

Research Assessment Exercise 2020 Impact Case Study

University: | Hong Kong Baptist University |
Unit of Assessment (UoA): | 09 Department of Chemistry |

Title of case study: | Chemical Sensing for Early Prostate Cancer Diagnosis |

(1) Summary of the impact

Prof. Ka Leung Wong and his team have identified spermine as a reliable urinary biomarker with >500 positive clinical prostate cancer samples and were the first to demonstrate that a combination of certain nanoparticles with spermine can diagnose prostate cancer at an early stage non-invasively with over 80% accuracy. This project is the second product of the HKBU spin-off company, New Life Medicine Technology Company Limited (NLMT). In particular, this work is being launched as a home-based kit in the market in 2020. It will give rise to significant impact by enhancing public awareness, especially for men at high risk. This work is beneficial to professionals in the medical field, as it becomes adopted as a supplementary method to the serum prostate specific antigen (PSA) test.

(2) Underpinning research

Prostate cancer is known to be one of the prominent causes of mortality and crucial public health impact in most of the developed countries. More than 1.5 million new cases are found per year globally. For men diagnosed with prostate cancer which has been spread to other parts of the body, the 5-year survival rate is 30%. Due to the latency of treatable prostate cancer and the lethality in its late stage, there is an urgent demand for more sensitive and accurate diagnostic methods to detect early prostate cancer so that the treatment outcome can be significantly improved and the need for an invasive biopsy will be reduced.

Urine-based analysis is vital for biomarker research since it is non-invasive and readily available. Most importantly, it can detect cancer-related metabolites excreted in urine. Spermine, a natural urinary polyamine biomarker, has been identified to differentiate prostate cancer from non-cancerous cases like Benign Prostatic Hyperplasia (BPH). Unlike PSA, the level of urinary spermine falls significantly in the presence of prostate cancer but remains high in the case of BPH. [Ref 1 & 2] Over 500 clinical samples from Prince Wales Hospital have been examined including patients diagnosed to have prostate cancer, BPH patients and healthy controls showing PSA greater than 4. Independent quantitation of the concentration of the biomarker was performed by using the 'gold standard', Ultra-high Performance Liquid Chromatography coupled with a triple quadrupole mass spectrometer (UPLC-MS/MS). The sensitivity and specificity of spermine in prostate cancer diagnosis were found to be 79% and 84% respectively. The accuracy of the diagnostic performance of spermine was over 80%, which is much higher than the positive-predictive value, 21%, of the PSA test.

With such a prominent biomarker, an aptasensor using gold nanoparticles (AuNPs) was developed specifically for fast and convenient spermine detection. Two sensing mechanisms of the aptasensor were under comprehensive investigation by adjusting the amount of DNA being added, which resulted either in the aggregation or precipitation of DNA-AuNPs. The response of the aggregation state by spermine can be easily viewed by the naked eye, due to the colour change. This sensor has also been applied in clinical urine samples from cancer patients for

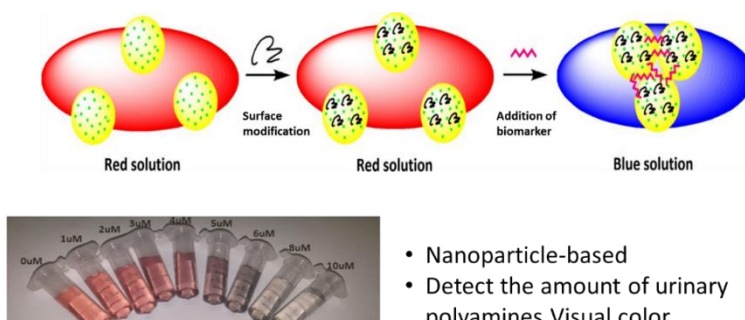


Figure 1. The principle of responsive gold nanomaterials for spermine as the potential early diagnosis prostate cancer kit. [Ref 1]

its intended purpose of detecting spermine content. The accuracy and direct use of urine samples without pre-treatment was verified by the accuracy of results obtained in spiked-sample analyses. (Figure 1) In this work, our design focused only on the detection of spermine, but we believe that the approach can be modified and expanded to enable analysis of other important markers, e.g. DNA or even cancer-related miRNA detection by using a suitable complementary DNA sequence for

adsorption. Also, other biomarkers in urine might be investigated which may allow more potential applications in clinical diagnosis. This approach has been evaluated for more than 500 clinical samples (prostate cancer positive by biopsy confirmation) in Hong Kong and China. [Ref 3 & 4]

