Breakthrough: With a chaperone, copper breaks through

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(PhysOrg.com) -- Information on proteins is critical for understanding how cells function in health and disease. But while regular proteins are easy to extract and study, it is far more difficult to gather information about membrane proteins, which are responsible for exchanging elements essential to our health, like copper, between a cell and its surrounding tissues.

Now Prof. Nir Ben-Tal and his graduate students Maya Schushan and Yariv Barkan of Tel Aviv University's Department of Biochemistry and Molecular Biology have investigated how a type of membrane protein transfers essential copper ions throughout the body. This mechanism,

Schushan says, could also be responsible for how the body absorbs Cisplatin, a common chemotherapy drug used to fight cancer. In the future, this new knowledge may allow scientists to improve the way the drug is transferred throughout the body, she continues.

Their breakthrough discovery was detailed in a recent issue of the Proceedings of the National Academy of Sciences.

Cellular gatekeepers and chaperones

Most proteins are water soluble, which allows for easy treatment and study. But membrane proteins reside in the greasy membrane that surrounds a cell. If researchers attempt to study them with normal technology of solubilization in water, they are destroyed — and can't be studied.

Copper, which is absorbed into the body through a membrane protein, is necessary to the healthy functioning of the human body. A deficiency can give rise to disease, while loss of regulation is toxic. Therefore, the cell handles copper ions with special care. One chaperone molecule delivers the copper ion to an "entrance gate" outside the cell; another chaperone then picks it up and carries it to various destinations inside the cell.

The researchers suggest that this delicate system is maintained by passing one copper ion at a time by the copper transporter, allowing for maximum control of the copper ions. "This way, there is no risk of bringing several copper ions into the protein at the same time, which ultimately prevents harmful chemical reactions between the ions and the abundant chemical reagents within the cell," explains Prof. Ben-Tal. Once the ion has passed through the transporter into the cell, the transporter is ready to receive another copper ion if necessary.

Improving cancer drugs — and more

The mechanism which transfers copper throughout the body may also be responsible for the transfer of the common chemotherapy drug Cisplatin . By studying how copper is transferred throughout the body, researchers may also gain a better understanding of how this medication and others are transferred into the cell.

With this information, says Prof. Ben-Tal, scientists could improve the transfer of the drug throughout the body, or develop a more effective chemotherapy drug. And that's not the only pharmaceutical dependent on the functioning of membrane proteins. "Sixty percent of drugs target membrane proteins," he explains, "so it's critical to learn how they function."

Provided by Tel Aviv University

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