PRESS RELEASE

Scientists Discover Mechanical Control of Embryonic Polarization

3 August 2017, Singapore – Temasek Life Sciences Laboratory (TLL) is pleased to announce the discovery of a key protein's function that plays an important role in the establishment of embryonic cell polarity which defines asymmetry within an embryo and the subsequent formation of somatic or germline cells. This research is conducted in collaboration with scientists from the Mechanobiology Institute (MBI) and the Institute of Molecular and Cell Biology (IMCB) in Singapore, that provides insights to the regulation of tumorigenesis as well as development of new medical interventions for human diseases.

Using *Caenorhabditis elegans* (*C. elegans*) as a model organism, a team led by Dr Fumio Motegi, Principal Investigator at TLL and a National Research Foundation Fellowship Award recipient (Class of 2012), have found the role of a key protein, PAR-3, in integrating mechanical and biochemical signals essential for the establishment of embryonic polarity. These findings have been published as a research article in the prestigious international journal *Nature Cell Biology* [doi: 10.1038/ncb3577].

The complex journey from one-celled embryo to an adult begins with the establishment of geometric asymmetry within an embryo. Embryonic asymmetry is used to make early critical decisions that determine whether cells will become somatic cell or germline cells. The ability of an embryo to define the asymmetry relies on inhomogeneous physical

properties of cellular materials, such as cytoskeletal elements and membranes. The mechanisms pertaining to how embryos sense the physical cues and translate the geometrical information to cellular fate were previously poorly understood.

The team has demonstrated that an evolutionally conserved protein, PAR-3, is responsible for mechano-transduction in newly fertilized embryos during the development of the nematode *C. elegans*. Mechano-transduction is a process by which a cell senses and responds to mechanical stimuli by converting them to biochemical signals that elicit specific cellular responses. The study showed that during *C. elegans*' embryonic polarization, cytoskeleton contractility and cortical tension stimulate clustering PAR-3 at the cortex. The cortical clustering of PAR-3 acts as a scaffold that mediates chemical signaling cascades for downstream cell fate determination.

Recent studies have identified PAR-3 as an important regulator in tumorigenesis and metastasis as this protein plays a role in tumor suppressor in breast and skin tumorigenesis. As a consequence, these tumor cells are likely to have defects in cellular polarity and mechano-transduction.

According to Dr Motegi, the discovery of PAR-3 as a new mechano-transducer is a significant step forward in the development of new molecular probes with which cellular mechanical forces can be visualized in living cells and tissues. Such tools may be used for the development of new diagnostic tools for a range of human diseases associated with alterations in mechanical properties of cells.

Peter Chia, TLL Chief Executive Officer, says, "Cross institutional collaboration is an important avenue for us in extending our research capacities to achieve impactful research outcomes and breed innovative ideas. This collaborative research between TLL,

NUS and A*Star in understanding the mechanisms that underlie mechanically-inducible protein clustering can be broadly applied to other pattern-forming systems in other eukaryotic cells. I congratulate Dr Motegi and the team for this significant finding and look forward to future developments from this research."

Citation

Wang S.C. et al., Cortical forces and CDC-42 control clustering of PAR proteins for *Caenorhabditis elegans* embryonic polarization. *Nature Cell Biology* (2017), http://dx.doi.org/10.1038/ncb3577

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.

About Mechanobiology Institute (MBI)

Instituted in 2009, the Mechanobiology Institute was created through joint funding by the National Research Foundation and the Ministry of Education with the goal of creating a new research centre in mechanobiology to benefit both the discipline and Singapore. MBI's primary focus is to identify, measure and describe how the forces for motility and morphogenesis are expressed at the molecular, cellular and tissue level.

For more information, please visit http://mbi.nus.edu.sg/

About Institute of Molecular and Cell Biology (IMCB)

Institute of Molecular and Cell Biology (IMCB) was launched on 23 January 1985, with the official opening ceremony held on 2 October 1987 at the National University of Singapore (NUS), to develop and support the biomedical R&D capabilities in Singapore. It subsequently became an autonomous research institute (RI) of the Agency for Science, Technology and Research (A*STAR), moving to Biopolis in 2004. For more information, please visit http://www.imcb.a-star.edu.sg/php/main.php

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