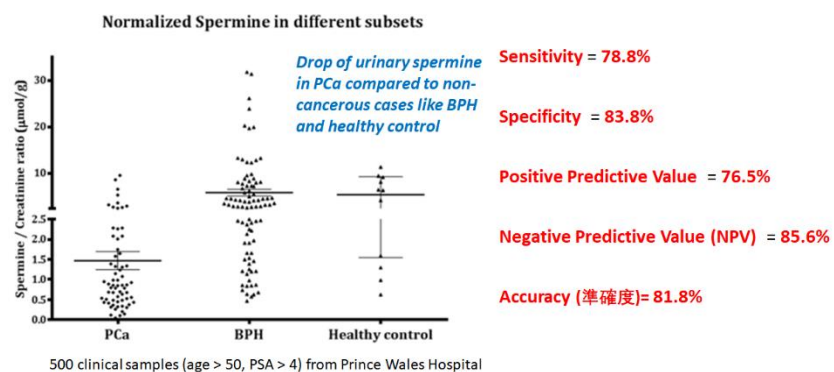


Figure 2. The selectivity and accuracy of spermine as biomarkers for prostate cancer identification. The conclusion is based on the 500 clinical urine samples. [Ref 2]

(3) References to the research

1. Tik-Hung Tsoi, Yan-Juan Gu, Wai-Sum Lo, Wai-Ting Wong, Wing-Tak Wong, Chi-Fai Ng, Chi-Sing Lee and Ka-Leung Wong,* 'Study on spermine-induced aggregation of DNA capped gold nanoparticles: a smart aptasensor for cancer screening', ChemPlusChem (2017) 802-809.
2. Tik-Hung Tsoi, Chi-Fai Chan, Wai-Lun Chan, Peter Ka-Fung Chiu, Wing-Tak Wong,* Chi-Fai Ng,* and Ka-Leung Wong,* 'Urinary polyamines: A pilot study on their roles as prostate cancer detection biomarkers', PloS One, 11 (2016) e0162217.
3. Ka-Leung Wong, 'Urinary Polyamines as Prostate Cancer Detection Biomarkers', US Patent, 15/935,572. Filed date: 16 Apr 2018
4. Ka-Leung Wong, 'Urinary Polyamines as Prostate Cancer Detection Biomarkers', US Patent, 15/784,269. Filed date: 16 Oct 2017

(4) Details of the impact

Prof. Wong commercialized his research summarized above in a spin-off company, New Life Medicine Technology Company Limited, which was founded in 2017 with the aid of Technology Start-up Support Scheme for Universities. Its mission is to develop a series of cost effective pioneering medical products to address the critical needs and provide worldwide clinicians advanced solutions to improve the effectiveness and efficiency of the existing methods in the medical field. The research outcome is described below in terms of academic, economic and societal aspects.

Increasing the effectiveness of public services - Studies have shown that prostate cancer is becoming more common all over the world and has even become the third leading cause of male cancer deaths in Hong Kong. Most patients are >50 years old in which many cases are diagnosed at later stage due to various factors such as cost of screening tests, pain caused by the tests etc. The common clinical prostate cancer screening methods are mainly relied on digital rectal examination (DRE) and serum PSA test, followed by ultrasound biopsy confirmation. DRE is a simple procedure, it not only brings discomfort to patients but also is a strongly-investigator-dependent technique; while PSA test shows a poor specificity towards prostate cancer diagnosis, which leads to poor accuracy of the result. Hence, many patients without prostate cancer are subjected to biopsy and thus its potential complications. Therefore, this work is likely to be used in hospitals or clinics where it is essential to include more efficient detection kits for accurate prostate cancer screening at an earlier stage for the sake of well-being. Due to its high sensitivity and non-intrusiveness, the cost is relatively lower compared to the existing methods. The public will have a higher motivation to get screened and the result can be obtained within an hour. We plan to provide services in clinics in which the urine samples are collected in the clinics and sent to our testing labs for results.

