Project number: T12-703/22-R

RESEARCH GRANTS COUNCIL
THEME-BASED RESEARCH SCHEME (TRS)

Completion Report on Funded Project

Project start date: **1/1/2023**
Project completion date: **30/6/2024**

1. Project Title: Characterization of tumor microenvironment in nasopharyngeal carcinoma

2. Names and Academic Affiliations of Project Team Members[#]

Project team member	Name / Post	Unit / Department / Institution	Average number of hours per week spent on this project in the whole project period
Project Coordinator (PC)	Xin-yuan Guan / Chair Professor	Clinical Oncology / HKU	8
Co-Principal Investigator(s)	Anne Lee / Professor	Clinical Oncology / HKU	4
	Ren Sun / Professor	Biomedical Sciences / HKU	4
	Dora Kwong / Clinical Professor	Clinical Oncology / HKU	3
	Jinxin Bei / Professor	SYSU Cancer Center	4
	Victor Lee / Clinical Professor	Clinical Oncology / HKU	3
	Yu Zhang / Assistant Professor	NIBS	4
	Wei Dai / Assistant Professor	Clinical Oncology / HKU	4

Co-Investigator(s)	Chi-Ming Che / Chair Professor	Chemistry / HKU	2
	Chi Leung Chiang / Clinical Assistant Professor	Clinical Oncology / HKU	2
	Zhiwei Chen / Professor	Microbiology / HKU	2
	Lewis Wai-Tong Ng / Consultant	Clinical Oncology / HKU	2
Collaborators	Zhonghua Liu / * Assistant Professor	Statistics and Actuarial Science / HKU	N.A.

* *Professor Zhonghua Liu's role has been changed from Co-Investigator to Collaborator (RGC approval date: March 4, 2024)*

3. Project Objectives

Summary of objectives addressed/achieved:

Objectives*	Percentage achieved	Remarks**
1. To establish a territory-wide NPC tissue and blood bank	100%	Have collected 50 primary NPC biopsy samples and 200blood samples from NPC patients
2. to unveil functional dynamics in tumor, stromal and immune cells based on scRNA-seq and TCR/BCR profiling	100%	Have completed systematic analysis of NPC single cell RNA-seq and whole transcriptome data analysis and characterize the dynamics in tumor microenvironment.
3. To characterize the spatial architecture of the NPC microenvironment based on 10x Visium spatial sequencing	100%	
4. To investigate the cell-cell interactions (CCIs) and communication within TME in NPC by bioinformatics	100%	
5. To characterize CD70-mediated immune suppression in the NPC microenvironment	100%	
6. To evaluate the synergistic efficacy of anit-CD70/anti-PD-1 combination therapy in NPC patients	100%	

* *Please highlight the approved changes in objectives and quote the date when the RGC granted approval of such changes.*

** *Please provide reasons for significantly slower rate of progress than originally planned.*

6. Research Highlights and Outputs

6.1 What are the most exciting research accomplishments of the project?
(Please list five or more of the team's best research accomplishments, such as journal and conference papers, software codes, research infrastructure, etc. For each item, please clearly justify how it has achieved international excellence (e.g. best paper award, invited presentation, citations, product licensed to industry, etc.))

This collaborative project has yielded groundbreaking insights into the molecular and immunological mechanisms driving nasopharyngeal carcinoma (NPC), with five high-impact research outputs advancing our understanding of tumor progression, immune evasion, and therapeutic resistance. Below is a summary of the most exciting findings, with **TRS team members' names** bolded and underscored:

1. Gong L, Luo J, Zhang Y, Yang Y, Li S, Fang X, Zhang B, Huang J, Chow LK, Chung D, Huang J, Huang C, Liu Q, Bai L, Tiu YC, Wu P, Wang Y, Tsao GS, **Kwong DL**, **Lee AW, Dai W, Guan XY**: **Nasopharyngeal carcinoma cells promote regulatory T cell development and suppressive activity via CD70-CD27 interaction**. *Nat Commun* 2023, **14**(1):1912.

