

# EMERGING INFECTIOUS DISEASES AND MICROBITA

## Fecal Microbiota Transplantation



Principal Investigator

Professor Siew Ng



Team Members

Francis Chan | Paul Chan | Joyce Mak | Lin Zhang | Qin Liu | Zhilu Xu | Jingwan Zhang | CP Cheung | Arthur Mak | Whitney Tang | Jessica Ching | Clinical FMT Team

### Research Progress Summary

Professor Siew Ng's team was awarded a competitive and prestigious grant by the Innovation and Technology Commission of the Hong Kong Special Administrative Region to establish a new Health@InnoHK Research Center at the Hong Kong Science Park - The

Microbiota I-Center (MagIC). The MagIC centre is established to develop effective and accessible microbiome medicine to improve human health, and will focus on advancing science in the human gut microbiome, knowledge transfer, and mentoring in entrepreneurship.

This year in the midst of the COVID-19 pandemic, the team was the first to discover a series of good bacteria missing in the gut of COVID-19 patients. Using big data analysis and machine learning, the team has successfully developed an oral microbiome immunity formula that aims to target gut dysbiosis, with the hope to boost immunity. Clinical data showed that the recovery of COVID-19 patients who received this microbiome immunity formula outperformed those with standard care in many aspects. These include the achievement of complete symptom resolution,

significant reduction of proinflammatory markers in their blood, increase in favourable bacteria in their stool and development of neutralising antibody. These important findings have been published in high impact journals including *Gastroenterology* and *Gut*, and selected for a global press release to over 7500 media and academics by BMJ group. The team has developed an oral microbiome immunity formula protection that has been licensed to a local biotechnology company for commercialisation. The commercial product of this formula has been launched in the market in December 2020.





In 2020, Prof. Ng's team was also awarded two major grants of 4.5M USD from the Hemsley Charitable Trust in New York. With this support, Prof. Ng's team will unravel the mystery of gut microbiota in early life to identify targets to prevent Crohn's disease. They will also be the partner with the University of Calgary to create one of the largest and most comprehensive Global Repository on the Epidemiology of Crohn's Disease with 29 newly industrialised countries. This support provides her team with a unique opportunity to realise new ways to translate the microbiome into medicine, with real impact for our communities challenged by debilitating diseases.



## Research and Scholarship

### Research Awards and Recognitions

Member's Name	Details	
	Award	Organisation
Siew Ng	Highly-cited Researchers 2020	Clarivate
	Alumni Hall of Fame Award	Penang Chinese Girls' School Centennial Celebration
	Richard Yu Award Lectureship	Hong Kong College of Physicians
	Croucher Senior Medical Research Fellowship	Croucher Foundation
	First in Asia as the Best Global Universities for Gastroenterology and Hepatology	US News and Report

### Fellowships

Member's Name	Details	
	Fellowship	Organisation
Lin Yu	HKPhD	Hong Kong PhD Fellowship Scheme (HKPFS)

### Academic Editorship

Member's Name	Details	
	Role	Journal
Siew Ng	Associate Editor	Gut
	Editorial Board Member	Journal of Gastroenterology and Hepatology
		Gastroenterology
		World Journal of Gastroenterology
		Journal of Crohn's and Colitis
		Alimentary Pharmacology & Therapeutics
Review Editor	Frontiers in Gastroenterology	
International Editorial Board Member	Indonesian Journal of Gastroenterology	

### Reviewer of Journal / Conference

Member's Name	Details	
	Role	Journal / Conference
Siew Ng	Chair Reviewer	American Gastroenterology Association (Digestive Disease Week)
	Reviewer	New England Journal of Medicine
		Nature Medicine
		Alimentary Pharmacology and Therapeutics
		Gastrointestinal Endoscopy
		Journal of Gastroenterology
		Gastroenterology
Journal of Gastroenterology and Hepatology		

