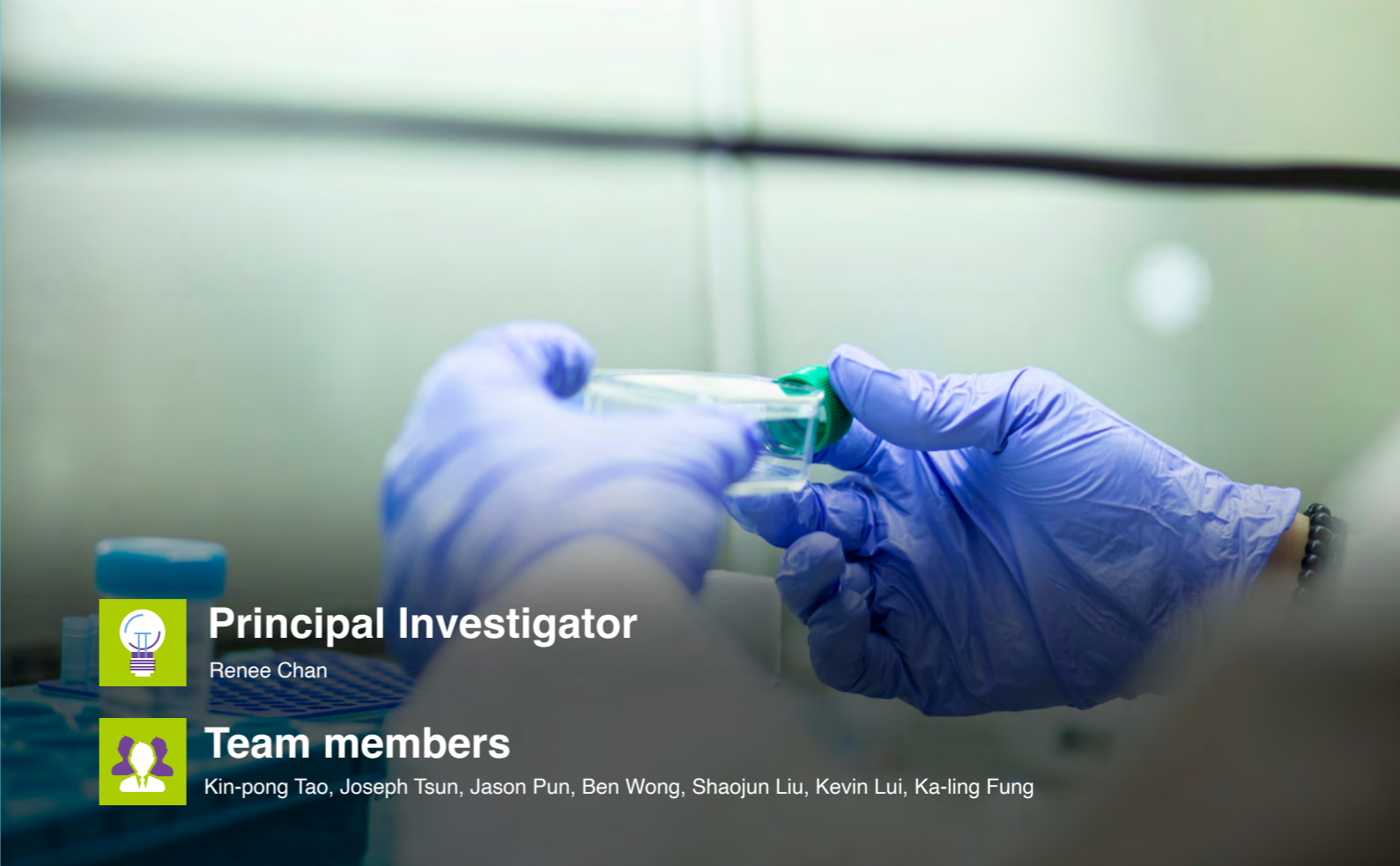


陳韻怡

RENEE CHAN



03 EMERGING INFECTIOUS DISEASES AND MICROBIOTA



Principal Investigator

Renee Chan



Team members

Kin-pong Tao, Joseph Tsun, Jason Pun, Ben Wong, Shaojun Liu, Kevin Lui, Ka-ling Fung

