

PRESS RELEASE

TLL Scientists Discover New Fundamental Class of Proteins Named "Guardian"

1 November 2017, Singapore – Scientists at Temasek Life Sciences Laboratory (TLL) have discovered the founding member of a new class of proteins that functions to protect newly translated and actively folding polypeptides from degradation. The research is led by Temasek Senior Investigator A/Prof Davis Ng and the team has named this new class of proteins as "Guardian". This novel finding has been recently published as a research article in the prestigious peer-reviewed scientific journal *Cell*.

As the basic building blocks of life, proteins have different functional roles in every living organisms. Newly synthesized proteins undergo a folding process which is dynamic and error prone before reaching their final conformations. Protein misfolding is the underlying cause of many human diseases such as Alzheimer's, Huntington's, and cystic fibrosis. Understanding the folding and quality control processes of protein synthesis is critical to developing therapies. The discovery of the guardian proteins by A/Prof Davis Ng and his team would build up our knowledge of defense mechanism which could help protect newly made proteins from any premature degradation and prevent diseases from occurring.

In this paper, A/Prof Davis Ng's team reported the discovery of a new class of proteins which they named "Guardian" that directly connect protein folding and quality control processes. The conserved membrane protein complex, consisting of Slp1 and Emp65 proteins, binds unfolded proteins and protects these immature proteins from cellular



degradation machinery. The newly-made polypeptides are initially unfolded and it was earlier not known how they are not subject to degradation. Without the guardian factor, newly made polypeptides are targeted for degradation inappropriately. The SIp-Emp65 complex guardian factor is found in all nucleated organism from single-cellular microbes to human. In the animals, this guardian factor is in every cell, emphasizing its fundamental function to life.

Over the years, much effort has been devoted to the world-wide research on protein homeostasis, particularly for the purpose of pharmaceutical drug development. Proteins are involved in every function of the living organism and the mechanisms which govern the production, logistics and elimination of the proteins are central to life. Collectively, these mechanisms comprise the protein homeostasis pathway of the cell, one of the most actively researched areas in medicine. Essentially, the proteins need to be translated correctly in order for the cellular mechanism to function normally. When such functions are compromised, diseases can occur and some examples of commonly known human associated diseases include cancer, Alzheimer's, Huntington's and emphysema. This discovery provides insight to the understanding of protein homeostasis for potential therapeutic intervention for these diseases.

"For my field, my team's discovery is important to understand protein folding and its quality control. As a scientist, the added excitement is to discover a new fundamental class of proteins. It's just like when the first transcription factor, kinase, DNA polymerase, or chaperone was discovered. Guardians are common building block of life that are needed to produce all the other building blocks." says A/Prof Davis Ng, Temasek Senior Investigator of TLL.



"At TLL, basic research forms the building block for innovation. I would like to congratulate Davis and his team on the publication of this work and look forward to successful translation of this discovery into areas that would bring about societal benefits and help improve lives.", said Peter Chia, Chief Executive Officer and Board Director of TLL.

Citation

Zhang et al., Slp1-Emp65: A Guardian Factor that Protects Folding Polypeptides from Promiscuous Degradation, *Cell* (2017) http://dx.doi.org/10.1016/j.cell.2017.08.036

About Temasek Life Sciences Laboratory (TLL)

TLL, established in 2002, is a beneficiary of the Temasek Trust and 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 www.tll.org.sg.

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