Press Release

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New study reveals the protein that makes phosphate chains in yeast

Phosphate chains store energy and have many more different functions in a cell

Heidelberg, 24 April 2009 – It can be found in all life forms, and serves a multitude of purposes, from energy storage to stress response to bone calcification. This molecular jack-of-all trades is polyphosphate, a long chain of phosphate molecules. Researchers at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, are now the first to uncover how this chain is assembled in eukaryotes (organisms whose cells have a nucleus). The study, published this week in *Science*, uncovers the function of a single protein with a wide range of potential implications ranging from improving crops to fighting diseases such as sleeping sickness.

Scientists have known for a long time how bacteria make phosphate chains, but how the same process works in eukaryotes has so far remained elusive. EMBL scientists now show that in yeast a protein called Vtc4p is responsible for the production of polyphosphates. Vtc4p is part of a protein complex called vacuolar transporter chaperone complex (VTC) that is usually found in the membranes of vacuoles – pouches in which cells store molecules for later use, transport or destruction.

"This protein is like a factory," says Klaus Scheffzek, whose group carried out the research at EMBL in collaboration with the Département de Biochimie at the Université de Lausanne, Switzerland, and others, "it sits in the vacuolar membrane, generates long chains of polyphosphates and we speculate that it sends them straight to the vacuole for storage."

Vtc4p is partly embedded in the membrane and has a 'tail' hanging into the cell, which removes a phosphate molecule from ATP, an important energy carrier in the cell. Vtc4p uses the energy that is released by that cleavage to add the newly-acquired phosphate to a growing chain of phosphates. Since the rest of Vtc4 straddles the membrane, scientists suspect this protein probably transfers the polyphosphate chain to the vacuole as it produces it.

The researchers determined Vtc4p's function by looking at its 3D structure.

"This study emphasises the importance of structural biology not just to show what molecules look like and how they work but also what that function is," says Michael Hothorn from Scheffzek's group at EMBL, who is presently at The Salk Institute for Biological Studies in California.

Since polyphosphate is a ubiquitous, multi-tasking molecule with many different functions, discovering how it is produced could have implications for many different fields. Although Vtc4p is not present in plants, the discovery could have implications for agriculture, for instance in the production of fertilizers and high-yield crops. Polyphosphate is important for plant growth, and the scientists suspect Vtc4p could play an important role in making it available to plants that have fungi living in their roots. Because the VTC can move from the membrane of the vacuole to that of the cell, it could assemble phosphate chains and transfer them to outside the fungus cell, where they would be available to the plant.

The research could also pave the way for new treatments for diseases such as sleeping sickness and Chagas disease, as the parasites that cause them need polyphosphate chains to survive. ●

Source Article

Hothorn, M., Neumann, H., Lenherr, E.D., Wehner, M., Rybin, V., Hassa, P.O., Uttenweiler, A., Reinhardt, M., Schmidt, A., Seiler, J., Ladurner, A.G., Herrmann, C., Scheffzek, K. & Mayer, A. Catalytic core of a membrane-associated eukaryotic polyphosphate polymerase. *Science*, 24 April 2009

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About EMBL

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