



COMMENTARY

MicroRNAs and Prostate Cancer Detection: A Continous Quest

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SUMMARY

Prostate cancer is one of the deadliest male malignancy in the worldwide. It has been estimated that 1.1 million cases of prostate cancer were diagnosed in 2012 and within coming 10 years, the prostate cancer cases will be increased by 15 per cent in men. The multifaceted molecular anomaly of prostate cancer has confronted it from being dated owing to the orchestrated carcinogenic functions of negative regulators which work in a network. An as yet blurred view of therapeutic interventions of prostate cancer has been acknowledged, resulting from the addition of substantial fraction of information. Prostate-specific antigen (PSA) screening is currently known as a method for early detection of prostate cancer but its validity as prostate cancer biomarker is still controversial. Information obtained from the sequencing data of prostate cancer tissue biopsy, it has been described that non-coding RNAs such as microRNAs are good source of information to detect the prostate cancer. This information can be used to detect, predict metastatic state and even the state of prostate cancer progression. In this commentary, the role of microRNAs has been discussed in prostate cancer detection.

Keywords: MicroRNAs, Prostate cancer, Prostate-specific antigen, Metastatic state

MicroRNAs are small non-coding RNAs which are found in almost all living organisms and are involved in the regulation of genes and a number of molecular mechanisms such as RNA silencing etc. It has been reported that miRNA expression is very tissue and cancer specific (1). So, it can be inferred that because of their specificity in tissues and type of cancer, they are very good source of information to diagnose, classify, predict stage and finally to propose for a therapeutic targets for cancers, especially for incurable hormone refractory prostate cancer (HRPC). Scientific reports have conceived the theory that miRNAs

have potential clinical values to detect cancer and propos a therapeutic strategy (2, 3).

The miRNA signatures can be used to distinguish normal and cancer tissues precisely and also to explain other cancer characteristics such as stages of cancer etc. microRNAs have been considered as a powerful tool in comparison with the mRNA isolated from the tissue and has been shown that 1 of 17 carcinomas could be distinguished by mRNA profile patterns, in contrary to microRNAs which can help to identify 12 of 17 carcinomas (1). Carcinogenesis can be defined as a complicated integration of alterations of multiple signal transduction pathways, so it is necessary that we

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should study microRNAs expression profile while diagnosing cancer very accurately as the simple mRNAs are not enough to justify the accuracy of tissue specific tumor. Thus to improve the accuracy of clinical diagnosis of cancer, we should study the expression patterns of hundreds of miRNAs (3).

Work has been done to verify the claim of microRNAs are significant in diagnosis, prognosis and classification of PCa, i.e. it has been studied that miR-21 expression was much higher in AI PCa cells as compared to the AD PCa cells (4). Therefore, detecting the expression level of miR-21 can be used to discriminate different stages of human PCa. Additionally, optimized high-through put miRNA expression profiling has revealed the possible of microRNAs, novel biomarkers to detect PCa (5). Mitchell et al. (6) have found that microRNAs are stable molecules both in plasma and serum of cancer patients and can be considered a potential biomarkers for blood-based cancer diagnosis. It has been proposed that PCa tissues released microRNAs in blood circulation and they are maintained at very constant level in blood. The sera of PCa metastatic patients revealed that the expression levels of miR-125b and miR-141 have 6.35-fold and 65-fold increase, respectively (7).

Prostate Specific Antigen (PSA)

As we have discussed earlier that PSA is a controversial tool for early diagnosis of PCs, but it has been studied that PSA detection could be useful when PSA threshold is changed and its detection is frequently repeated. PSA screening could be an associated tool along with the modern and very accurate cancer screening molecular markers such as microRNAs (8). There is a long history of research on prostate-specific antigen (PSA) to made it an integral part of prostate cancer management but its authenticity as an recommended prostate cancer marker is still remained controversial (9). Scientists also attempted to improve the PSA based screening methods but still the answer is unclear on

recommending the PSA as prostate cancer diagnosis (10).

Androgen Receptor (AR)

Expression of androgen receptor (AR) has been found in prostate cancer (PCa) cells and the necessity of androgens for PCa cells survival has been documented. Due to the increased expression in PCa cells at the start of PCa metastasis, androgen suppression therapy show remarkable response in prostate cancer therapy but with the passage of time and continuation of hormonal therapy, results in very low response. Androgen receptor (AR) is an important factor playing central role in the normal growth and development of the prostate gland. Researches have reported the role of AR in prostate carcinogenesis (11-13).

Others Non-Invasive Approaches

Developments also have been seen in some non-invasive approaches to detect prostate cancer at early stage such as an advanced MRI technique known as restriction spectrum imaging (RSI) MRI, multi-parametric (mp) MRI (14, 15) as well as multi-parametric (mp) ultrasound (16) etc. These approaches still are not cheap and radiation based which are not highly recommended as a technique for early detection and screening of cancer.

It can be concluded from some controversial literature that blood based micro-RNAs could be the accurate and precise screening method to detect prostate cancer allying with PSA as biomarkers as a combination based early screening approach.

Conflict of Interest

I declare, there is no any conflict of interest regarding this commentary with any person or organization.

