

MOLECULAR MICROBIOLOGY

(Clinical Meta-genomics)



Principal Investigator

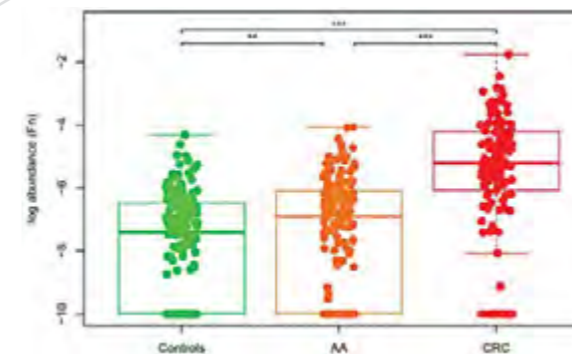
Professor Sunny Wong

Team

Thomas Kwong, Xiansong Wang, Avis Shiu, Rudin Dai, Tai-cheong Chow

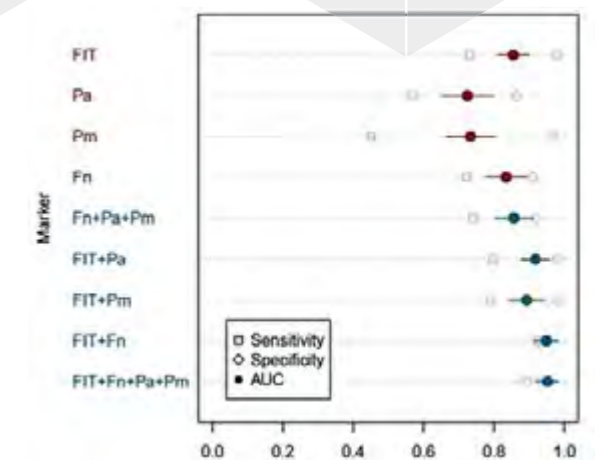
Research Progress Summary

The mucosal surfaces of the gut are colonised by large numbers of micro-organisms that contribute to human health and diseases. These micro-organisms, collectively surpassing the number of the host cells, provide an extensive biochemical repertoire to carry out important metabolic, developmental and immunological functions. Increasing evidence suggests that the gut microbiota also take part in the pathogenesis of common diseases, including obesity, atherosclerosis, inflammatory bowel diseases, colorectal cancer and *Clostridium difficile* infection. Disruption of the microbial ecology and alternations in bacterial abundance are frequently observed. Such detailed observations are now possible with the advent of sequencing technology and bioinformatic tools, which have enabled them to describe the microbial environment at an unprecedented depth. Together with the functional studies in human and animal models, metagenomics is unfolding the secluded mechanisms of many common diseases.



Relative abundance of the microbial marker Fn in colorectal cancer, advanced adenoma and controls.

Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially.

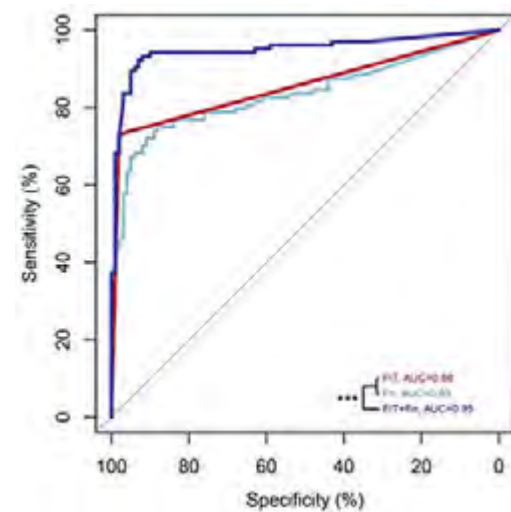


Diagnostic performance with the AUC, sensitivities and specificities of fecal immunochemical test, individual microbial markers and their combinations for the diagnosis of colorectal cancer.

Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially.

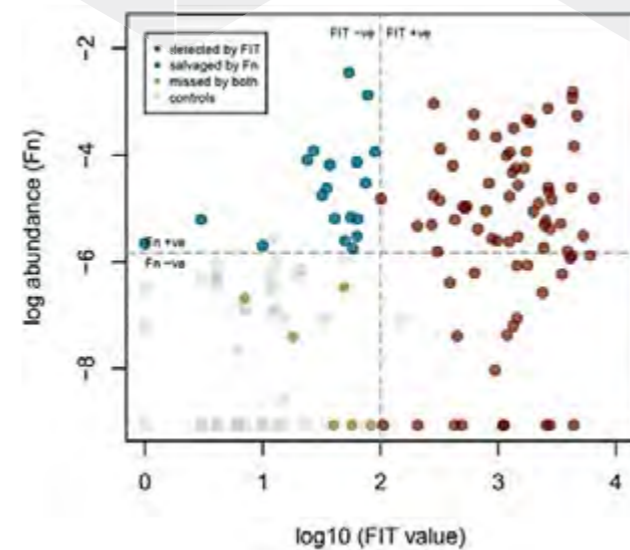
In this regards, the team works to investigate the gut microbiota and host-microbe interaction in various digestive diseases. For colorectal cancer, the team has continued the previous metagenomic studies to newly identify a *Fusobacterium* microbial marker for the detection of advanced colorectal neoplasia (Wong et al., *Gut* 2016). In the study, they have consistently observed a higher *Fusobacterium* abundance in patients with colorectal cancer and advanced neoplasia, whereas addition of the marker can significantly improve performance of the fecal immunochemical test in detecting the lesions. The marker, when combined with the immunochemical test, has showed superior sensitivity (92.3% vs 73.1%, $p < 0.001$) and area under curve (0.95 vs 0.86, $p < 0.001$) than stand-alone immunochemical test in detecting colorectal cancer. This approach takes them one step further towards a non-invasive and more accurate diagnosis of advanced colorectal neoplasia.

