NEW HOT PAPERS - 2009

November 2009

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Amy L. Davidson talks with *ScienceWatch.com* and answers a few questions about this month's New Hot Paper in the field of Microbiology. The author has also sent along images of their work.

Article Title: Structure, function, and evolution of bacterial ATP-binding cassette systems
Authors: Davidson, AL;Dassa, E;Orelle, C;Chen, J
Journal: MICROBIOL MOL BIOL REV, Volume: 72, Issue: 2, Page: 317-364, Year: JUN 2008
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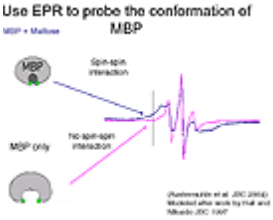
SW: Why do you think your paper is highly cited? Does it describe a new discovery, methodology, or synthesis of knowledge?

Our team of authors put a lot of time and effort into compiling as complete a review of ATP-binding cassette (ABC) transporters in bacteria as we could, and combined that with an up-to-date discussion of progress in understanding of the structure and mechanism of ABC transporters. It's definitely a synthesis of knowledge.

SW: Would you summarize the significance of your paper in layman's terms?

ABC transporters use the energy generated from ATP hydrolysis to transport solutes across the membrane. In bacteria, these proteins are critical for survival, since they function in the uptake of nutrient and in the secretion of toxins and antimicrobial agents. In humans, several genetic defects in these proteins are implicated in more than a dozen disease states involving transport deficiencies including cystic fibrosis, hyperinsulinemia, and macular degeneration.

Broad-based multidrug resistance, as seen in a variety of human cancers can also be traced to ABC transporters that function as nonspecific efflux pumps. Furthermore, the expression of ABC transporters at the blood-brain barrier has been shown to limit the penetration of drugs and other agents into the brain. By deciphering the mechanism of action of a diverse set of ABC transporters, such as those present in bacteria, we may discover new ways to inhibit microbial growth and improve the drug delivery process.



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SW: How did you become involved in this research, and were there any problems along the way?

I started work on the maltose transport system as a postdoctoral fellow at the University of California, Berkeley, with the goal of reconstituting transport activity *in vitro*, in artificial membrane vesicles. Reconstitution requires the functional overexpression of these membrane proteins, which is often a challenge, but, once successful, it really opens up the door to biochemical, biophysical, and structural analysis.

I was fortunate to be able to team up with two outstanding crystallographers, Dr. Jue Chen, and Dr. Florante Quiocho, who worked very hard for many years to solve the structure of this transporter.

SW: Where do you see your research leading in the future?

We hope to understand how different types of substrates are moved across the membrane by ABC transporters now that we have an understanding of how small nutrients are brought into the cell. Devising mechanisms for inhibition of ABC transporters is an important goal if we are to translate this basic research problem into a clinically important discovery.

SW: Do you foresee any social or political implications for your research?

Any ways that we can devise to inhibit ABC transport function has the potential to help the human condition, either by decreasing bacterial virulence or improving drug delivery to cells.

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KEYWORDS: GRAM-NEGATIVE BACTERIA; MULTIDRUG EFFLUX PUMP; MALTOSE TRANSPORT-SYSTEM; PROTEIN-DEPENDENT TRANSPORT; OUTER-MEMBRANE-PROTEIN; ENTERICA SEROVAR TYPHIMURIUM; RESISTANCE P-GLYCOPROTEIN; X-RAY-STRUCTURE; ELECTRON-PARAMAGNETIC-RESONANCE; ARCHAEON THERMOCOCCUS-LITORALIS.

PDF

back to top

2009 : November 2009 - New Hot Papers : Amy L. Davidson on ATP-binding Cassette Systems

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