References

1. Lu J, Getz G, Miska EA, Alvarez-Saavedra E, Lamb J, Peck D, Sweet-Cordero A, Ebert BL, Mak RH, Ferrando AA, Downing JR, Jacks T, Horvitz HR, Golub TR. MicroRNA expression profiles classify human cancers. Nature. 2005 Jun

- 9;435(7043):834-8. PMID: 15944708. DOI: nature03702 [pii] 10.1038/nature03702.
2. Lan H, Lu H, Wang X, Jin H. MicroRNAs as Potential Biomarkers in Cancer: Opportunities and Challenges. *BioMed Research International*. 2015;2015:1-17. DOI: 10.1155/2015/125094.
3. Jackson BL, Grabowska A, Ratan HL. MicroRNA in prostate cancer: functional importance and potential as circulating biomarkers. *BMC Cancer*. 2014;14(1):930. DOI: 10.1186/1471-2407-14-930.
4. Li T, Li D, Sha J, Sun P, Huang Y. MicroRNA-21 directly targets MARCKS and promotes apoptosis resistance and invasion in prostate cancer cells. *Biochem Biophys Res Commun*. 2009 Jun 5;383(3):280-5. PMID: 19302977. DOI: S0006-291X(09)00543-9 [pii] 10.1016/j.bbrc.2009.03.077.
5. Mattie MD, Benz CC, Bowers J, Sensinger K, Wong L, Scott GK, Fedele V, Ginzinger D, Getts R, Haqq C. Optimized high-throughput microRNA expression profiling provides novel biomarker assessment of clinical prostate and breast cancer biopsies. *Mol Cancer*. 2006;5:24. PMID: 16784538. DOI: 1476-4598-5-24 [pii] 10.1186/1476-4598-5-24.
6. Mitchell PS, Parkin RK, Kroh EM, Fritz BR, Wyman SK, Pogosova-Agadjanyan EL, Peterson A, Noteboom J, O'Brian KC, Allen A, Lin DW, Urban N, Drescher CW, Knudsen BS, Stirewalt DL, Gentleman R, Vessella RL, Nelson PS, Martin DB, Tewari M. Circulating microRNAs as stable blood-based markers for cancer detection. *Proc Natl Acad Sci U S A*. 2008 Jul 29;105(30):10513-8. PMID: 18663219. DOI: 0804549105 [pii] 10.1073/pnas.0804549105.
7. Pang Y, Young CYF, Yuan H. MicroRNAs and prostate cancer. *Acta Biochimica et Biophysica Sinica*. 2010;42(6):363-9. DOI: 10.1093/abbs/gmq038.
8. Cuzick J, Thorat MA, Andriole G, Brawley OW, Brown PH, Culig Z, Eeles RA, Ford LG, Hamdy FC, Holmberg L, Ilic D, Key TJ, Vecchia CL, Lilja H, Marberger M, Meyskens FL, Minasian LM, Parker C, Parnes HL, Perner S, Rittenhouse H, Schalken J, Schmid H-P, Schmitz-Dräger BJ, Schröder FH, Stenzl A, Tombal B, Wilt TJ, Wolk A. Prevention and early detection of prostate cancer. *The Lancet Oncology*. 2014;15(11):e484-e92. DOI: 10.1016/s1470-2045(14)70211-6.
9. Manley BJ, Andriole GL. History of Prostate-Specific Antigen, from Detection to Overdiagnosis. 2016:3-16. DOI: 10.1007/978-3-319-21485-6_1.
10. Murthy V, Rishi A, Gupta S, Kannan S, Mahantshetty U, Tongaonkar H, Bakshi G, Prabhash K, Bhanushali P, Shinde B, Inamdar N, Shrivastava S. Clinical impact of prostate specific antigen (PSA) inter-assay variability on management of prostate cancer. *Clinical Biochemistry*. 2016;49(1):79-84. DOI: 10.1016/j.clinbiochem.2015.10.013.
11. van der Kwast TH, Tetu B. Androgen receptors in untreated and treated prostatic intraepithelial neoplasia. *Eur Urol*. 1996;30(2):265-8. PMID: 8875210.
12. Sadi MV, Walsh PC, Barrack ER. Immunohistochemical study of androgen receptors in metastatic prostate cancer. Comparison of receptor content and response to hormonal therapy. *Cancer*. 1991 Jun 15;67(12):3057-64. PMID: 1710537.
13. Tilley WD, Lim-Tio SS, Horsfall DJ, Aspinall JO, Marshall VR, Skinner JM. Detection of discrete androgen receptor epitopes in prostate cancer by immunostaining: measurement by color video image analysis. *Cancer Res*. 1994 Aug 1;54(15):4096-102. PMID: 7518349.
14. McCammack KC, Kane CJ, Parsons JK, White NS, Schenker-Ahmed NM, Kuperman JM, Bartsch H, Desikan RS, Rakow-Penner RA, Adams D, Liss MA, Mattrey RF, Bradley WG, Margolis DJA, Raman SS, Shabaik A, Dale AM, Karow DS. In vivo prostate cancer detection and grading using restriction spectrum imaging-MRI. *Prostate Cancer and Prostatic Disease*. 2016. DOI: 10.1038/pcan.2015.61.
15. Mertan FV, Berman R, Szajek K, Pinto PA, Choyke PL, Turkbey B. Evaluating the Role of mpMRI in Prostate Cancer Assessment. *Expert Review of Medical Devices*. 2015. DOI: 10.1586/17434440.2016.1134311.
16. Grey A, Ahmed HU. Multiparametric ultrasound in the diagnosis of prostate cancer. *Current Opinion in Urology*. 2016;26(1):114-9. DOI: 10.1097/mou.0000000000000245.