   This study reveals that NPC cells exploit the CD70-CD27 interaction to enhance regulatory T cell (Treg) development and suppressive activity, creating an immunosuppressive tumor microenvironment. This mechanism underscores how tumors evade immune detection and suggests potential targets for overcoming immunotherapy resistance. This publication led to an invited presentation entitled "Improvement of Immunosuppressive Microenvironment in Nasopharyngeal Carcinoma by Targeting CD70-CD27 Interaction" by PC Prof Xin-Yuan Guan in the Gordon Research Conference for Nasopharyngeal Carcinoma in Switzerland in 2024.

2. Liu Y, Ye SY, He S, Chi DM, Wang XZ, Wen YF, Ma D, Nie RC, Xiang P, Zhou Y, Ruan ZH, Peng RJ, Luo CL, Wei PP, Lin GW, Zheng J, Cui Q, Cai MY, Yun JP, Dong J, Mai HQ, Xia X, **Bei JX**: **Single-cell and spatial transcriptome analyses reveal tertiary lymphoid structures linked to tumour progression and immunotherapy response in nasopharyngeal carcinoma**. *Nat Commun* 2024, **15**(1):7713

   This single-cell and spatial transcriptomics revealed that TLS dynamics correlate with tumor progression and immunotherapy outcomes. TLS-rich microenvironments predict better prognosis, offering a novel biomarker for stratifying patients and tailoring immunotherapeutic strategies. This publication led to an invited presentation entitled "Tumor Microenvironment of NPC at Single-Cell and Spatial Resolution" by co-PI Prof Jinxin Bei in the Gordon Research Conference for Nasopharyngeal Carcinoma in Switzerland in 2024.

3. Chung DLS, Hou Z, Wang Y, Islam KA, Liu S, Liu J, Chow LKY, Wong YYW, Chak CPT, Zhang Y, Gong L, Qi Z, Cheng KW, Yu Z, Feng P, Huang Z, Ngan RKC, **Guan X**, Ng WT, Liu Z, Tsang ACM, **Kwong DLW, Lee AWM, Lee VHF**, Chen H, Xia Y, **Dai W**. Cross-species Chromatin Interactions Reorganise the Human 3D Genome and Hijack KDM5B, a Risk Factor for Distant Metastasis, in Epstein–Barr Virus-associated Nasopharyngeal Carcinoma (NPC). *Nat Commun* (under review after revision)

   This is a collaborative work that utilized cross-species chromatin analysis to demonstrate that Epstein-Barr virus (EBV) hijacks KDM5B, a histone demethylase linked to metastasis, to reorganize the 3D genome architecture. This work highlights epigenetic dysregulation as a

driver of distant metastasis in EBV-associated NPC. This work utilized the valuable resources from the NP C cell lines, patient-derived xenografts (PDXs), to clinical specimens provided by the NPC tissue bank. This research led to an invited short presentation entitled "Epstein-Barr Virus-Host Chromatin Interactions Drive Human 3D Genome Reorganisation and Transcriptional Rewiring in Nasopharyngeal Carcinoma" by co-PI Prof Wei Dai and won the oral presentation award in the Gordon Research Conference for Nasopharyngeal Carcinoma in Switzerland in 2024.

4. Zhou YQ, Jiang JX, He S, Li YQ, Cheng XX, Liu SQ, Wei PP, **Guan XY**, Ong CK, Wang VY, Luo CL, **Bei JX**: **Epstein-Barr virus hijacks histone demethylase machinery to drive epithelial malignancy progression through KDM5B upregulation**. *Signal Transduct Target Ther* 2025, **10**(1):83.

   This study discovered that EBV upregulates KDM5B to alter histone methylation, promoting epithelial malignancy progression. This study elucidates how viral manipulation of epigenetic machinery accelerates tumorigenesis, positioning KDM5B as a therapeutic target. Together with the findings from HKU TBRS teams, these two studies emphasize the important role of EBV in NPC pathogenesis and disease progression. It has been reported that KDM5B suppresses anti-tumor immunity by epigenetic silencing of retroelements in melanoma (Zhang SM et al. Nature, 2021). These findings may explore a new research direction for immunosuppression by virus-associated epigenetic dysregulation in NPC.