Research Progress Summary

Renee Chan and her team have been awarded the Innovation and Technology Fund – Partnership Research Programme by the Innovation and Technology Commission of the Hong Kong Special Administrative Region of China to expand her work on the respiratory mucosal immunity projects:

Pioneer in using nasal strip for SARS-CoV-2 detection

Hospitalised paediatric patients with coronavirus disease 2019 (COVID-19) experienced frequent nasopharyngeal swabs during their inpatient period. The unpleasant feelings of these children inspired Renee’s team to look for an alternative method for these kids. They pioneered to tailor-made nasal strip using special absorbent material for the collection of nasal epithelial lining fluid (NELF) from children. The length of nasal strips

is much shorter (2-3cm long) than that of the nasopharyngeal swab and can be customised in different sizes to fit subjects at different ages to detect viruses. It can be self-administered by the users even at their school-age (Demonstration available at <https://youtu.be/R5L0eLeprwA>). Another key benefit is that specimens collected by the nasal strip are stable at room temperature for at least 72 hours. This stability of nasal strip samples at room temperature potentially allows the specimens to be posted to the laboratory which usually takes at least a day. These findings have been published in the *Journal of Infection*. With this niche, mucosal samples can be collected in a longitudinal manner unprecedentedly. It also ensures the low dropout rate throughout our prospective studies, as the biological sample can be collected by themselves and mailed to the laboratory directly.

Mucosal antibody induced by SARS-CoV-2 infection

The nasal strip sample is exciting because it also allows the measurements of the mucosal antibody, microbiota and host mediators in a standardised fashion. The team expanded the use of the NELF samples to monitor and elucidate the important role of SARS-CoV-2 specific nasal immunoglobulin A (IgA) between asymptomatic and symptomatic paediatric patients (n=34) and adult patients (n=47) of different severities at different timepoints of the disease course for six months. They reported that children had higher nasal antibodies and lower viral loads early after diagnosis compared to adults with a mild infection. The early occurrence of the IgA on the mucosal surface would relate to the decline in viral load. Their mucosal immunity study is scant in the field and unique in Hong Kong. The mucosal immunity is remarkably important as it is directly guarding the site of infection, however, available research was overwhelmed with the serological readouts. These findings have been uploaded to the preprint server *medRxiv*.

Mucosal antibody induced by SARS-CoV-2 vaccine

Renee's team also evaluated the mucosal and serological antibody induction by the two SARS-CoV-2 vaccines in 88 adults in Hong Kong for three months. The team found that Comirnaty (mRNA vaccine) induces S1-specific IgA and IgG responses with neutralising activity in the nasal mucosa while a similar response is not seen with CoronaVac (inactivated vaccine) which may provide additional protection. However, whether such widespread immunological response by Comirnaty may produce inadvertent adverse effects in other tissues warrants further investigation. These findings have been published in the *Frontiers in Immunology*.

This study opens up a new arm of research in studying respiratory diseases related to acute and chronic local inflammations, such as neonatal sepsis, obstructive sleep apnoea and rhinitis within the Department.

Research and Scholarship

Research Awards and Recognitions

Member's Name	Details	
	Award	Organisation
Shaojun Liu	Nature Review Immunology Poster Prize at 15 th World Immune Regulation Meeting	Swiss Institute of Allergy and Asthma Research

Academic Editorship

Member's Name	Details	
	Role	Journal
Renee Chan	Associate Editor	Frontiers in Medicine: Infectious Diseases - Surveillance, Prevention and Treatment
	Review Editor	Frontiers for Young Minds – Human Health
	Academic Editor	PLoS One
	Editorial Board Member	Journal of Virological Methods

