic markers helpful to differentiate indolent type from aggressive type of PCa but less attention was given to unfold the hidden molecular mechanisms responsible for initiation and progression of cancer.[4] Among females, breast cancer is very common both in advanced as well as under developed countries, killing over 508,000 females in 2011.[5] Research on breast cancer is also focused on tumor markers related to its prognosis, treatment options, survival rate and linkages with sub-types of breast cancer[6] e.g., BRCA-1 and BRCA-2, PTEN, MSH1 / MLH2, and p53 etc.[7]

Cancer develops as a result of change in the cell's microenvironment e.g., inflammation, oxidative stress, damage to DNA.[8] According to modern cancer biology, signaling pathways controlling cell reproduction, it's survival and death are common in normal mammalian cells. Disturbance of signaling web at either level i.e., molecular or

cellular, can result in cancerous state.[9]

The concentration on CK2 in perspective of neoplasias is a very hot topic for research.[10] CK2 expression is found to be elevated in cancers.[11] CK2, a serine / threonine kinase[12] and anti-apoptotic agent, has additional role of cancer driver generating encouraging cellular environment for cancer.[13] CK2 expression and kinase activity are found to be elevated in breast cancer.[14] Based on its elevated expression in cancers and ability to back tumorigenesis, CK2 is a possible candidate for therapy. Hence it is important to figure out CK2 mediated cellular substrates and events.[15] Over 300 substrates of CK2 have been known but the functional relationship between CK2 and those substrates are still unknown.[16]

Among the known substrates of CK2 is a proto-oncogene i.e., c-Myc. c-Myc is essential for normal development but its expression is elevated in cancers, the reason being unknown.[17] Tissues with high proliferation rate over express c-Myc.[18] An extreme intensification in lymphogenesis is observed as result of c-Myc and CK2 co-expression. It was evident that, inhibition of CK2 activity in cell lines resulted in decreased proliferation as well as decreased c-Myc expression. Therefore CK2 can be considered as an important supervisor of the control of c-Myc protein. c-Myc has capability to get phosphorylated via CK2, hence they may have an operating communication.[19]

Based on the research findings all over the world and contributing our part to solve the mysteries of cancer, the study was designed to investigate the expression of CK2 and c-Myc in both breast and prostate cancers (Published data). The correlation was also determined between CK2 and c-Myc in prostate as well breast cancers. The present study aimed to figure out the difference between correlation level of CK2 and c-Myc between the two cancers.

MATERIAL AND METHODS

This study is based on comparing the results of already published data. Previously the immunohistochemical staining was done to assess the level of expression of CK2 and c-Myc in both breast and prostate cancer patients with sample size n=30 for each cancer group using relevant internal controls. 30 cases of BPH patients were also studied. The level of CK2 and c-Myc expression and their correlation was analyzed in both cancers including BPH samples. Now in this article, the correlation level between the two proteins i.e., CK2 and c-Myc between the different cancer groups will be compared.