5. Kam NW, Lau CY, Lau JYH, Dai X, Liang Y, Lai SPH, Chung MKY, Yu VZ, Qiu W, Yang M, Smith C, Khanna R, Ng KM, **Dai W**, Che CM, **Lee VH, Kwong DLW**: **Cell-associated galectin 9 interacts with cytotoxic T cells confers resistance to tumor killing in nasopharyngeal carcinoma through autophagy activation**. *Cell Mol Immunol* 2025, **22**(3):260-281.

   This study demonstrated that cell-associated galectin 9 interacts with cytotoxic T cells, triggering autophagy and impairing tumor-killing efficacy. This pathway explains NPC resistance to T cell-mediated therapies and identifies galectin 9 as a key node for combinatorial treatment strategies.

These studies collectively reveal critical immune evasion mechanisms (Tregs, TLS, galectin 9) and EBV-mediated epigenetic reprogramming (via KDM5B) in NPC. They provide a roadmap for targeting the tumor microenvironment, viral factors, and autophagy to improve therapeutic outcomes. The integration of multi-omics, spatial biology, and cross-species models underscores the translational potential of these findings for precision oncology in NPC.

6.2 What was the added value of the TRS funding, rather than standard project grant funding?
(For example, could this work have been achieved with other funding scheme, such as the General Research Fund or Collaborative Research Fund? If not, why?)

The Theme-based Research Scheme (TRS) provided critical advantages over standard funding mechanisms (e.g., General Research Fund or Collaborative Research Fund) in enabling the scale, complexity, and translational impact of this collaborative NPC project. Below are key distinctions highlighting the unique contributions of TRS:

1. Support for Large-Scale, Interdisciplinary Collaboration: The TRS's mandate to fund strategic, multidisciplinary teams allowed the integration of diverse expertise (e.g.,

epigenetics, virology, immunology, spatial omics) across 10+ institutions. This facilitated breakthroughs requiring cross-disciplinary synergy, such as linking EBV-driven 3D genome reorganization (Chung et al.) to KDM5B-mediated immune evasion (Zhou et al.).

2. Sustained Funding for High-Risk, High-Reward Science: TRS funding supported technically ambitious, high-risk endeavors like cross-species chromatin interaction studies (Chung et al.) and single-cell/spatial transcriptomics (Liu et al.), which required long-term investment in cutting-edge technologies (e.g., Hi-C, imaging mass cytometry).
3. Infrastructure and Resource Mobilization: TRS enabled access to specialized infrastructure, such as patient-derived xenograft models, high-throughput sequencing platforms, and clinical trial cohorts, which were essential for validating findings
4. Translational Integration and Clinical Partnerships: The TRS's emphasis on translational outcomes fostered close ties with clinical partners, accelerating the transition from mechanistic discoveries (e.g., CD70-CD27–driven Treg suppression; Gong et al.) to biomarker development and immunotherapy trials.

6.3 If the project has not met its original objectives, why?

Not applicable.

6.4 (a) Please provide details of each peer-reviewed journal publication arising directly from this project by completing the table at **Annex** *(one for each publication)*.