Apart from colorectal cancer, the team has also published on other digestive diseases including *C. difficile* infection and inflammatory bowel diseases. Given the increasing number of *C. difficile* cases as a major gastrointestinal nosocomial infection, they have carried out a microbiological study and identified ribotype 002 as a major pathogenic subtype in Hong Kong (Wong et al., *J Infect* 2016). This work has led to a few on-going projects on this bacterium, including a successful grant approved by the Research Grant Council (RGC). Furthermore, the team has worked on the microbe-based testing of latent tuberculosis in patients with inflammatory bowel (Wong et al., *Inflamm Bowel Dis* 2014) and other autoimmune diseases (Wong et al., *Thorax* 2016). These works are only possible with the enormous support from the Li Ka Shing Institute of Health Sciences.



The diagnostic performance of fecal immunochemical test, marker Fn and their combined test indicated by the ROC analysis.

Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially.



The colorectal cancer samples detected by fecal immunochemical test, missed by fecal immunochemical test and detected by marker Fn (blue), and missed by both tests (yellow).

Open Access article distributed in accordance with the Creative Commons Attribution-NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially.



Recognitions

Awards and Fellowships

Member's Full Name	Details
Sunny Wong	Fellowship of the Hong Kong Academy of Medicine
Sunny Wong	Fellowship of the Hong Kong College of Physicians
Sunny Wong	Distinguished Research Paper Award for Young Investigators, Hong Kong College of Physicians
Sunny Wong	Exemplary Teachers' Award, Department of Medicine and Therapeutics

Grants and Consultancy

Full Name of PI	Project Title	Funding Source	Start Date (dd/mm/yyyy)	End Date (dd/mm/yyyy)	Amount (HK\$)
Sunny Wong	Clarifying the Mechanisms of Ribotype 002 Virulence in <i>Clostridium difficile</i> Infection	Research Grant Council - General Research Fund / Early Career Scheme	01/07/2016	31/12/2020	1,050,589
Sunny Wong	CRISPR-Cas9 Mediated Gene Splicing as a Novel Therapy for <i>Clostridium difficile</i> Infection	Shenzhen Science and Technology Innovation Commission	01/03/2016	31/12/2017	239,210
Sunny Wong	A Metagenomic Study on Patients with Pre-malignant Neoplastic Polyps	Croucher Foundation	30/12/2013	29/12/2017	500,000