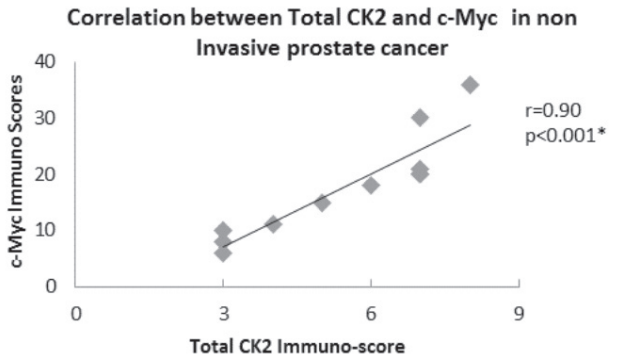
RESULTS

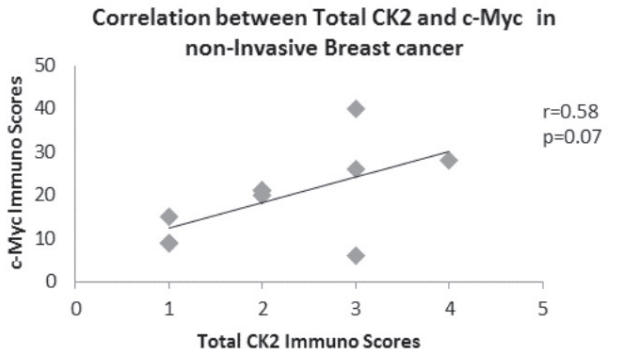
Thirty prostate cancerous tissues including 30% patients with lympho-vascular invasion and 50% patients with perineural invasion were examined for IHC of CK2 and c-Myc. Mean Gleason score calculated was 7.33 (SD ±1.124). Similarly 30 breast cancer tissues including 20 patients of perineural invasion were studied for IHC of CK2 and c-Myc. Mean nottingham index score was found to be 6.0 (SD ± 1.17) in invasive cases and 4.06 (SD ± 0.751) in noninvasive cases (already published data).

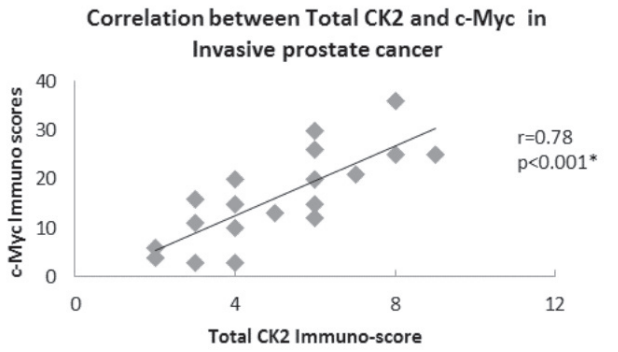
The IHC data of CK2 and c-Myc published before is shown in Table-I. A significantly strong positive correlation was found between total CK2 and c-Myc expression in invasive cases of both cancers i.e., prostate and breast cancer and noninvasive prostate cancer (Figure-1). A significantly strong positive correlation was found between nuclear CK2 and c-Myc expression in invasive cases of both cancers i.e., prostate and breast cancer but not in noninvasive cases of both cancers (Figure-2). A significantly strong positive correlation was found between cytoplasmic CK2 and c-Myc expression in invasive cases of both cancers i.e., prostate and breast cancer and noninvasive prostate cancer (Figure-3).

DISCUSSION

CK2 is a protein kinase[20] whose expression is found to be elevated in human cancers[19] but the mechanism of this elevated expression in carcinogenesis is not clear. CK2 has been marked as a signature for prognosis of squamous cell carcinoma lungs patients.[21] c-Myc is an onco-protein and CK2 substrate and plays role in cell proliferation.[22]