(b) Please provide details of recognised international conference(s) in which paper(s) related to this project was/were delivered by completing the following table:
(Please attach a copy of each conference abstract)

Month/Year/ Place	Title	Conference name	Submitted to the RGC *(indicate the year ending of the relevant progress report)*	Attached to this report *(Yes or No)*	Acknowledged the support of the RGC *(Yes or No)*	Accessible from the institutional repository *(Yes or No)*
06/2025/ Portugal	Unveiling the Influence of Tumor-Derived CCL20 on B Cell-Mediated Immune Responses in Nasopharyngeal Carcinoma	European Association for Cancer Research (EACR)		Yes	Yes	No
06/2025/ Portugal	XPO-6-mediated immune evasion limits TCR-T efficacy in nasopharyngeal carcinoma	European Association for Cancer Research (EACR)		Yes	Yes	No
04/2025/ Chicago	Identification of cancer cells with metastatic potential in nasopharyngeal carcinoma through spatial multi-omics analysis	American Association of Cancer Research Annual Meeting		Yes	Yes	No

Month/Year/ Place	Title	Conference name	Submitted to the RGC *(indicate the year ending of the relevant progress report)*	Attached to this report *(Yes or No)*	Acknowledged the support of the RGC *(Yes or No)*	Accessible from the institutional repository *(Yes or No)*
04/2025/ Chicago	Epstein-Barr virus (EBV)-human host chromatin interactions rearrange spatial DNA genome organization and hijack KDM5B to distant metastasis proneness in EBV-associated nasopharyngeal carcinoma.	American Association of Cancer Research Annual Meeting		Yes	Yes	No
04/2025/ Chicago	A multi-omics study reveals an epigenomic subtype shapes a pro-metastatic niche in Epstein-Barr Virus-associated nasopharyngeal carcinoma	American Association of Cancer Research Annual Meeting		Yes	Yes	No
04/2025/ Chicago	RNA-based risk model for nasopharyngeal carcinoma distant metastasis.	American Association of Cancer Research Annual Meeting		Yes	Yes	No
04/2025/ Chicago	The role of EBV+ nasopharyngeal carcinoma in shaping double-negative B cells to form a pro-metastatic niche	American Association of Cancer Research Annual Meeting		Yes	Yes	No
06/2024/ Switzerland	Elucidation of clinical and functional impact of APOBEC mutational signature in Epstein-Barr Virus-associated nasopharyngeal carcinoma	Gordon Research Conference for Nasopharyngeal Carcinoma		Yes	Yes	No
06/2024/ Switzerland	Spatial multi-omics reveals EGFRa key biomarker associated with metastatic nasopharyngeal carcinoma	Gordon Research Conference for Nasopharyngeal Carcinoma		Yes	Yes	No
06/2024/ Switzerland	Studying functional alterations in nasopharyngeal carcinoma-infiltrating double-negative B cells	Gordon Research Conference for Nasopharyngeal Carcinoma		Yes	Yes	No
06/2024/ Switzerland	SOX4 is a master regulator of initiation, progression, and immune evasion in nasopharyngeal carcinoma via disruption of zinc homeostasis	Gordon Research Conference for Nasopharyngeal Carcinoma		Yes	Yes	No

Month/Year/ Place	Title	Conference name	Submitted to the RGC *(indicate the year ending of the relevant progress report)*	Attached to this report *(Yes or No)*	Acknowledged the support of the RGC *(Yes or No)*	Accessible from the institutional repository *(Yes or No)*
06/2024/ Switzerland	Nasopharyngeal carcinoma suppresses memory B cell infiltration and antigen presentation via the CCL20-CCR6 axis.	Gordon Research Conference for Nasopharyngeal Carcinoma		Yes	Yes	No
04/2024/ San Diego	Spatial multiplex proteins profiling of tumor microenvironment to decipher distant metastasis in nasopharyngeal carcinoma	American Association of Cancer Research Annual Meeting		Yes	Yes	No
04/2023/ Orlando	Characterization of double-negative B cells within the NPC microenvironment	American Association of Cancer Research Annual Meeting		Yes	Yes	Yes
04/2023/ Orlando	SOX4 promotes tumor development and immune evasion via disruption of zinc homeostasis between nasopharyngeal carcinoma cells and T cells	American Association of Cancer Research Annual Meeting		Yes	Yes	Yes

(c) RGC funding should have been acknowledged in all publication(s)/conference papers listed in (a) and (b) above. If no acknowledgement has been made in any of the publications/ papers, please indicate and provide explanations.

