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MOLECULAR DIAGNOSTICS

Plasma Nucleic Acids Research

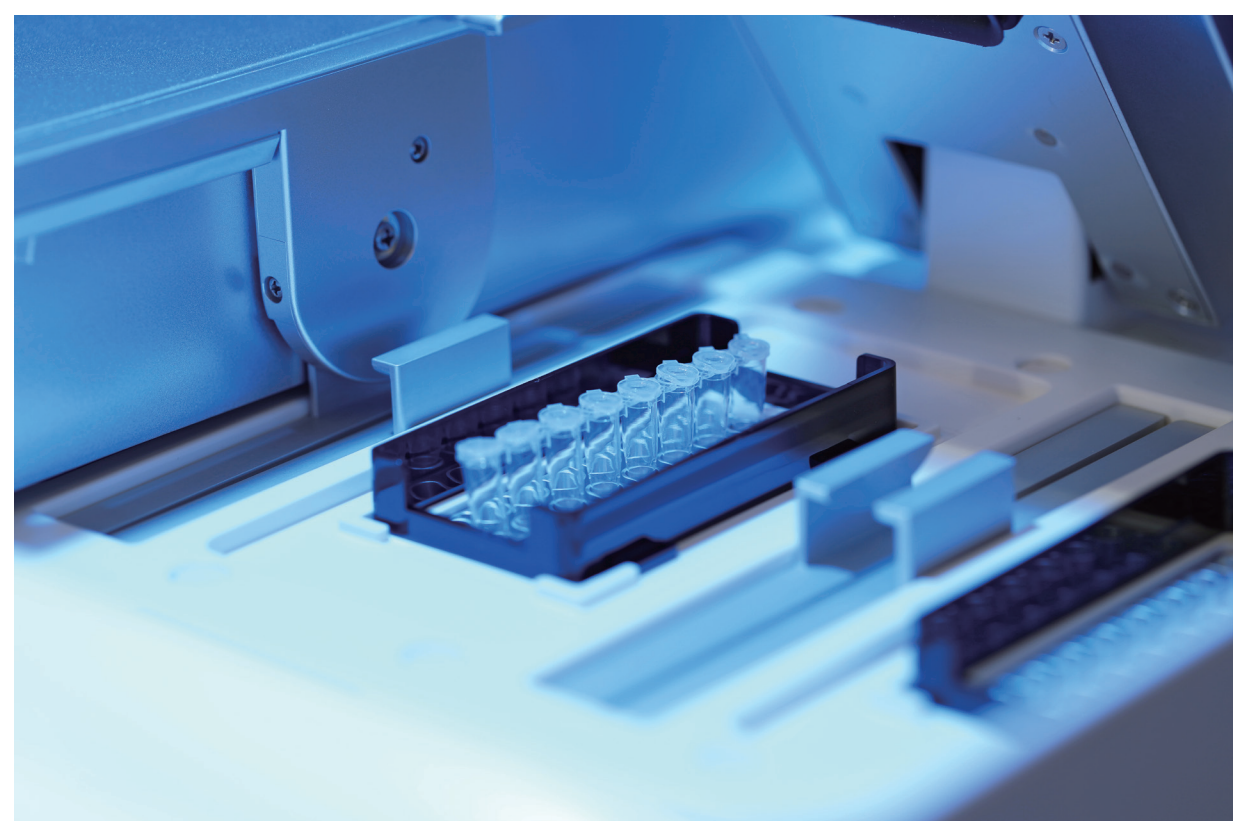
 **Principal Investigator**
Professor Allen Chan

 **Team Members**
Jacky Lam | Irene Tse | Vivien Lin | Patrick Lee

Research Progress Summary

Professor Allen Chan and his team have been actively researching the diagnostic applications of circulating cell-free DNA. Since 2013, the team started a large-scale prospective study to evaluate the potential use of circulating DNA for the screening of early nasopharyngeal cancer (NPC). Through the screening of over 20,000 subjects, they demonstrated that plasma Epstein-Barr virus (EBV) DNA analysis is useful for screening NPC in asymptomatic individuals. Patients identified by screening had superior survival compared with those who had not been screened. This study was published in the *New England Journal of Medicine* and was selected as one of the ten notable articles published in 2017. To recognise this work, Prof. Chan was awarded the Annual Achievement Award from the Chinese Society of Clinical Oncology in 2018 and the Lo Ying Shek Chi-wai scholarship.