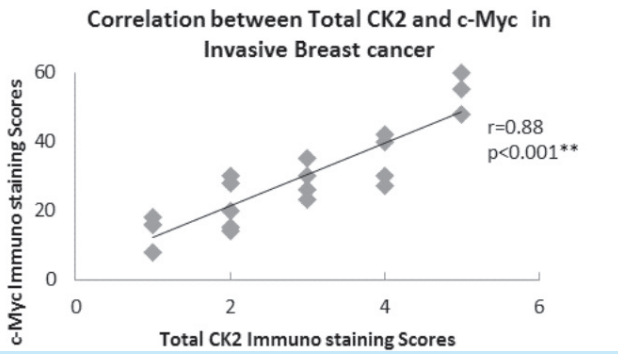
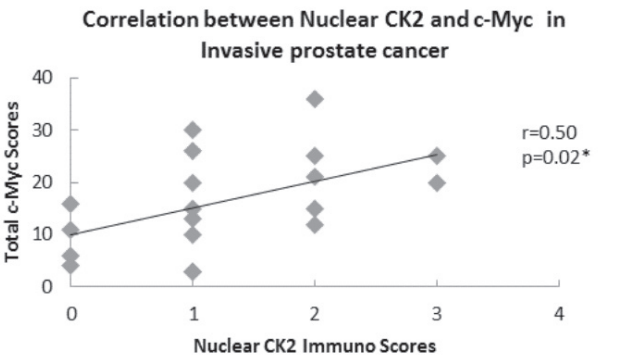
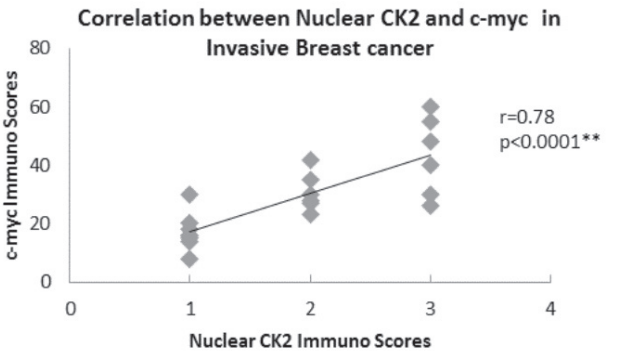
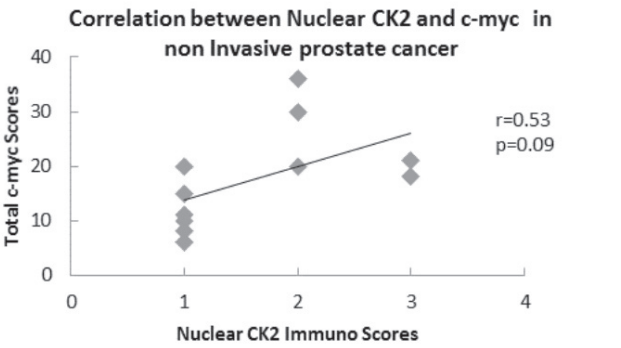


Figure 1: Comparison of correlation total CK2 and c-Myc expression in Prostate and Breast cancer tissues







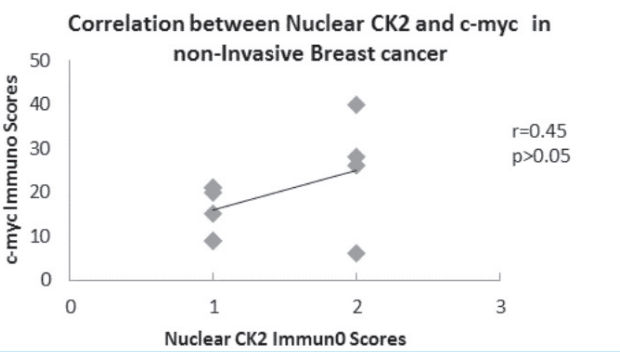


Figure-2. Comparison of correlation nuclear CK2 and c-Myc expression in Prostate and Breast cancer tissues