### Grants and Consultancy

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Siew Ng	IBD GIVES-21: Global IBD Visualization of Epidemiology Studies (GIVES) in the 21 <sup>st</sup> Century	The Leona M. & Harry B. Helmsley Charitable Trust	09/2020	08/2023	15,564,946
	Health@InnoHK: Microbiota I-Center (MagIC)	Innovation and Technology Commission	05/2019	06/2024	400,000,000
	Role of Gastrointestinal Tract and Gut Microbiota in Pathogenesis of Coronavirus Disease 2019 (COVID-19): A Missing Site for Viral Replication & Transmission	Food and Health Bureau – Health and Medical Research Fund	06/2020	05/2021	4,076,580
	Mother-to-Infant Transfer of Bacteriome, Virome, Fungome and Metabolome in health and Crohn's disease (Mommy-CD)	The Leona M. & Harry B. Helmsley Charitable Trust	10/2019	09/2022	19,727,952
	A Randomised, Placebo-controlled Study on Fecal Microbiota Transplantation for Patients with Irritable Bowel Syndrome with Fecal and Mucosal Microbiota Assessment (FMT-IBS Study)	Food and Health Bureau – Health and Medical Research Fund	06/2019	05/2021	1,301,112
	When Should Low-dose Aspirin be Resumed after Peptic Ulcer Bleeding? A Double-blind, Randomized Controlled Trial	Research Grants Council – General Research Fund	01/2018	12/2020	972,000

### Grants and Consultancy

Name	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Siew Ng	PACIFIC: Prevalence, Characteristics and Genetics of Adherent-Invasive Escherichia Coli in Crohn's Disease Patients: Comparative Study between France and Hong Kong	ANR/RGC Joint Research Scheme	02/2018	01/2022	2,611,942
	The ENIGMA Studies – Eastern Inflammatory Bowel Disease Gut Microbiota	The Leona M. & Harry B. Helmsley Charitable Trust	03/2017	02/2020	14,259,211
	Recurrence Rates in High-risk Subjects with Baseline Advanced Colorectal Adenomas Followed up at Different Surveillance Intervals: A Multi-centre Randomised Controlled Trial in Four Chinese Cities	Food and Health Bureau – Health and Medical Research Fund	09/2020	09/2023	1,460,388
	Early Detection and Surveillance of COVID-19 Infection by Non-invasive Ophthalmic Evaluations	Food and Health Bureau – Commissioned Studies	08/2020	07/2022	4,822,810

## Publications

### A. Journal Papers

- Ng SC, Mak JWY, Hitz L, Chow Y, Bernstein CN, Silverberg MS. COVID-19 pandemic: Which IBD patients need to be scoped – who gets scoped now, who can wait, and how to resume to normal. *Journal of Crohn's and Colitis*. 2020;14(Supplement\_3):S791-S797. doi:10.1093/ecco-jcc/jjaa128. (Supplement)
- Ng SC, Mak JWY, Pal P, Banerjee R. Optimising management strategies of inflammatory bowel disease in resource-limited settings in Asia. *The Lancet Gastroenterology and Hepatology*. 2020;5(12):1089-1100. doi:10.1016/S2468-1253(20)30298-3. (Series)
- Banerjee R, Pal P, Mak JWY, Ng SC. Challenges in the diagnosis and management of inflammatory bowel disease in resource-limited settings in Asia. *The Lancet Gastroenterology and Hepatology*. 2020;5(12):1076-1088. doi:10.1016/S2468-1253(20)30299-5. (Series)
- Zuo T, Sun Y, Wan Y, Yeoh YK, Zhang F, Cheung CP, Chen N, Luo J, Wang W, Sung JJY, Chan PKS, Wang K, Chan FKL, Miao Y, Ng SC. Human-gut-DNA virome variations across geography, ethnicity, and urbanization. *Cell Host & Microbe*. 2020;28(5):741-751.e4. doi:10.1016/j.chom.2020.08.005.
- Mak JWY, Weng M, Wei SC, Ng SC. Zero COVID-19 infection in inflammatory bowel disease patients: Findings from population-based inflammatory bowel disease registries in Hong Kong and Taiwan. *Journal of Gastroenterology and Hepatology*. 2021;36(1):171-173. doi:10.1111/jgh.15164. (Epub ahead of print)
- Ng SC, Tilg H. COVID-19 and the gastrointestinal tract: More than meets the eye. *Gut*. 2020;69(6):973-974. doi:10.1136/gutjnl-2020-321195. (Commentary)