Publications

A. Journal Papers

1. Wong SH, Kwong TN, Chow TC, Luk AK, Dai RZ, Nakatsu G, Lam TY, Zhang L, Wu JC, Chan FK, Ng SS, Wong MC, Ng SC, Wu WK, Yu J, Sung JJ. Quantitation of faecal *Fusobacterium* improves faecal immunochemical test in detecting advanced colorectal neoplasia. *Gut*. 2016; gutjnl-2016-312766.
2. Wong SH, Gao Q, Tsoi KK, Wu WK, Tam LS, Lee N, Chan FK, Wu JC, Sung JJ, Ng SC. Effect of immunosuppressive therapy on interferon gamma release assay for latent tuberculosis screening in patients with autoimmune diseases: a systematic review and meta-analysis. *Thorax*. 2016; 71(1): 64-72.
3. Wong SH, Ip M, Hawkey PM, Lo N, Hardy K, Manzoor S, Hui WW, Choi KW, Wong RY, Yung IM, Cheung CS, Lam KL, Kwong T, Wu WK, Ng SC, Wu JC, Sung JJ, Lee N. High morbidity and mortality of *Clostridium difficile* infection and its associations with ribotype 002 in Hong Kong. *Journal of Infection*. 2016; 73(2): 115-22.
4. Li Z, Wong SH, Shen J, Chan MT, Wu WK. The Role of MicroRNAs in Ankylosing Spondylitis. *Medicine (Baltimore)*. 2016; 95(14): e3325.
5. Tse G, Lai ET, Yeo JM, Tse V, Wong SH. Mechanisms of Electrical Activation and Conduction in the Gastrointestinal System: Lessons from Cardiac Electrophysiology. *Frontiers in Physiology*. 2016; 7: 182. (Review)
6. Tse G, Lai ET, Lee AP, Yan BP, Wong SH. Electrophysiological Mechanisms of Gastrointestinal Arrhythmogenesis: Lessons from the Heart. *Frontiers in Physiology*. 2016; 7: 230. (Review)
7. Ho J, Chan H, Wong SH, Wang MH, Yu J, Xiao ZG, Liu XD, Choi G, Leung CCH, Wong WT, Li Z, Gin T, Chan MTV, Wu WK. The involvement of regulatory non-coding mRNAs in sepsis: A systematic review. *Critical Care* 2016; 20.
8. Bai AH, Wu WK, Xu L, Wong SH, Go MY, Chan AW, et al. Dysregulated Lysine Acetyltransferase 2B Promotes Inflammatory Bowel Disease Pathogenesis Through Transcriptional Repression of Interleukin-10. *Journal of Crohns & Colitis*. 2016; 10(6): 726-34.
9. Hirai HW, Tsoi KK, Chan JY, Wong SH, Ching JY, Wong MC, et al. Systematic review with meta-analysis: faecal occult blood tests show lower colorectal cancer detection rates in the proximal colon in colonoscopy-verified diagnostic studies. *Alimentary Pharmacology & Therapeutics*. 2016; 43(7): 755-64.
10. Ho J, Yu J, Wong SH, Zhang L, Liu X, Wong WT, Leung CC, Choi G, Wang MH, Gin T, Chan MT, Wu WK. Autophagy in sepsis: degradation into exhaustion? *Autophagy*. 2016; 12(7): 1073-82. (Review)
11. Li XC, Wu WK, Xing R, Wong SH, Liu YX, Fang XD, Zhang YL, Wang MY, Wang JQ, Li L, Zhou Y, Tang SW, Peng SL, Qiu KL, Chen LY, Chen KX, Yang HM, Zhang W, Chan MT, Lu YY, Sung JJ, Yu J. Distinct subtypes of gastric cancer defined by molecular characterization include novel mutational signatures with prognostic capability. *Cancer Research*. 2016; 76(7): 1724-32.
12. Ng WK, Wong SH, Ng SC. Changing epidemiological trends of inflammatory bowel disease in Asia. *Intestinal Research*. 2016; 14(2): 111-9. (Review)
13. Tang SW, Wu WK, Li XC, Wong SH, Wong N, Chan MTV, Sung JJY, Yu J. Stratification of digestive cancers with different pathological features and survival outcomes by miRNA expression. *Scientific Reports*. 2016; 6.
14. Zhang L, Wu WK, Gallo RL, Fang EF, Hu W, Ling TK, Shen J, Chan RL, Lu L, Luo XM, Li MX, Chan KM, Yu J, Wong VW, Ng SC, Wong SH, Chan FKL, Sung JJ, Chan MT, Cho CH. Critical role of antimicrobial peptide cathelicidin for controlling helicobacter pylori survival and infection. *Journal of Immunology*. 2016; 196(4): 1799-809.

B. Book Chapters

1. Wong SH, Chan FK. Adverse Effects of NSAIDs in the Gastrointestinal Tract: Risk Factors of Gastrointestinal Toxicity with NSAIDs. In: Lanasa A, ed. *NSAIDs And Aspirin: Recent Advances And Implications For Clinical Management*. New York: Springer Healthcare LLC; 2016:45-59.

C. Conference Papers

1. Wong SH, Tang W, Wu JC, Ng SC. *Clostridium difficile* infections in inflammatory bowel disease patients is associated with increased use of immunosuppressant and higher rates of colectomy: results from a population-based cohort. In: *Digestive Disease Week*; San Diego, USA; 2016 May 21-24.
2. 'Effect of immunosuppressive therapy on interferon-gamma release assay for latent tuberculosis screening in patients with autoimmune diseases', Oral Presentation at the Annual Scientific Meeting, Hong Kong College of Physicians.
3. Wong SH, Kwong TN, Wang N, Tang RS, Ng SC, Sung JJ. Bacteraemia from mucosal microbiota is associated with subsequent occurrence of colorectal cancer. In: *United European Gastroenterology Week*; Vienna, Austria; 2016 Oct 28 - Nov 1.
4. Wong SH, Kwong TN, Chow TC, Luk AK, Dai RZ, Nakatsu G, Lam TY, Zhang L, Wu JC, Chan FK, Ng SS, Wong MC, Ng SC, Wu WK, Yu J, Sung JJ. Quantification of fecal *Fusobacterium* and fecal immunochemical test in detecting colorectal cancer and advanced neoplasia. In: *Asia Pacific Digestive Week*; Kobe, Japan; 2016 Nov 2-5.