To enhance the accuracy of this cancer screening method, they have developed next-generation-sequencing based methods to differentiate EBV DNA released from cancer and non-cancer cells. The new methods were based on the size and methylation difference between EBV DNA released by cancer and non-cancer cells. The positive predictive values of the two new methods improved to 19% and 35%, compared with 11% of the original study. These two improved methods were published in the *Proceedings of the National Academy of Sciences of the United States of America (PNAS)* and *Nature Communications*, respectively.



Research and Scholarship

Academic Editorship

Member's Name	Details	
	Role	Journal
Allen Chan	Member of Editorial Board	Expert Review Molecular Diagnostics

Reviewer of Journal / Conference

Member's Name	Details	
	Role	Journal / Conference
Allen Chan	Reviewer	Clinical Chemistry
		Expert Review Molecular Diagnostics
		Prenatal Diagnosis
		Clinical Cancer Research

Grants and Consultancy

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Allen Chan	Centre for Novostics	Innovation and Technology Commission – Innovation and Technology Fund	01/05/2020	30/04/2025	483,000,000
	Plasma DNA as a Platform Technology for Cancer Detection	Research Grants Council – Theme-based Research Scheme	01/07/2016	30/06/2020	40,000,000
	Prospective 20,000-Person Nasopharyngeal Carcinoma (NPC) Screening Programme Using Plasma Epstein-Barr Virus (EBV) DNA Analysis	Kadoorie Charitable Foundation	01/04/2013	31/03/2023	9,400,000

Publications

A. Journal Papers

- Chan RWY, Serpas L, Ni M, Volpi S, Hiraki LT, Tam LS, Rashidfarrokhi A, Wong PCH, Tam LHP, Wang Y, Jiang P, Cheng ASH, Peng W, Han DSC, Tse PPP, Lau PK, Lee WS, Magnasco A, Buti E, Sisirak V, AlMutairi N, Chan KCA, Chiu RWK, Reizis B, Lo YMD. Plasma DNA profile associated with DNASE1L3 gene mutations: Clinical observations, relationships to nuclease substrate preference, and *in vivo* correction. *American Journal of Human Genetics*. 2020;107(5):882-894. doi:10.1016/j.ajhg.2020.09.006.

- Jiang P, Xie T, Ding SC, Zhou Z, Cheng SH, Chan RWY, Lee WS, Peng W, Wong J, Wong VWS, Chan HLY, Chan SL, Poon LCY, Leung TY, Chan KCA, Chiu RWK, Lo YMD. Detection and characterization of jagged ends of double-stranded DNA in plasma. *Genome Research*. 2020;30(8):1144-1153. doi:10.1101/gr.261396.120.
- Ma ML, Yakovenko S, Zhang H, Cheng SH, Apyrshko V, Zhavoronkov A, Jiang P, Chan KCA, Chiu RWK, Lo YMD. Fetal mitochondrial DNA in maternal plasma in surrogate pregnancies: Detection and topology. *Prenatal Diagnosis*. 2020; 41(3):368-375. doi:10.1002/pd.5860.
- Lam WKJ, Ji L, Tse OYO, Cheng SH, Jiang P, Lee PHP, Lin SV, Hui EP, Ma BBY, Chan ATC, Chan KCA, Chiu RWK, Lo YMD. Sequencing analysis of plasma Epstein-Barr Virus DNA reveals nasopharyngeal carcinoma-associated single nucleotide variant profiles. *Clinical Chemistry*. 2020;66(4):598-605. doi:10.1093/clinchem/hvaa027.
- Jiang P, Sun K, Peng W, Cheng SH, Ni M, Yeung PC, Heung MMS, Xie T, Shang H, Zhou Z, Chan RWY, Wong J, Wong VWS, Poon LC, Leung TY, Lam WKJ, Chan JYK, Chan HLY, Chan KCA, Chiu RWK, Lo YMD. Plasma DNA end-motif profiling as a fragmentomic marker in cancer, pregnancy, and transplantation. *Cancer Discovery*. 2020;10(5):664-673. doi:10.1158/2159-8290.CD-19-0622.
- Sin STK, Jiang P, Deng J, Ji L, Cheng SH, Dutta A, Leung TY, Chan KCA, Chiu RWK, Lo YMD. Identification and characterization of extrachromosomal circular DNA in maternal plasma. *Proceedings of the National Academy of Sciences of the United States of America*. 2020;117(3):1658-1665. doi:10.1073/pnas.1914949117.



Second phase nasopharyngeal cancer screening to address if plasma Epstein-Barr virus DNA analysis can predict risk of future development of the cancer.

Source: Professor Allen Chan