Reviewer of Journal / Conference

Member's Name	Details	
	Role	Journal / Conference
Renee Chan	Reviewer	The Lancet Child & Adolescent Health
		JAMA Paediatrics
		Emerging Microbes & Infections
		Stem Cell Research & Therapy
		Frontiers in Medicine
		Frontiers for Young Minds
		Journal of Pediatric Infectious Diseases
		Respiratory Research
	PLoS One	
	Abstract Rating Reviewer	Joint annual Scientific Meeting 2021 - The Hong Kong Paediatric Society, Hong Kong College of Paediatricians, Hong Kong Paediatric Nurses Association and Hong Kong College of Paediatric Nursing
ATS 2021 - Assembly on Allergy, Immunology, and Inflammation		

Grants and Consultancy

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Renee Chan	Nasal Epithelial Lining Fluid - A Single Specimen for the Detection of SARS-CoV-2 Antigen and SARS-CoV-2 Specific Antibody	The Chinese University of Hong Kong Research Committee – Direct Grant	08/06/2021	07/06/2022	32,000

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Renee Chan	SARS-CoV-2 Receptor Distribution, Replication and Immune Response Induced in the Respiratory Epithelial Cells of Paediatric and Adult and the Existence of Alternative Receptor	Food and Health Bureau – Commissioned Research on the Novel Coronavirus Disease (COVID-19)	01/05/2020	30/04/2022	1,810,820
	A Mechanistic Investigation of the Inhibition of Apoptotic Pathways by Rhinovirus C in Asthmatic Nasopharyngeal Epithelial Cells	The Chinese University of Hong Kong Research Committee – Direct Grant	30/06/2020	29/06/2021	62,000
	Development of a Rapid Test for SARS-CoV-2 Mucosal Antigen and Antibody	Innovation and Technology Commission – Partnership Research Programme	01/11/2021	30/04/2023	1,760,000
	The Establishment of Non-invasive Nasal Epithelial Lining Fluid Collection Method for the Detection of Localized IgA and Mucosal Immune Response	Hong Kong Institute of Allergy Research Grant	01/09/2020	31/08/2021	90,000
	Functional Grouping of Rhinovirus by its Association with Clinical Outcomes for Better Disease Management and Therapeutic Development	Research Grants Council – General Research Fund	01/02/2020	31/12/2022	874,450
	Role of the Heme Oxygenase-1/Carbon Monoxide Axis in the Regulation of Ion Transport and Pro-inflammatory Cytokine Secretion in Airway Epithelia: <i>in Vitro</i> and <i>in Vivo</i> Studies	Research Grants Council – General Research Fund	01/01/2021	31/12/2023	996,285
	A Study to Assess the Efficacy of Plasma and Urine Biomarkers for Early Detection of Necrotizing Enterocolitis	The Chinese University of Hong Kong Research Committee – Direct Grant	15/06/2021	14/06/2022	149,700
	The Safety of High Flow Nasal Cannula and Noninvasive Ventilation for Treatment of Patients with COVID-19 Complicated by Respiratory Failure	Food and Health Bureau – Commissioned Research on the Novel Coronavirus Disease (COVID-19)	01/05/2020	31/10/2021	767,623

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Renee Chan	Optimization of Clinical Treatment of Severe Influenza to Reduce Morbidity and Mortality	Food and Health Bureau – Commissioned Programme for Influenza Research	01/09/2019	31/08/2022	4,996,960

