

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Hon Wai Koon	POSITION TITLE Assistant Professor (UCLA)		
eRA COMMONS USER NAME Koonhw2			
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
The Hong Kong Polytechnic University, Hong Kong.	B.Sc. (Hons)	1996	Applied Biology with Biotechnology
The University of Hong Kong, Hong Kong. The University of Hong Kong, Hong Kong.	M.Phil. Ph.D.	1999 2004	Pharmacology Molecular Biology
Harvard Medical School / Beth Israel Deaconess Medical Center, Boston, MA	Research fellow	2007	Gastroenterology

A. Personal Statement

My research involves identification of in vivo and signaling mechanisms by which neuropeptides and their G protein-coupled receptors modulate intestinal inflammation relevant to the pathogenesis of IBD. My most recent independent area of research funded by a K Award and the Crohn's and Colitis Foundation concerns the role of the antimicrobial peptides cathelicidins in IBD pathogenesis with particular emphasis on the importance of intestinal epithelial cells in this response. I have been working with the PI of this proposal since 2003 and helped developed relevant animal models and approaches to study neuropeptide involvement in intestinal inflammation using diverse colitis models. My role in the current proposal will be to serve as collaborator to Dr. Pothoulakis. In this role, I will provide my experience and expertise in assisting his research related to colitis and intestinal fibrosis animal models. Along these lines I have recently published three manuscripts related to the animal model of fibrosis proposed in this application

B. Positions and Honors.

Positions and Employment

- 7/2007-6/2009 Assistant Researcher, Division of Digestive Diseases, David Geffen School of Medicine, the University of California, Los Angeles.
- 7/2009-6/2010 Associate Researcher, Division of Digestive Diseases, David Geffen School of Medicine, the University of California, Los Angeles.
- 7/2010-Present Assistant Professor, Division of Digestive Diseases, David Geffen School of Medicine, the University of California, Los Angeles.

Honors and Awards

- 1993-1996 Hong Kong Jockey Club Scholarship for full undergraduate tuition fee payments.
- 1996-2003 Studentship for postgraduate training stipend (The University of Hong Kong)
- 2000-2001 Chairman of Postgraduate Students Association (The University of Hong Kong)
- 2005 AGA Poster of Distinction, title 'Substance P-Stimulated Cyclooxygenase-2 and Prostaglandin E₂ Expression in Human Colonic Epithelial Cells Involves Stat Activation'
- 2005 AGA Poster of Distinction, title 'Substance P-Stimulated Interleukin-8 Expression in Human Colonic Epithelial Cells Involves PKC δ Activation'
- 2006 **Crohn's and Colitis Foundation of America (CCFA) Research Fellowship Award (2006-2008)**
- 2006 Oral Presentation at Digestive Disease Week 2006, title "Substance P Mediates Anti-apoptotic Pathways Through Akt/Protein Kinase B Activation in Human Colonic Epithelial Cells"
- 2007 **Pilot and Feasibility Study grant, CURE Center, UCLA.**
- 2007 AGA Poster of Distinction, title 'Substance P (SP) stimulates expression of the pro-angiogenic factor cyr61 in colonic epithelial cells. Evidence for a SP-cyr61 communication during experimental colitis.'

- 2007 Invited reviewer for the Journal of Pharmacology and Experimental Therapeutics (www.jpvet.org).
- 2008 Poster of Distinction, CURE annual research meeting, title 'Protective mechanism of cathelicidin in colonic inflammation.'
- 2008 Oral presentation at Center for Neurobiology of Stress Symposium, title "Substance P promotes angiogenesis during colitis"
- 2008 Oral Presentation at Digestive Disease Week, title "NT induces IL-6 secretion in mouse preadipocytes and adipose tissues during TNBS colitis".
- 2008 Oral Presentation at Digestive Disease Week, title "Substance P mediates development of colon tumors in DSS-exposed Apc/Min mice and cultured human colon cancer cells".
- 2009 Travel Award for International Symposium on Regulatory Peptides.
- 2009 Oral Presentation in Digestive Disease Week, title "Substance P mediates colonic fibrosis in chronic trinitrobenzene sulfonic acid (TNBS)-treated and collagen synthesis in human colonic fibroblasts".
- 2010 Oral Presentation at CURE Annual Scientific Meeting, title "Role of cathelicidin in intestinal inflammation.'
- 2010 AGA Poster of Distinction, title 'Bacterial DNA mediated cathelicidin secretion from monocytes during colonic inflammation.'
- 2010 Invited reviewer for the Journal of Biological Chemistry (www.jbc.org).
- 2010 **Crohn's and Colitis Foundation of America (CCFA) Career Development Award (2010-2013)**
- 2010 **NIH/NIDDK Mentored Research Scientist Development Award (K01) 2010-2015.**
- 2010 Oral Presentation at CCFA clinical & research conference, title "Roles of endogenous and exogenous cathelicidin during colonic inflammation."
- 2011 Faculty mentor of UCLA undergraduate research programs (SRP99 & MIMG199).