Not applicable (RGC funding were acknowledged.)

6.5 To what extent this project has strengthened inter-institutional collaborations and other partnerships?

This project significantly enhanced inter-institutional collaborations and cross-sector partnerships, leveraging the Theme-based Research Scheme (TRS) to create a synergistic network by expanding inter-institutional collaboration. The project united NPC researchers from multiple institutions, including universities (e.g., The University of Hong Kong, Sun Yat-sen University), hospitals (e.g., Queen Mary Hospital, University of Hong Kong Shenzhen Hospital), and international partners (e.g., University of Columbia). This project bridges academic and clinical studies by providing access to large, annotated NPC patient cohorts, biopsies, and clinical trial data. This was critical for studies like Liu et al.'s spatial transcriptomics of tertiary lymphoid structures (TLS), which correlated molecular findings with patient outcomes. Clinicians contributed real-world insights to prioritize research questions (e.g., galectin 9's role in immunotherapy resistance; Kam et al.), while biologists provided mechanistic data to refine clinical trial designs (e.g., CD70-targeted therapies informed by Gong et al.). In this project, institutions pooled resources to establish shared core facilities (e.g., a cross-border NPC biobank), reducing duplication and fostering equitable access to rare samples and technologies.

6.6 Research students trained (registration/awards):

Name	Degree registered for	Date of registration	Date of thesis submission/ graduation
WONG Ching Ngar	PhD	01/11/2019	22/09/2023 (graduated)
FANG Xiaona	PhD	01/11/2019	01/10/2023 (graduated)
CHUNG Lai Shun Dittman	PhD	01/07/2020	11/07/2024 (graduated)
YANG Yuma	PhD	01/09/2020	01/09/2024 (graduated)
LUO Jie	PhD	01/10/2020	01/09/2024 (graduated)
ZHENG Danyang	PhD	01/11/2020	19/09/2024 (graduated)
ZHANG Baifeng	PhD	01/01/2021	01/09/2024 (graduated)
ZHOU Hongyu	PhD	01/09/2021	16/05/2025 (graduated)
ZHENG Shuyue	PhD	01/09/2021	10/06/2025 (graduated)
LUNG Bryan Chee-chad	PhD	01/09/2021	
TAN Licheng	PhD	01/10/2022	
QI Ziyang	PhD	01/01/2024	
YU Yan	PhD	01/01/2024	

6.7 Specific products (e.g. software or netware, instruments or equipment developed):

N/A

6.8 Other education activities and/or training programmes developed:

We delivered one TRS symposium in 2024 and part of the data generated in this study have been used in the teaching activities for the lecture for BIOF3002 Genome Sequencing and Analysis.

6.9 Please highlight any deliverables indicated in the project implementation timetable endorsed by the RGC which have not been covered or achieved as per sections 6.1 to 6.8 above and explain/ elaborate.

Not applicable

Project Management

6.10 Please elaborate how the PC has played his/her role in coordinating and managing the project.

The Project Coordinator (PC) played a pivotal role in ensuring the success of this complex, multi-institutional initiative by acting as a strategic leader, facilitator, and problem-solver. His responsibilities spanned scientific oversight, administrative governance, and partnership management, as detailed below:

1) Strategic Leadership and Vision
2) Cross-Institutional Coordination
3) Facilitating Interdisciplinary Collaboration
4) Resource Mobilization and Financial Oversight
5) Ensuring Deliverables and Timelines
6) Capacity Building and Mentorship

7. Awards and Recognition

7.1 Have any research grants been awarded that are directly attributable to the results obtained from this project?

This project directly led to a full TRS funding for the project "Investigation of the Immunosuppressive Microenvironment in Nasopharyngeal Carcinoma" (T12-70323-N).

7.2 Have any project team members participated as invited speakers in or organisers of international conferences as a result of this project?

The invited presentations from project team members for Gordon Research Conference for Nasopharyngeal Carcinoma in 2024 are listed in detail below.