Publications

A. Journal Papers

- Cao L, Zhao S, Lou J, Zheng H, Chan RWY, Chong MKC, Chen Z, Chan PKS, Zee BCY, Wang MH. Differential influence of age on the relationship between genetic mismatch and A(H1N1) pdm09 vaccine effectiveness. *Viruses-Basel*. 2021;13(4):619. doi:10.3390/V13040619.
- Chan RWY, Chan KCC, Lui GCY, Tsun JGS, Chan KYY, Yip JSK, Liu S, Yu MWL, Ng RWY, Chong KKL, Wang MH, Chan PKS, Li AM, Lam HS. Mucosal antibody response to SARS-CoV-2 in paediatric and adult patients: A longitudinal study. *medRxiv*. Published online September 29, 2021. doi:10.1101/2021.09.27.21264219.
- Chan RWY, Liu S, Cheung JY, Tsun JGS, Chan KC, Chan KYY, Fung GPG, Li AM, Lam HS. The mucosal and serological immune responses to the novel coronavirus (SARS-CoV-2) vaccines. *Frontiers in Immunology*. 2021;12. doi:10.3389/fimmu.2021.744887.
- Leung KKY, Hon KL, Ip P, Chan RWY. Critically ill children in paediatric intensive care unit are no less susceptible to infectious diseases amid the COVID-19 pandemic. *Hong Kong Medical Journal*. 2021;27(6):461-463. doi:10.12809/hkmj209029. (Commentary)
- Qu F, Zhao S, Cheng G, Rahman H, Xiao Q, Chan RWY, Ho YP. Double emulsion-pretreated microwell culture for the *in vitro* production of multicellular spheroids and their *in situ* analysis. *Microsystems & Nanoengineering*. 2021;7(1):1-12. doi:10.1038/s41378-021-00267-w.
- Tao KP, Chong M, Pun JC, Tsun JG, Chow SM, Ng CS, Wang MH, Chan Z, Chan PK, Li AM, Chan RW. Suppression of influenza virus infection by rhinovirus interference at the population, individual and cellular levels. *medRxiv*. Published online August 10, 2021. doi:10.1101/2021.08.09.21256656.
- Zhao S, Lou J, Cao L, Zheng H, Chen Z, Chan RWY, Zee BCY, Chan PKS, Chong MKC, Wang MH. An early assessment of a case fatality risk associated with P.1 SARS-CoV-2 lineage in Brazil: An ecological study. *Journal of Travel Medicine*. 2021;28(7). doi:10.1093/jtm/taab078. (Editorial)
- Zhao S, Lou J, Cao L, Zheng H, Chong MKC, Chen Z, Chan RWY, Zee BCY, Chan PKS, Wang MH. Real-time quantification of the transmission advantage associated with a single mutation in pathogen genomes: A case study on the D614G substitution of SARS-CoV-2. *BMC Infectious Diseases*. 2021;21(1):1-8. doi:10.1186/S12879-021-06729-w.
- Zhao S, Lou J, Chong MKC, Cao L, Zheng H, Chen Z, Chan RWY, Zee BCY, Chan PKS, Wang MH. Inferring the association between the risk of COVID-19 case fatality and N501Y substitution in SARS-CoV-2. *Viruses-Basel*. 2021;13(4):638. doi:10.3390/v13040638.