C. Publications (in chronological order)

Original and Research Articles:

- 1 **Koon HW**, Zhao D, Na X, Moyer MP, Pothoulakis C. Metalloproteinases and transforming growth factor- α mediate substance P-induced mitogen-activated protein kinase activation and proliferation in human colonocytes. **J Biol Chem**. 2004 279:45519-27.
- 2 Zhao D, Zhan Y, Zeng H, **Koon HW**, Moyer MP, Pothoulakis C. Neurotensin stimulates interleukin-8 expression through modulation of I κ B α phosphorylation and p65 transcriptional activity: involvement of protein kinase C α . **Mol Pharmacol**. 2005 67:2025-31.
- 3 Na X, Zhao D, **Koon HW**, Kim H, Husmark J, Moyer MP, Pothoulakis C, LaMont JT. Clostridium difficile toxin B activates the EGF receptor and the ERK/MAP kinase pathway in human colonocytes. **Gastroenterology**. 2005 128:1002-11.
- 4 **Koon HW**, Zhao D, Zhan Y, Moyer MP and Pothoulakis C. Substance P-stimulated interleukin-8 expression in human colonic epithelial cells involves PKC δ activation. **J Pharmacol Exp Ther**. 2005 Sep;314(3):1393-400. PMID: PMC2607294
- 5 **Koon HW**, Zhao D, Zhan Y, Rhee SH, Moyer MP and Pothoulakis C. Substance P stimulates cyclooxygenase-2 and prostaglandin E $_2$ expression through JAK-STAT activation in human colonic epithelial cells. **J Immunol**. 2006 Apr 15;176(8):5050-9. PMID: PMC2593099
- 6 Zhao D, Zhan Y, Zeng H, **Koon HW**, Moyer MP, Pothoulakis C. Neurotensin stimulates expression of early growth response-gene-1 and EGF receptor through MAP kinase activation in human colonic epithelial cells. **Int J Cancer**. 2007 Jan 17;120(8):1652-1656. PMC Journal – In process.

- 7 **Koon HW**, Zhao D, Zhan Y, Moyer MP and Pothoulakis C. Substance P mediates anti-apoptotic responses in human colonocytes via Akt activation. **Proc Natl Acad Sci U S A**. 2007 Feb 6;104(6):2013-8. PMID: PMC1794289
- 8 Gross K, Karagiannides I, Thomou T, **Koon HW**, Bowe C, Kim H, Giorgadze N, Tchkonja T, Pirtskhalava T, Kirkland JL and Pothoulakis C. Substance P promotes expansion of human mesenteric preadipocytes through proliferative and anti-apoptotic pathways. **Am J Physiol Gastrointest Liver Physiol**. 2009 May;296(5):G1012-9. PMID: PMC2681337.
- 9 **Koon HW**, Kim YS, Xu H, Kumar A, Zhao D, Karagiannides, Dobner PR and Pothoulakis C. Neurotensin induces IL-6 secretion in mouse preadipocytes and adipose tissues during 2,4,6,-trinitrobenzenesulphonic acid-induced colitis. **Proc Natl Acad Sci U S A**. 2009 May 26;106(21):8766-71. PMID: PMC2688970.
- 10 **Koon HW**, Shih D, Karagiannides I, Zhao D, Fazelbhoj Z, Hing TC, Xu H, Lu B, Gerard N, Pothoulakis C. Substance P modulates chronic inflammation induced colonic fibrosis. *Am J Pathol*. 2010 Nov;177(5):2300-9. Epub 2010 Oct 1. PMID: PMC2966789.
- 11 Zhao D, Bakirtzi K, Zhan Y, Zeng H, **Koon HW**, Pothoulakis C. Insulin-like growth factor-1 receptor transactivation modulates the inflammatory and proliferative response of neurotensin in human colonic epithelial cells. **J Biol Chem**. 2011 Feb 25;286(8):6092-9. Epub 2011 Jan 6. PMID: PMC3057861
- 12 Shih DQ, Barrett R, Zhang X, Yeager N, **Koon HW**, Phaosawasdi P, Song Y, Ko B, Wong MH, Michelsen KS, Martins G, Pothoulakis C, Targan SR. Constitutive TL1A (TNFSF15) Expression on Lymphoid or Myeloid Cells Leads to Mild Intestinal Inflammation and Fibrosis. *PLoS One*. 2011 Jan 11;6(1):e16090. PMID: PMC3019214
- 13 **Koon HW**, Shih DQ, Chen J, Bakirtzi K, Hing TC, Law I, Ho S, Ichikawa R, Zhao D, Xu H, Gallo R, Dempsey P, Cheng G, Targan SR, Pothoulakis C. Cathelicidin Signaling via the Toll-like receptor protects against colitis in mice. *Gastroenterology* 2011 Nov;114(5):1852-1863.e3 Epub 2011 Jul 14. PMID: PMC3214015.
- 14 **Koon HW**, Shih DQ, Hing TC, Chen J, Ho S, Zhao D, Targan SR, Pothoulakis C. Substance P induces CCN1 expression via histone deacetylase activity in human colonic epithelial cells. *Am J Pathol* 2011 Nov;179(5):2316-26. Epub 2011 Sep 23. PMID: PMC3204086.
- 15 Barrett R, Zhang X, **Koon HW**, Vu M, Chang JY, Yeager N, Nguyen MA, Michelson KS, Berel D, Pothoulakis C, Targan SR, Shih DQ. Constitutive TL1A Expression under Colitogenic Conditions Modulates the Severity and Location of Gut Mucosal Inflammation and Induces Fibrostenosis. *Am J Pathol* 2011 Dec 1 [Epub ahead of print] PMC – Journal in Process

D. Research Support

Ongoing research support:

Career Development Award Koon (PI) 01/01/2010-12/31/2012

Funding Agency: Crohn's and Colitis Foundation of America, Inc

Title: Role of cathelicidin in intestinal inflammation **Role:** Principal Investigator

The goal of this proposal is to study the pathophysiological mechanism(s) by which cathelicidin in colons modulate the development of colitis.

K-01 DK084256 Koon (PI) 07/01/2010-06/31/2015

Funding Agency: NIH, NIDDK

Title: Role of cathelicidin in intestinal inflammation **Role:** Principal Investigator

The overall goal of this proposal is to study the molecular mechanism(s) by which cathelicidin in colons modulate the development of colitis.

Completed research support:

None