

Landmark discovery of 'engine' that drives cell movement

October 6 2008

This research by Thomas Leung, Ph.D., and his team in the GSK-IMCB Group at the Institute of Molecular and Cell Biology (IMCB), under Singapore's Agency for Science, Technology and Research, is fundamental to the understanding of how assembles its internal machinery required for cell movement.

The findings have widespread implications in the fields of cancer growth and spread, wound- healing, learning and memory, and developmental biology.

The researchers discovered a complex of three proteins that directly regulates the myosin network within a cell, thus generating traction force to propel the cell forward. (Myosin is the most common protein found in muscle cells, and is responsible for the elastic and contractile properties of muscle. A different form of myosin is involved in cell movement.)

This action of the tripartite protein complex may be likened to a spring in a toy motorcar – when the protein complex assembles and moves backwards within the cell, it resembles the wound up "engine" of the toy car that has been pulled backwards.

Subsequent disassembling of the protein complex and the resultant forward movement of the cell can be likened to the released spring which unleashes the earlier stored potential energy to propel the car forward.

Michael Sheetz, Ph.D., who is William R Kenan Jr Professor of Cell Biology at the Department of Biological Sciences, Columbia University, and also Distinguished Visiting Professor at the National University of Singapore, said, "This is an exciting paper because Leung's group has discovered an unexpected step in cell migration and contractility — a complex of three proteins including a form of myosin, that is responsible for assembling most of the other myosin components involved in motile processes. The assembly mechanism has been a major mystery and is critical in a variety of diseases from cardiovascular to aging. Now we have a new tool to understand the bases of these critical processes."

Of the three proteins MRCK, LRAP35a and MYO18A, MRCK was discovered by the GSK-IMCB group 10 years ago, while the other two had hitherto unknown functions. Dr. Leung of IMCB said, "The success of the work relies on the commitment and perseverance of the team. A major contributor, Dr. Ivan Tan, is a home-grown scientist who has been working on this project for many years and he has had several clues as to how the system functions for some time, but it was only recently that the jigsaw puzzle was put together. The system has the potential to unravel other as yet undiscovered mechanisms that coordinate the different 'engines' for proper cell migration."

The research by the GSK-IMCB Group is supported by the GlaxoSmithKline (Singapore) Research Fund that was set up in 1989. Louis Lim, Ph.D., head of the GSK-IMCB Group, said, "The 2008 Cell paper represents the culmination of many years of industry and dedication on the part of Dr. Thomas Leung and Dr. Ivan Tan. Dr. Leung has been responsible for defining the role of other signalling enzymes along with other members of the GSK-IMCB Group, and we are very glad to acknowledge the support of the GSK Singapore Research Fund throughout these years."

Source: Agency for Science, Technology and Research (A*STAR),

Singapore

Citation: Landmark discovery of 'engine' that drives cell movement (2008, October 6) retrieved 19 April 2024 from <https://phys.org/news/2008-10-landmark-discovery-cell-movement.html>

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