B. Conference Papers

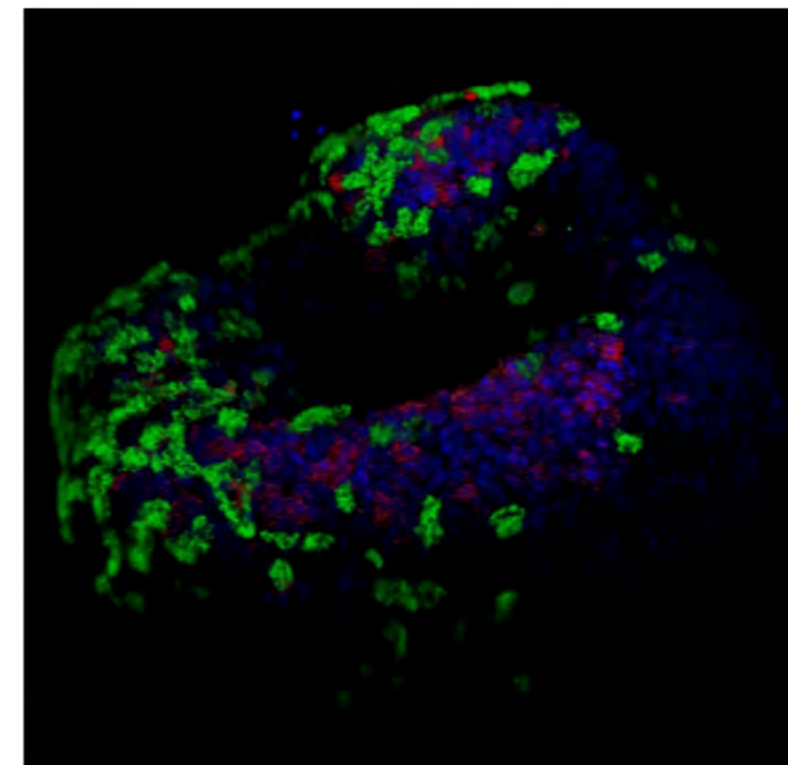
1. Chan RWY, Tao KP, Tsun JGS, Hui KPY, Wong GWK, Chan MCW, Hui DSC, Chan PKS, Chan KCC, Lam HS, Li AM. SARS-CoV-2 replication and immune response induced in the respiratory epithelial cells of paediatric and adult subjects. In: *Health Research Symposium 2021*. Hong Kong. 2021 November 23.
2. Chan RWY, Liu SJ, Cheung JY, Tsun JGS, Chan KC, Chan KYY, Fund GPG, Li AM, Lam HS. Study on the mucosal and serological immune response to the novel coronavirus (SARS-CoV-2) Vaccines. In: *Joint Annual Scientific Meeting 2021 (Hybrid meeting) The Hong Kong Paediatric Society, Hong Kong College of Paediatricians, Hong Kong Paediatric nurses Association & Hong Kong College of Paediatric Nursing*. Hong Kong. 2021 October 30.
3. Wong BKS, Tsun JGS, Chan LLY, Tao KP, Long X, Chow SMW, Ng CSH, Lau RWH, Leung TF, Li AM, Chan RWY. Innate immune response of human influenza A virus and Rhinovirus A16 in patients' nasopharyngeal aspirates and human airway models. In: *Joint Annual Scientific Meeting 2021 (Hybrid meeting) The Hong Kong Paediatric Society, Hong Kong College of Paediatricians, Hong Kong Paediatric nurses Association & Hong Kong College of Paediatric Nursing*. Hong Kong. 2021 October 30.
4. Islam MA, Tsun JGS, Tao KP, Yu JW, Wong BKS, Wai CY, Chan RWY. Rhinovirus-C replication kinetics in neonatal mice lung explant. In: *European Academy of Allergy and Clinical Immunology Hybrid Congress 2021*. Kraków, Poland. 2021 July 10-12.
5. Chan RWY, Chan KCC, Lui GCY, Tsun JGS, Chan KYY, Yip JSK, Liu SJ, Ng RWY, Chong KKL, Chan PKS, Li AM, Lam HS. Mucosal antibody response to SARS-CoV-2 in paediatric and adult patients: A longitudinal study from active infection to convalescent phase. In: *World Immune Regulation Meeting XV: Immune Activation, Effector Functions and Immune Tolerance*. Virtual. 2021 June 30 - July 3.
6. Tsun JGS, Liu S, Lui GCY, Chan KCC, Chan KYY, Ng RWY, Chan PKS, Li AM, Lam S, Chan RWY. The dual-use of nasal strip in the surveillance of active and convalescent SARS-CoV-2 cases. In: *European Respiratory Society International Congress 2021*; 2021 September 5-8. doi:10.1183/13993003.congress-2021.pa3484



Renee Chan and her team have introduced a nasal strip test as a sensitive and accurate method to detect SARS-CoV-2 and the mucosal antibody against the virus. It could be a superior tool for community based surveillance test since it is a simple, less irritative and low risk method which is easy to administer in subjects of a wide age range.

From left: Renee Chan, Assistant Professor; Simon Lam, Professor; Albert Li, Chairman; and Kate Chan, Assistant Professor, of the Department of Paediatrics at CU Medicine.

Source: Renee Chan



Human bronchial organoid at its apical out orientation. It recapitulates the cell population of human bronchial epithelium and is utilized for drug screening. This image shows one organoid with its ciliated cells stained in green, basal cells stained in red and the nucleus in blue.

Source: Renee Chan