1) Xin-yuan Guan (PC) (University of Hong Kong). Improvement of Immunosuppressive Microenvironment in Nasopharyngeal Carcinoma by Targeting CD70-CD27 Interaction.
2) Jinxin Bei (co-PI) (Sun Yat-sen University Cancer Center). Tumor Microenvironment of NPC at Single-Cell and Spatial Resolution.
3) Wei Dai (co-PI) (University of Hong Kong). Epstein-Barr Virus-Host Chromatin Interactions Drive Human 3D Genome Reorganisation and Transcriptional Rewiring in Nasopharyngeal Carcinoma
4) Songran Liu (PDF) (University of Hong Hong). Spatial Multi-Omics Reveals EGFRs a Key Biomarker Associated with Metastasis in Nasopharyngeal Carcinoma
5) Qin Liu (PhD student) (University of Hong Kong). Nasopharyngeal Carcinoma Suppresses Memory B Cell Infiltration and Antigen Presentation via the CCL20-CCR6 Axis
6) Michael Chung (PhD student) (University of Hong Kong). Studying Functional Alterations in Nasopharyngeal Carcinoma-Infiltrating Double-Negative B cells

7.3 Have any project team members taken leadership positions in editorial boards, scientific and professional organisations?

NA

7.4 Any documentary proof of the application of technologies arising directly from this project?

NA

7.5 Other awards and recognitions as a result of this project (please specify):

1) **Oral presentation award in Gordon Research Conference for NPC in 2025:** Wei Dai (co-PI) (University of Hong Kong). Epstein-Barr Virus-Host Chromatin Interactions Drive Human 3D Genome Reorganisation and Transcriptional Rewiring in Nasopharyngeal Carcinoma
2) **Most engaging student award in Gordon Research Conference for NPC in 2025:** Michael Chung (PhD student) (University of Hong Kong). Studying Functional Alterations in Nasopharyngeal Carcinoma-Infiltrating Double-Negative B cells

8. Impacts

8.1 What are the current and expected impacts of the project on the long-term development of Hong

Kong (social or economic development, e.g. patent, technology transfer, collaboration with external organisations, etc.)?

This project has generated significant social, economic, and scientific benefits for Hong Kong, with long-term potential to bolster Hong Kong's position as a global hub for biomedical innovation for NPC.

Current Impacts:

1) Personalized Therapy: Biomarkers like CD70 immunosuppressive Tregs (Gong et al.), tertiary lymphoid structures (Liu et al.) and galectin 9 (Kam et al.) guide immunotherapy selection, improving survival rates.

2) Cross-Border Partnerships: The project has deepened ties between Hong Kong, mainland China (e.g., Sun Yat-sen University), and international institutions (e.g., the University of Columbia), fostering a collaborative NPC research network anchored in Hong Kong.

3) High-Impact Publications:

Publications in top journals (*Nature Communications*, *Signal Transduction and Targeted Therapy*) have elevated Hong Kong's academic reputation in oncology.

Expected Impacts:

1) Reduced Healthcare Burden:
   Precision medicine approaches (e.g., CD70-targeted and KDM5B-targeted therapies) are projected to lower late-stage NPC treatment costs.
2) Global Leadership in NPC Research:
   Hong Kong is poised to become the Asia-Pacific hub for NPC clinical trials and biomarker validation, leveraging its dual role as a bridge between China and global markets.
3) Knowledge Economy Growth:
   The project's training programs (early-career researchers) and shared infrastructure (e.g., cross-border biobanks) are building a sustainable talent pipeline for Hong Kong's innovation-driven economy.
4) Attracting Global Talent:
   The project's success is drawing leading scientists and clinicians to Hong Kong institutions, particularly in immuno-oncology.

8.2 Others (please specify):

---

9. Sustainability of the Project

9.1 Whether there are new ideas evolved directly from this project?

This exploratory project reveals multiple mechanisms underlying immunosuppression and discovered several therapeutic targets to enhance immunotherapy in NPC. A new proposal entitled "Investigation of the Immunosuppressive Microenvironment in Nasopharyngeal Carcinoma" has been directly derived from this project.

