

Microbiology: On the trail of bacterial saboteurs

Published online 29 September 2010

A previously unidentified bacterial protein variant gums up the gears of a lastresort cellular suicide mechanism

Pathogenic bacteria that successfully penetrate the interior of a cell find themselves living on borrowed time before the infected cell self-destructs via the programmed cell death mechanism known as apoptosis. However, certain pathogens are able to protect themselves by producing cell death-delaying factors that target the mitochondria, key metabolic organelles within the cell that also represent 'ground zero' for the onset of apoptosis.

The identity of these anti-apoptotic molecules has remained a mystery, but new research from a team led by A*STAR Institute of Molecular and Cell Biology and National University of Singapore researcher Victor Yu has now uncovered a surprising culprit¹. After screening soluble proteins produced by *Escherichia coli* K1, a

pathogen responsible for neonatal sepsis and meningitis, postdoctoral fellow Sunil Sukumaran identified the protein FimA as the most likely candidate apoptotic inhibitor. "FimA is known to be a component of the bacterial pili, which is a structure useful for



Fig. 1: Shortly after infecting a cell, the pathogenic bacterium, *E. Coli* K1 (blue), releases a soluble variant of the FimA protein, which binds to mitochondrial surfaces (red) and thereby blocks the onset of cell death.

© 2010 V. Yu

adhesion to host cells and other substrates," explains Yu. "Hence, FimA was not known to be a soluble protein."

Nevertheless, the researchers observed clear evidence of FimA localization at host cell mitochondria within an hour of infection (Fig. 1); similar findings were also observed with other disease-causing, FimA-expressing bacteria such as *Salmonella* or *Shigella*. FimA was largely no longer associated with mitochondria by 12 to 14 hours post-infection, which is when infected cells normally begin to undergo apoptosis.

Bacterial FimA appears to exert its anti-apoptotic effects by binding to the mitochondrial voltage-dependent ion channel-1 (VDAC1) and subsequently stabilizing its interaction with the hexokinase (HK) protein. "Many cancer researchers already have data suggesting that the VDAC–HK complex plays an important role in turning off the suicide program in cancer cells," says Yu. "This work may therefore offer new insights into the role of these pathogens in promoting cancer of the gut, such as stomach and colon cancers."

Although Yu and his co-workers examined only a handful of bacteria species in this study, FimA is ubiquitously expressed among many other pathogenic bacteria residing within the human gut. Yu suggests that at least some of these are likely to employ a similar mechanism, and hopes to more closely characterize the production and activity of soluble FimA in future animal studies. "It would also be very useful if we could find small molecular-weight compounds for probing the mechanism of action of FimA–VDAC–HK, and explore their potential as drug candidates for treating cancers and infectious diseases caused by pathogenic bacteria in the human gut."

Recent Highlights

- Crystal engineering: Composition of functions
- Applied physics: A headto-head comparison
- Biochemistry: Out of the loop
- Microbiology: On the trail of bacterial saboteurs

Archive

Resources
Recommend Article
Share
崔 Follow Us On Twitter
S RSS

Oui	ick	Lin	ks
20		_	1.5

- select -

Jobs

Research Fellow Modulation & Coding, Institute for Infocomm Research, A*STAR, Singapore,

Senior Project Team Leader Experimental Therapeutics Centre (ETC) A*STAR

Centre (ETC), A*STAR, Singapore

Senior / Research Engineer

Materials Analysis & Characterization, Institute of Materials Research and Engineering (IMRE), A*STAR, Singapore

Research Fellow/Senior Research Fellow Artificial Cognitive Memory, Data Storage Institute (DSI), The A*STAR-affiliated researchers contributing to this research are from the Institute of Molecular and Cell Biology and the Institute of Medical Biology

Reference

 Sukumaran, S.K., Fu, N.Y., Tin, C.B., Wan, K.F., Lee, S.S. & Yu, V.C. A soluble form of the pilus protein FimA targets the VDAC-hexokinase complex at mitochondria to suppress host cell apoptosis. *Molecular Cell* 37, 768–783 (2010). | article A*STAR, Singapore

More Jobs **•**

Events

- 27th HUGO-IABCR Congress 2010: Genomics, Biology and Breast Cancer Treatment, 5th-7th October, Biopolis, Singapore
- 'Decade Of The Mind VI' Conference, Cognitive Science & Neurotechnologies, 18th-20th October 2010, Fusionopolis, Singapore
- ISSB: International Symposium on Synthetic Biology, 18th-19th October 2010, Singapore
- 4th International Singapore Symposium for Immunology, 17th-18th January 2011, Biopolis, Singapore

More Events



Agency for Science, Technology and Research

Track <u>A*STAR</u> on the nature asia-pacific PUBLISHING INDEX

SINGA Singapore International Graduate Award Apply now!

Related Information

Tag Clouds

A*STAR Research EISSN 2010-0523	
Terms & Conditions Privacy Statement Sitemap	© 2010 Agency for Science, Technology and Research