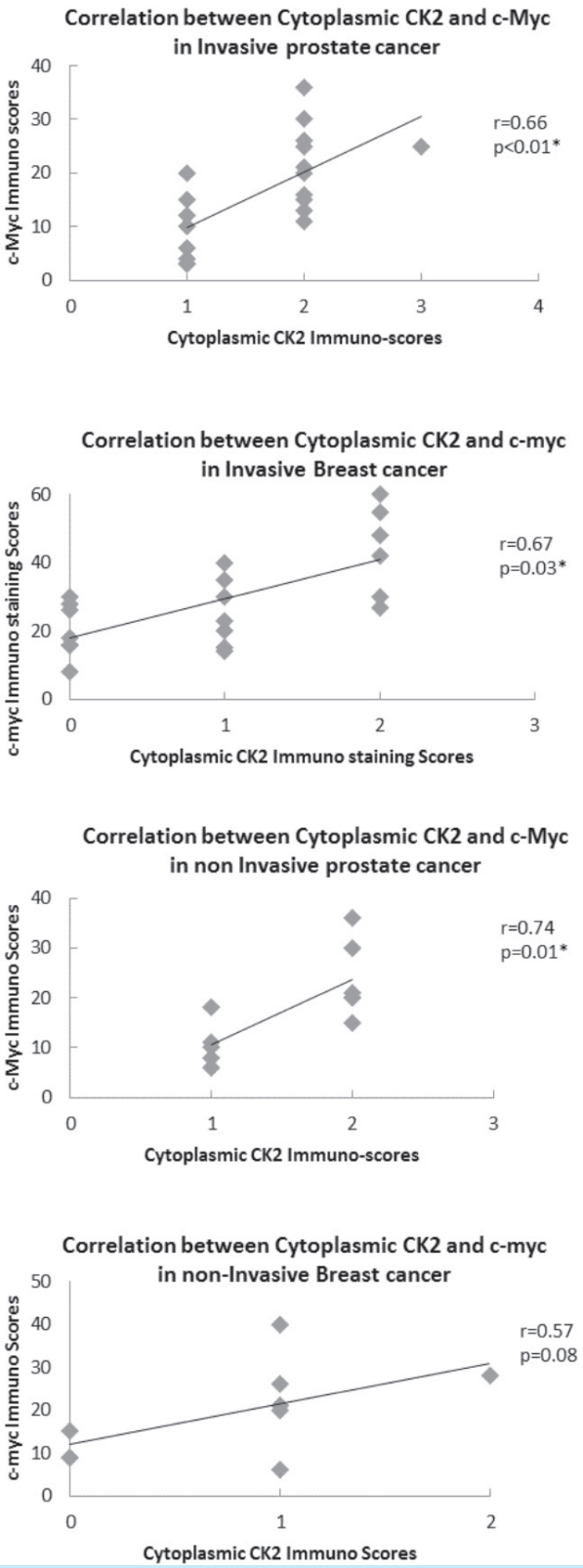


Figure-3. Comparison of correlation cytoplasmic CK2 and c-Myc expression in Prostate and Breast cancer tissues

Because of the association between CK2 and c-Myc, co-expression was studied in prostate and breast cancer. In this study, the correlation between CK2 and c-Myc was also discussed and compared between the two cancers. Overall a positive correlation was found between CK2 and c-Myc in both cancers.

Elevated expression of CK2 as well as c-Myc has been observed in breast cancer[23] and has resulted in lymphoma development.[24] It has been reported previously that in T cell lymphomas, CK2 functionally interacts with c-Myc[25,26] c-Myc and CK2 expression has been found to have positive correlation in lung cancers[27], phenotypically invasive immortalized cancer cells.[28]

Elevated CK2 activity is observed to promote elevated levels of stable c-Myc thus promoting cellular proliferation and plays role in cancer development.[29]

CK2α inhibition by small-interfering RNA (siRNA) inhibited proliferation of colorectal cancer cells and resulted in decreased c-Myc expression.[30] In this study, CK2 and c-Myc were found to be in positive correlation in both cancers especially in invasive cases. So it is suggested especially in prostate cancer that CK2 is over-expressed and it may be utilizing more efficiently the constitutive expression of c-Myc for cancer progression.

CONCLUSION

CK2 and c-Myc expressions are significantly correlated in invasive cases in both the prostate and breast cancers. Hence CK2 and c-Myc co-expression can be useful for prediction of cancer phenotype.

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Fake friends believe in rumors.
Real friends believe in you.

– Unknown –

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2	Abdul Khaliq Naveed	Supervision of research.	
3	Palvasha Waheed	Proof reading, Stats.	
4	Fatima Qaiser	Data analysis.	
5	Shoaib. N. Hashmi	Histopathological Scoring.	