Economic benefits to companies: entering into HK, China and global market -The research on the early prostate cancer detection aroused the interest of a local listed pharmaceutical company, Jacobson Pharma Corporation, who have invested capital of US\$ 8 million in NLMT, in a partnership deal (25% of shares acquired from NLMT). The deal was completed on 21 Dec 2018. With this capital funding, the business valuation of NLMT is now considered to be over US\$ 32 million. The NLMT company has led to significant and increasing local job creation: 20 full-time staff are employed including 7 people for administration while 13 work in for research and development. Of these, 18 are graduates from Hong Kong local universities. The research and development team consist of 4 PhDs, 3 Masters and 6 Bachelors, in charge of analytical and new biomarkers/sensor development. The company business, NLMT has two main directions:

1) Early diagnosis prostate cancer screening service: NLMT and Jacobson are now able to provide an early stage prostate cancer screening service to local clinics. Each test will be charged at HKD 500. The service is launched in the winter of 2019 and will cover more than 100 clinics in HK.

2) Home-based early prostate cancer diagnostic kit: a prototype of the home-based prostate cancer early diagnosis kit has been designed and 1000 clinical samples are going to be tested to validate it. The FDA and CE certification of the screening kit is being sought and the kit will be first launched in Hong Kong in late 2019. Our prototype has already drawn attention in Asia, and as a result the testing and licensing agreements for the Japanese market are underway.

OTC SCREENING KIT INSTRUCTIONS



Figure 3. The design of the commercial home-based early prostate cancer diagnostic kit and will be launched in 2020 Feb. |

To support the development of NLMT on early diagnosis prostate cancer kits, ISO-15189 and ISO-13485 accredited labs have been established in Hong Kong and Zhongshan. NLMT has secured major support from the Zhongshan government, with 1600 m² of new laboratory space and over RMB 20 million allocated for the production of the hospital/laboratory based early diagnosis prostate cancer kits.



Figure 4. The agreement signing ceremony from NLMT and Zhongshan government. The chief of Zhongshan government is presented in the signing ceremony. |

Global impact: Multi-centre clinical study - A multi-centre clinical study is in progress for future scientific research purposes. A total of 10,000 clinical samples are expected to be collected in the UK, France, Australia and Japan at the end of 2020 to further expand the data base on this project. (150 samples are collected) NLMT technical team has been sent out to above sample collection site for sampling. This not only helps with the expansion of the company but also allows the staff to expand their horizon in overseas working environment. Four hospitals are using this biomarker combine with the traditional method PSA to evaluate the potential of prostate cancer in patients. The European Medical Accreditation (EMA) is under application with the submission of 700 clinical data from all over the world. |

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(5) Sources to corroborate the impact

1. Jacobson agreement and exclusive licensing agreement (Confidential);
2. Supportive letter from Jacobson
3. NLMT company structure - <https://www.nlmedtech.com.hk/>
4. Prototype design and test information (Jacobson Provisional Patent)
5. PCA screening service (Letter from Prof. Anthony Ng, CUHK)
6. Zhongshan-HKBU-NLMT agreement reported by Greater Bay Area Medium
<https://mp.weixin.qq.com/s/BpKF3OuH1mfNxFczcVzUtQ>
7. Zhongshan-HKBU-NLMT laboratory opening reported by Greater Bay Area Medium
<https://mp.weixin.qq.com/s/TVKeRatLT8n0cefyxwRxwA>
8. Prostate cancer biomarker qualification application doc- European Medical Accreditation (Confidential) |