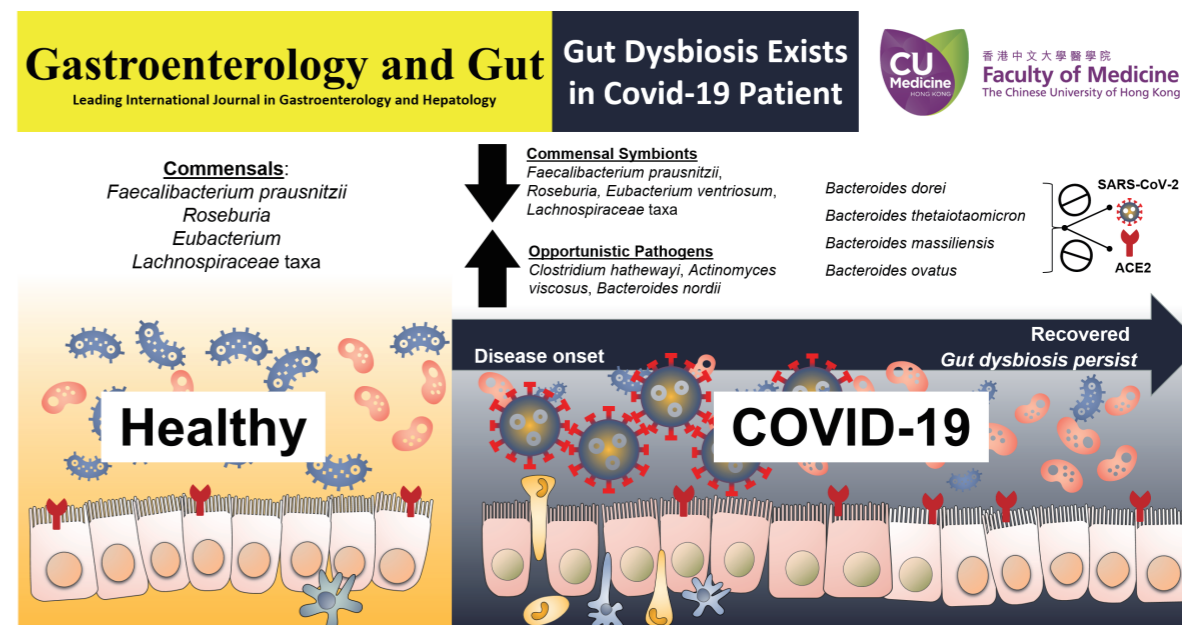
7. Zuo T, Zhan H, Zhang F, Liu Q, Tso EYK, Lui GCY, Chen N, Li A, Lu W, Chan FKL, Chan PKS, Ng SC. Alterations in fecal fungal microbiome of patients with COVID-19 during time of hospitalization until discharge. *Gastroenterology*. 2020;159(4):1302-1310.e5. doi:10.1053/j.gastro.2020.06.048.
8. Zuo T, Zhang F, Lui GCY, Yeoh YK, Li AYL, Zhan H, Wan Y, Chung ACK, Cheung CP, Chen N, Lai CKC, Chen Z, Tso EYK, Fung KSC, Chan V, Ling L, Joynt G, Hui DSC, Chan FKL, Chan PKS, Ng SC. Alterations in gut microbiota of patients with COVID-19 during time of hospitalization. *Gastroenterology*. 2020;159(3):944-955.e8. doi:10.1053/j.gastro.2020.05.048.
9. Chiu PWY, Ng SC, Inoue H, Reddy DN, Ling Hu E, Cho JY, Ho LK, Hewett DG, Chiu HM, Rerknimitr R, Wang HP, Ho SH, Seo DW, Goh KL, Tajiri H, Kitano S, Chan FKL. Practice of endoscopy during COVID-19 pandemic: Position statements of the Asian Pacific Society for digestive endoscopy (APSDE-COVID statements). *Gut*. 2020;69(6):991-996. doi:10.1136/gutjnl-2020-321185.
10. Mak JWY, So J, Tang W, Yip TCF, Leung WK, Li M, Lo FH, Ng KM, Sze SF, Leung CM, Tsang SWC, Shan EHS, Chan KH, Lam BCY, Hui AJ, Chow WH, Chan FKL, Ng SC. Cancer risk and chemoprevention in Chinese inflammatory bowel disease patients: A population-based cohort study. *Scandinavian Journal of Gastroenterology*. 2020;55(3):279-286. doi:10.1080/00365521.2020.1731760.
11. You JHS, Jiang X, Lee WH, Chan PKS, Ng SC. Cost-effectiveness analysis of fecal microbiota transplantation for recurrent *Clostridium difficile* infection in patients with inflammatory bowel disease. *Journal of Gastroenterology and Hepatology*. 2020;35(9):1515-1523. doi:10.1111/jgh.15002.
12. Ananthakrishnan AN, Kaplan GG, Ng SC. Changing global epidemiology of inflammatory bowel diseases: Sustaining health care delivery into the 21<sup>st</sup> century. *Clinical Gastroenterology and Hepatology*. 2020;18(6):1252-1260. doi:10.1016/j.cgh.2020.01.028. (Review)
13. Ng SC, Kamm MA, Yeoh YK, Chan PKS, Zuo T, Tang W, Sood A, Andoh A, Ohmiya N, Zhou Y, Ooi CJ, Mahachai V, Wu CY, Zhang F, Sugano K, Chan FKL. Scientific frontiers in faecal microbiota transplantation: Joint document of Asia-pacific association of gastroenterology (APAGE) and Asia-pacific society for digestive endoscopy (APSDE). *Gut*. 2020;69(1):83-91. doi:10.1136/gutjnl-2019-319407.
14. Segal JP, Mak JWY, Mullish BH, Alexander JL, Ng SC, Marchesi JR. The gut microbiome: An under-recognised contributor to the COVID-19 pandemic? *Therapeutic Advances in Gastroenterology*. 2020;13:175628482097491. doi:10.1177/1756284820974914. (Review)
15. Guillo L, Rabaud C, Choy EH, D'Amico F, Danese S, Ng SC, Peyrin-Biroulet L. Herpes zoster and vaccination strategies in inflammatory bowel diseases: A practical guide. *Clinical Gastroenterology and Hepatology*. 2020;0(0). doi:10.1016/j.cgh.2020.10.027. (Review)
