Institute of Molecular and Cell Biology
A*STAR

PRESS RELEASE
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SINGAPORE SCIENTISTS THE FIRST TO UNCOVER KEY PROTEIN THAT CAN POTENTIALLY CAUSE THE DEATH OF CANCER CELLS

1. Researchers from A*STAR's Institute of Molecular and Cell Biology (IMCB) have become the first to discover and characterize a human protein called Bax-beta (Bax*β*), which can potentially cause the death of cancer cells and lead to new approaches in cancer treatment. The finding is published in the 16 January report of the esteemed science journal, *Molecular Cell*.

2. Detection of Bax*β* has eluded scientists until now. Said Dr Victor Yu, the Principal Investigator of the research team at IMCB, "Our research findings reveal that Bax*β* protein levels are normally kept at essentially undetectable levels in healthy cells by the protein degradation machine in cells known as the "proteasomes"[1]. The proteasomes are there to keep the lethal Bax*β* in check. This is exciting — if the proteasome-mediated degradation of Bax*β* could be inhibited specifically in cancer cells, it could cause the harmful cancer cells to go through apoptosis[2]".

3. Until the discovery of Bax*β* by Dr Yu's team, only one single protein called Bax-alpha (Baxα) has ever been extensively studied in cells[3]. The researchers also

[1] Proteasome: A "protein-digesting machine" that regulates cellular levels of various proteins including that of the lethal Bax*β*, by breaking them into smaller components within the cell.
[2] Apoptosis: An important physiological process by which unwanted, damaged and infected cells are eliminated from multi-cellular organisms through a series of highly regulated cellular events resulting in the safe destruction of the target cells.
[3] Earlier evidence had suggested that more than one protein was encoded by the *Bax* gene. However, only a single protein called Bax*α* had ever been detected and extensively studied in cells. *Bax* is known to be a key gene needed for the execution step of an important physiological process called apoptosis, or programmed cell death.

found that Bax*β* is able to associate with, and promote, Bax*α* activation, and that Bax*β,* in its native form, is 100 times more potent than its sibling Bax*α* in triggering a key step in apoptosis. The future development of novel compounds that can selectively elevate levels of Bax*β* or stimulate its interaction with Bax*α* could also lead to new drug approaches to cancer treatment, as these compounds are likely to enhance the apoptotic signals triggered by many conventional cancer drugs, which frequently cause toxic side effects in patients when higher doses of drugs are needed.

4. David Andrews, Professor of Biochemistry and Biomedical Sciences at McMaster University, Canada added, "The beta-isoform[4] of Bax has been enigmatic for several years. Although earlier research had hinted at its existence, the protein has proven extremely difficult to detect or examine functionally. Even attempts to produce the protein in the laboratory have been largely unsuccessful. In this study the Yu group resolves these issues by demonstrating that in cells Bax*β* is normally rapidly degraded and kept at low levels, and when it is not degraded, it is profoundly apoptotic on its own and works in concert with Bax*α*. These studies provide information necessary for the elucidation of the importance of Bax*β* in cell physiology."

AGENCY FOR SCIENCE, TECHNOLOGY AND RESEARCH

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[4] Isoform: An alternative form of a protein that may differ in characteristics such as its functions and/or distribution.

Notes to the Editor:

The research findings described in the press release can be found in the article "Bax*β*: A Constitutively Active Human Bax Isoform that Is under Tight Regulatory Control by the Proteasomal Degradation Mechanism", in the January 16, 2009 print issue of ***Molecular Cell***.

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About the Institute of Molecular and Cell Biology (IMCB)

The Institute of Molecular and Cell Biology (IMCB) is a member of Singapore's Agency for Science, Technology and Research (A*STAR) and is funded through A*STAR's Biomedical Research Council (BMRC). It is a world-class research institute that focuses its activities on six major fields: Cell Biology, Developmental Biology, Structural Biology, Infectious Diseases, Cancer Biology and Translational Research, with core strengths in cell cycling, cell signalling, cell death, cell motility and protein trafficking. Its recent achievements include leading an international consortium that successfully sequenced the entire pufferfish (Fugu) genome. The IMCB was awarded the Nikkei Prize 2000 for Technological Innovation in recognition of its growth into a leading international research centre and its collaboration with industry and research institutes worldwide. Established in 1987, the Institute currently has 35 independent research groups with more than 400 staff members.

For more information about IMCB, please visit www.imcb.a-star.edu.sg.

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