

PRESS RELEASE

Scientists at TLL Identify an Important Mechanism That Terminates Protein Folding Failures

11 June 2013, Singapore – Scientists at Temasek Life Sciences Laboratory (TLL) have identified an important mechanism that neutralizes the detrimental effects of unfolded proteins by removing the potentially harmful proteins from the system. This discovery may provide a new avenue of therapeutic intervention and is applicable to a diverse range of diseases.

A team led by Associate Professor Davis Ng, Temasek Senior Investigator at TLL, has discovered a cellular mechanism dedicated to terminating protein folding failures. This remarkable mechanism works by modifying unfolded proteins with hydrophilic (water-loving) molecule thus disables folding and at the same time, prevents aggregation which is a process that causes unfolded proteins to accumulate and become toxic. Basically, proteins that took longer time to fold are tagged in a way that is able to stop their failed attempts and be removed from the cell's folding compartment. These findings have been published in the May issue of the prestigious *Science* journal.

Proteins are the basic building blocks of life and they carry out thousands of functions in all living organisms. One of the most fundamental activities of a cell is the correct and orderly folding of proteins during synthesis. In recent years, it has been revealed that protein folding failures are the underlying cause of many common and devastating human diseases such as Alzheimer's, Huntington's, and Parkinson's diseases, as well as cancer, childhood emphysema, and cystic fibrosis. Unfortunately, the understanding of those mechanisms that promote protein folding and how they maintain quality control is inadequate and has impeded potential therapeutic development.



The termination mechanism for protein folding was previously not known. In most models of chaperone-mediated protein folding, the concept of termination was conceived but there was no evidence for it. Davis's team is one of the first to discover such mechanism. The protein folding and quality control mechanisms that his team focuses are functionally and genetically conserved from yeast to humans. This discovery unravels the basic mechanism that affects many proteins in the cell which may be a target for multiple diseases and has many consequences for human health.

"A termination mechanism for protein folding failures was widely envisioned but has eluded researchers for decades. It was an interesting problem for us because while protein folding is one of the most fundamental processes of life, better understanding it has important medical implications," said Davis. "Conformational protein diseases affect tens of millions worldwide every year. We hope that this research can contribute to effective therapeutic interventions."

Davis received his postdoctoral training at the University of California, San Francisco. In 1998, he established his independent research group at the Pennsylvania State University focusing on protein biosynthesis. He continues to pursue his research interest after joining TLL in 2005 and focuses on the quality control mechanisms of protein folding. Davis is the editor and member of several international editorial boards and has trained more than 10 graduate students; one of them is Mr Xu Chengchao, a graduate student and Ph.D. candidate of NUS, who has contributed significantly to this discovery.

Professor Chan Soh Ha, Executive Director of TLL, says, "In TLL, our vision is to build a preeminent organization of global talent to undertake bio-molecular science research and applications to benefit people in Asia and beyond. Davis's work describes a novel and important mechanism that is related to the underlying cause of diseases and has the potential to create positive impact to improve lives. I would like to congratulate Davis and his team for their publication in the highly regarded international journal *Science* and look forward to future developments from this research."



About Temasek Life Sciences Laboratory (TLL)

TLL, established in 2002, is a beneficiary of Temasek Trust and is affiliated to the National University of Singapore and Nanyang Technological University. The research institute focuses primarily on understanding the cellular mechanisms that underlie the development and physiology of plants, fungi and animals. Such research provides new understanding of how organisms function, and also provides foundation for biotechnology innovation.

For more information, please visit <u>www.tll.org.sg</u>.

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