16. Ungaro RC, Brenner EJ, Geary RB, Kaplan GG, Kissous-Hunt M, Lewis JD, Ng SC, Rahier JF, Reinisch W, Steinwurz F, Underwood FE, Zhang X, Colombel JF, Kappelman MD. Effect of IBD medications on COVID-19 outcomes: Results from an international registry. *Gut*. Published online 2020. doi:10.1136/gutjnl-2020-322539. (Epub ahead of print)
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19. Danese S, Sands B, Ng SC, Peyrin-Biroulet L. The day after COVID-19 in IBD: How to go back to 'normal.' *Nature Reviews Gastroenterology & Hepatology*. 2020;17(8):441-443. doi:10.1038/s41575-020-0322-8. (Editorial)
20. Al-Ani AH, Prentice RE, Rentsch CA, Johnson D, Ardan Z, Heerasing N, Garg M, Campbell S, Sasadeusz J, Macrae FA, Ng SC, Rubin DT, Christensen B. Review article: Prevention, diagnosis and management of COVID-19 in the IBD patient. *Alimentary Pharmacology & Therapeutics*. 2020;52(1):54-72. doi:10.1111/apt.15779. (Review)
21. Labarile N, Ghosh S, Ng SC, Walters J, Iacucci M. Tests that now deserve to be more widely adopted in IBD clinical practice. *Therapeutic Advances in Gastroenterology*. 2020;13:175628482094408. doi:10.1177/1756284820944088. (Review)
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23. Su S, Shen J, Zhu L, Qiu Y, He JS, Tan JY, Iacucci M, Ng SC, Ghosh S, Mao R, Liang J. Involvement of digestive system in COVID-19: Manifestations, pathology, management and challenges. *Therapeutic Advances in Gastroenterology*. 2020;13:175628482093462. doi:10.1177/1756284820934626. (Review)
24. Brenner EJ, Ungaro RC, Geary RB, Kaplan GG, Kissous-Hunt M, Lewis JD, Ng SC, Rahier JF, Reinisch W, Ruemmele FM, Steinwurz F, Underwood FE, Zhang X, Colombel JF, Kappelman MD. Corticosteroids, but not TNF antagonists, are associated with adverse COVID-19 outcomes in patients with inflammatory bowel diseases: Results from an international registry. *Gastroenterology*. 2020;159(2):481-491.e3. doi:10.1053/j.gastro.2020.05.032.
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26. Mao R, Qiu Y, He JS, Tan JY, Li XH, Liang J, Shen J, Zhu LR, Chen Y, Iacucci M, Ng SC, Ghosh S, Chen MH. Manifestations and prognosis of gastrointestinal and liver involvement in patients with COVID-19: A systematic review and meta-analysis. *The Lancet Gastroenterology & Hepatology*. 2020;5(7):667-678. doi:10.1016/S2468-1253(20)30126-6. (Review)
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28. Trakman GL, Lin W, Wilson-O'Brien AL, Stanley A, Hamilton AL, Tang W, Or L, Ching J, Morrison M, Yu J, Ng SC, Kamm MA. Development and validation of surveys to estimate food additive intake. *Nutrients*. 2020;12(3):812. doi:10.3390/nu12030812.
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### B. Conference Papers

