Dr Terry Kwok-Schuelein

Head, Microbial Oncogenesis Laboratory

Monash Biomedicine Discovery Institute
Infection and Immunity Program

OTHER PROGRAM AFFILIATIONS

Cancer

EMAIL terry.kwok@monash.edu

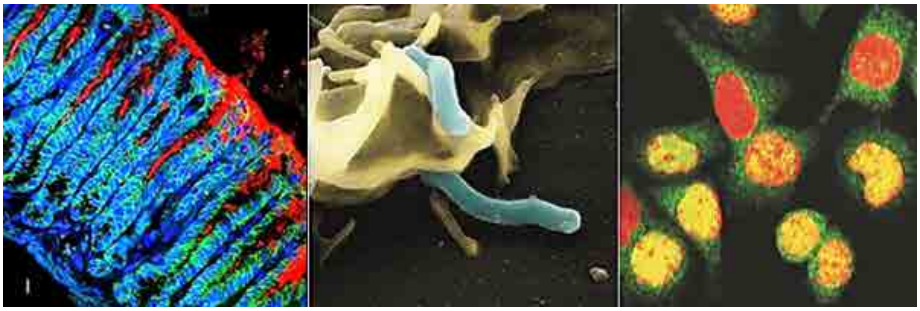
TELEPHONE +61 3 9902 9216

WEB med.monash.edu/biochem/staff/kwok-schuelein.html

Helicobacter pylori (Hp) is a prototype of a cancer-inducing pathogen. This motile rod-shaped Gram negative bacterium colonises persistently in the human stomach, causing chronic gastritis and gastric cancer in susceptible individuals. Virulent *Hp* expresses a Type IV secretion system (T4SS), a major virulence factor which functions as macromolecular machine gun that "shoots" virulence proteins and peptidoglycan molecules into the host cells. Recently, we discovered that a novel adhesin of Hp, CagL, is expressed on the surface of T4SS and is able to dock onto integrin receptors on human gastric epithelial cells, turn on integrins and simultaneously trigger the secretion of other virulence molecules into the stomach cells. Once intracellular, the Hp virulence factors including CagA and peptidoglycan then interact with specific host signalling molecules to trigger activation of host tyrosine kinases, nuclear factor kappa B (NFκB) and/or downstream proinflammatory responses such as the secretion of cytokines. Meanwhile, the vacuolating toxin secreted by Hp dysregulates normal host cell functions, causes severe cytotoxicity and disrupts the gastric epithelium. The molecular basis of how Helicobacter infection progresses into cancers however remains largely a mystery. Our lab is interested in using a multi-disciplinary approach to understand the pathogenesis of *Helicobacter*-associated malignancies.

Research Projects

1. **The molecular mechanisms by which *Helicobacter pylori* causes stomach cancer**



Left: Cross-section of *H. pylori* (red)-infected mouse stomach (blue and green); scale bar = 10 mm Middle: *H. pylori* (blue) interacting with gastric epithelial cells (yellow). Right: Activation of the human transcription factor, nuclear factor kappa B (yellow), in gastric epithelial cells by *H. pylori.*

Selected significant publications:

1. Gorrell RJ, Zwickel N, Reynolds J, Bulach D, **Kwok T**. 2016. Helicobacter pylori CagL hypervariable motif: a global analysis of geographical diversity and association with gastric cancer. *J Infect Dis* pii: jiw060.
2. Deen NS, Gong L, Naderer T, Devenish RJ, **Kwok T**. 2015. Analysis of the relative contribution of phagocytosis, LC3-associated phagocytosis, and canonical autophagy during Helicobacter pylori infection of macrophages. *Helicobacter* 20(6):449-59.
3. Pang SS, Nguyen ST, Perry AJ, Day CJ, Panjikar S, Tiralongo J, Whisstock JC, **Kwok T**. 2014. The three-dimensional structure of the extracellular adhesion domain of the sialic acid-binding adhesin SabA from Helicobacter pylori. *J Biol Chem* 289(10): 6332-40.
4. Gorrell RJ, Guan J, Xin Y, Tafreshi MA, Hutton ML, McGuckin MA, Ferrero RL, **Kwok T**. 2013. A novel NOD1- and CagA-independent pathway of interleukin-8 induction mediated by the Helicobacter pylori type IV secretion system. *Cell Microbiol* (4):554-70.
5. **Kwok T**, Zabler D, Urman S, Rohde M, Hartig R, Wessler S, Misselwitz R, Berger J, Sewald N, König W, Backert S. 2007. Helicobacter exploits integrin for type IV secretion and kinase activation. *Nature* 449(7164): 862-6.