**H. pylori study in NCKU and overcome difficult-issues of digestive tract**

Bor-Shyang Sheu*

Department of Medicine, College of Medicine, National Cheng Kung University

sheubs@mail.ncku.edu.tw

【106 MOST Outstanding Research Award】Special Issue

Prof. Bor-Shyang Sheu has a central belief: clinical research is to “improve the need of patients”. Prof. Sheu has been nominated as Distinguished Professor of NCKU since 2007, and as chairman of Internal medicine Committee of National Science Council, ROC 2011-2013. Prof. Sheu also served as deputy superintendent in NCKU hospital in 2011-2015. Prof. Sheu is now served as superintendent of Tainan Hospital, Ministry of Health & Welfare, due to the co-promotion with NCKU hospital. Prof. Sheu’s achievements are categorized in 4 aspects:

1> **H. pylori virulence for gastric colonization- vaccination target beneath gastric mucin gel**

Colonization of *H. pylori* to the gastric epithelium is the first step to establish infection. Our team explored two putative pathways for colonization (Figure 1): 1> the interaction between gastric Lewis B on epithelium and BabA of bacteria (2003, *Gut*), and 2> while host lack or shortage with Lewis B antigen, between sialyl-Lewis X and SabA of bacteria (2006, *Am J Gastroenterol*). Prof. Sheu was award as “Emerging Leader Lectureship” on 2009 Asia-Pacific Digestive Week, for milestone contribution to define *H. pylori* vaccination targets (2010, *JGH*).
H. pylori virulence for gastric carcinogenesis- a bug-mediated high-pH vicious cycle

*H. pylori* is type I WHO carcinogen, our team discovered *H. pylori* cagL amino-acid sequence in as Y58/E59 can mediate a stronger binding to the integrin α5β1 receptor of gastric epithelium and facilitate type IV secretion system (T4SS) to inject *H. pylori* CagA into cells to trigger up adverse carcinogenetic cascade. During chronic *H. pylori* infection, an achlorhydria environment can prime up integrin α5β1 receptor to adapt with CagL-Y58E59 with a vicious cycle (Figure 2). Screening out the high virulent *H. pylori* or adjust the intra-gastric environment can stop the vicious cycle to improve gastric cancer control (2013, PLoS ONE).

Screening and long-term surveillance to *H. pylori*-related precancerous lesions

Intestinal metaplasia (IM) is an important precancerous lesion of *H. pylori* infection. It is too late to eradicate *H. pylori* for gastric cancer control, once IM has developed. Prof. Sheu’s team composed a novel histological marker as corpus-predominant gastritis index (CGI), earlier marker than IM to identify out high-risk group for early *H. pylori* eradication (2013, APT). Moreover, our team conducted screening and long-term surveillance for risky IM in *H. pylori*-infected subjects with chemoprevention to reverse the IM progression since 2003 until now. Our team shall be highly original to illustrate 70% IM cases have persisted IM with COX-2 overexpression, despite of *H. pylori* eradication (2003, Clin Cancer Res). Because a better IM regression by *H. pylori* eradication in the long-term COX-2 inhibitor user (2007, APT), Prof. Sheu conducted clinical trial (2014, Helicobacter) to suggest COX-2 inhibitor can be safe to prevent IM progression after *H. pylori* eradication. Prof. Sheu composed the 1st Taiwan national-wide *H. pylori* consensus to highlight successful Taiwan experience for globalization (2017, Helicobacter).

The breakthroughs to difficult clinical issues of upper gastrointestinal diseases
4-1 Upper gastrointestinal bleeding (UGIB)

Upper gastrointestinal bleeding is a fatal clinical disease, especially in senile comorbid background. Our team is novel to illustrate double oral dose of PPI can be highly cost-beneficial to achieve well control of rebleeding for high risky patients with Rockall scores > 6 comorbid illness (2014, Gut). The study has breakthrough contribution to offer the optimal dosage and duration of PPI to improve the recurrent bleeding control in such risky patient. The cornerstone results were included in UGIB guideline in USA and in Taiwan.

4-2 Gastroesophageal reflux disease (GERD)

GERD is an important clinical burden worldwide in need to improve refractory case control. Prof. Sheu disclosed higher body mass index (BMI > 25 kg/m²) is an independent factor to determine PPI response in Grade AB & CD cases (2007 & 2008, Am J Gastroenterol). Prof. Sheu illustrated double-dosed PPI can improve the GERD control for overweight and obesity (2010, Am J Gastroenterol). Prof. Sheu also suggested to eradicate H. pylori infection to prevent progression of precancerous lesion during long-term PPI for GERD (2009, Am J Gastroenterol). Herein, Prof. Sheu was invited to compose the national Taiwan GERD consensus on 2014.

Awardee remarks:
Research is to find, to face, to resolve the problem with attitude, ability and self-refreshment. Based on the lucky support with good logistics, persistent motivation, and adequate resource, I start my H. pylori journey in NCKU. I appreciate all the events happen to me, including both positive vs. negative, even though the latter seems to be more. I shall keep “Patient is my best research teacher” with this late coming honor. There will be no change in my consistent persistence to research on tomorrow’s sun rise. By this way, I express my deep appreciation to my wife to let me “always believe there will be unlimited possibility in life”.

References:

10. Cheng HC, Wu CT, Chang WL, Cheng WC, Chen WY, Sheu BS*. Double oral esomeprazole after a 3-day
intravenous esomeprazole infusion reduces recurrent peptic ulcer bleeding in high-risk patients: a randomised controlled study. Gut 2014; 63:1864-72

Copyright 2018 National Cheng Kung University