1. Xu Z, Yang K, Liu Q, Tang W, Zuo T, Li A, Lau L, Lui R, Mak J, Cheung K, Ching J, Wong V, Wong SH, Kong APS, Chow EYK, Wong S, Ho I, Chan P, Chan FKL, Ng SC. A 24-week, double-blind, randomized trial of fecal microbiota transplantation on microbial acquisition in obese patients with type 2 diabetes. In: *Digestive Disease Week 2020*. Chicago, USA.
2. Zhang J, Liu Q, Teh JJ, Hamilton A, Wilson O'Brien A, Ching J, Yang K, Xu Z, Wong SH, Sung JJY, Kamm MA, Morrison M, Yu J, Ng SC. Further evidence that proteus mirabilis is a key bacterium in Crohn's disease pathogenesis. The ENIGMA Study. In: *Digestive Disease Week 2020*. Chicago, USA.
3. Yang K, Niu J, Xu Z, Sun Y, Zuo T, Tang W, Zhang J, Liu Q, Ng EKW, Wong SKH, Chan PKS, Chan FKL, Miao Y, Ng SC. Metagenomic analysis of fecal virome showed geography and population specific signatures in obesity. In: *Digestive Disease Week 2020*. Chicago, USA.
4. Mak JWM, Ho C, Wong K, Cheng TY, Yip TCF, Leung WK, Li M, Lo FH, Ng KM, Sze SF, Leung CM, Tsang SWC, Shan EHS, Chan KH, Lam BCY, Hui AJ, Chow WH, Ng SC. Elderly-onset inflammatory bowel disease is associated with higher risks of infections, cancers and hospitalization: Results from a territory-wide Hong Kong IBD registry. In: *Digestive Disease Week 2020*. Chicago, USA.
5. Arkenbosch JHC, Mak JWY, Hol JCL, Beelen EMJ, Erler N, de Graaf EJ, Bodelier AGL, Hoentjen F, Dijkstra G, de Boer NKH, Romberg-Camps M, van der Woude CJ, Ng SC, de Vries AC. Indications, postoperative management and prognosis of Crohn's disease after ileocecal resection: A multicenter study comparing East versus West. In: *Digestive Disease Week 2020*. Chicago, USA.



The team of Laboratory of Fecal Microbiota Transplantation (FMT) is the first to discover a series of good bacteria missing in the gut of COVID-19 patients. The team has confirmed this discovery with a large number of healthy subjects and COVID-19 patients (Data published in *Gastroenterology and Gut*). Using metagenomics and big data analysis, the team has successfully developed a probiotic formula that aims to target gut dysbiosis. The patent-pending formula has been licensed out to a local biotechnology company for launch to market in December 2020.

Source: Professor Siew Ng



40% of Hong Kong people show gut dysbiosis comparable to that of COVID-19 patients CUHK microbiome immunity formula hastens recovery of COVID-19 patients and offers hope to boost immunity.

Source: Press conference on 19 November 2020