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[Bio-Medical Tech] Academia Sinica Disclose Membrane Protein Structure; the Results May Aid in Development of Antibiotics

[Bio-Medical Tech] Academia Sinica Disclose Membrane Protein Structure; the Results May Aid in Development of Antibiotics (Chinese Version)

Academia Sinica Newsletter (2009/05/21) reported, this week, Assistant Research Fellow, Che Alex MA and colleagues at the Academia Sinica Genomics Research Center, Academia Sinica, published a complete 3-dimensional model structure of the membrane protein (penicillin-binding protein 1b; PBP1b) that resides on the surface of the bacteria Escherichia coli in the online Proceedings of the National Academy of Sciences. This is the first time that a mechanism that holds the key to bacterial cell wall formation has been disclosed in detail and could lead to the development of a new class of antibiotics.

Antibiotics are effective because they block certain key enzymes that help bacteria construct their cell walls as they divide and multiply. Dr. MA started his research five years ago, as part of project to solve the mystery of bacterial cell wall synthesis. Initially, Dr. MA and his group studied the activity of PBPs and published their work in early 2008 (PNAS 2008, 105, 431-436).

Their next task was to discover exactly how PBP1b conducts the task of making bacterial cell walls. For their latest report, the research team coaxed this purified membrane protein into crystals and used x-ray crystallography to obtain its 3-dimensional structure, and proposed a model giving a clear picture of how PBP1b binds a substance called lipid II, performing a kind of a knitting job to finally make a new skin when the bacteria divides.

Their work also revealed the interaction between moenomycin and PBP1b. Moenomycin is an attractive target in the search of new antibiotics that function by inactivating transglycosylases. Furthermore, the team identified one particular area within the structure named "the UB2H domain" that they propose to be a key player in coordinating the cell wall formation and DNA synthesis/repair.

This research is part of a campaign to solve the drug resistance bacterial infection issue, led by President of Academia Sinica Dr. Chi-Huey WONG, as well. Dr. WONG, along with Dr. MA, is also a lead corresponding author of the publication.

This is the first membrane protein structure that has ever been determined in Taiwan. Membrane proteins, which make up over 30% of all proteins, play critical roles in different biological processes and represent more than 50% of current drug targets. Of nearly 60,000 structures of biological macromolecules available in the Protein Data Bank now, less than 1% are membrane proteins.

The publication entitled "Crystal structure of the membrane-bound bifunctional transglycosylase PBP1b from Escherichia coli," Proc. Nat. Acad. Sci. U.S.A., (2009) can be found at the PNAS website :
http://www.pnas.org/content/early/2009/05/19/0904030106.abstract
The complete list of authors is: M.-T. Sung, Y.-T. Lai, C.-Y. Huang, L.-Y. Chou, H.-W. Shih, W.-C. Cheng, C.-H. Wong and C. Ma.

Media Contacts:
Dr. Che Alex MA, Assistant Research Fellow, Genomics Research Center, Academia Sinica
(Tel) +886-2-2787-1233
Ms. Mei-Hui LIN, Public Relations Office, Central Office of Administration, Academia Sinica
mhlin313@gate.sinica.edu.tw (Tel) +886-2-2789-8821, (Fax) +886-2-2782-1551, (M) 0921-845-234

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