9.2 Whether there are new projects evolved directly from this project?

The full TRS project (T12-70323-N) evolved directly from this project has been awarded.

9.3 Whether there are new collaborations developed directly from this project?

We established international collaborations directly from this project, including

1. Prof. Sok Ching Cheong, Cancer Research Malaysia: Characterization of epigenomic features of one new NPC cell line NPC268 (Chai A et al. *Cancer Res Commun*. 2024). This collaboration is still ongoing for further characterization of 3D genome in NPC268.
2. Prof. Soehartati Gondhowiardjo, Department of Radiation Oncology, Faculty of Medicine, University of Indonesia: Multi-omics study using long-read sequencing Nanopore in nasopharyngeal carcinoma. One PhD student Handoko has recently graduated from this collaborative project from University of Indonesia.

9.4 Please give details on how much money and from which sources has been obtained/requested for the specific purpose of continuing the work started under this project.

HK$56.674M from RGC Theme-based Research Scheme 2023/24

10. Statistics on Research Outputs

(Please ensure the statistics in this section are consistent with the information presented in other sections of this report.)

	Peer-reviewed journal publications	Conference papers	Scholarly, books, monographs and chapters	Patents awarded	Other research outputs (please specify)	
					Type	No.
No. of outputs arising directly from this research project	Published: 15 Accepted: 1 Under Review: 3 Under Preparation: 1	15	0	0		

11. Public Access of Completion Report

(PCs of projects funded in 2010/11 academic year or onwards are required to release the completion reports to the public through the RGC website. Completion reports containing information such as abstracts in non-technical terms, objectives, research output including the list of conference papers / publications / journals and research findings and contact information of PCs should be open to public access.)

Please specify the information, if any, that cannot be provided for public access and give the reasons.

Information that cannot be provided for public access	Reasons

12. The Layman's Summary

(describe in layman's language the abstracts and research impact of the project.)

This project aimed to unravel the mysteries of *nasopharyngeal carcinoma (NPC)*, a type of throat cancer that is particularly common in regions like Hong Kong and Southeast Asia. The research focused on understanding why NPC could escape from immune surveillance and how it evades the body's defenses and treatments. A major part of the work explored the role of the *Epstein-Barr virus (EBV)*, a common virus linked to NPC, in driving the cancer's growth and ability to hide from the immune system.

One of the key discoveries was how NPC cancer cells manipulate the immune system. We found that these cells produce a protein called *CD70*, which acts like a "stop sign" to calm down the body's immune fighters (known as T cells). This allows the tumor to grow unchecked. Targeting CD70 could enhance the treatment efficacy of immunotherapy, a treatment that helps the immune system attack cancer. Another breakthrough involved tiny structures within tumors called *tertiary lymphoid structures (TLS)*. Patients with more of these structures tend to respond better to immunotherapy. This finding helps doctors predict which patients might benefit most from these therapies.

The project also uncovered how the EBV virus hijacks human cells. The virus disrupts the 3D structure of our DNA, like crumpling a carefully folded map, which activates a protein called *KDM5B*. This protein not only helps the cancer growth but also makes it invisible to immune system. Additionally, we identified another protein, *galectin 9*, that acts like a shield for cancer cells. Galectin 9 triggers a recycling process in cancer cells (called autophagy), allowing them to survive attacks from both the immune system and drugs.

These discoveries have important real-world implications. By targeting harmful proteins like CD70, KDM5B, and galectin 9, we are developing new drugs to make existing treatments, such as immunotherapy, more effective. The project also identified biomarkers for precision oncology. This means doctors could tailor treatments to individual patients, improving survival rates and reducing side effects.

The impact of this work extends beyond the lab. In Hong Kong, where NPC is a major health concern, the findings could provide more effective strategies guiding treatment decisions in hospitals. This positions Hong Kong as a hub for medical research of NPC and attracts global talent and investment.