Scientists discover essential biochemical process driven by alternative cellular fuel

Discovery opens window for development of novel classes of antibiotics

An international team of scientists have discovered a novel biochemical process that is based on an alternative energy carrier. This discovery improves the understanding of bacterial cell physiology - and creates opportunities in the search for novel antibiotics.

The blueprint to build a living cell is encoded within the DNA on chromosomes. The DNA in - for example - a human cell measures two meters, so chromosomes need to be tied up and organized in a way that allows instructions contained in the DNA to be read. The precise solutions to the problem may vary between organisms, but the fundamental challenge is shared between bacteria and higher organisms including humans.

While working to understand the basic nature of chromosome organization, an international team of scientists spearheaded by a group at the Department of Fundamental Microbiology at the University of Lausanne together with colleagues at the Research Institute of Molecular Pathology (IMP) in Vienna discovered a novel enzymatic activity of a protein called ParB, which could have far-reaching implications beyond their field.

ParB proteins are key players involved in the organization of bacterial DNA. They are present on chromosomes as well as on small mobile DNA elements, which are used to share genetic information between cells. This phenomenon contributes to the problematic spreading of antibiotic resistances. On the bacterial chromosome itself, ParB proteins serve as major regulators of large-scale DNA organization. Although being involved in critical cellular processes, their mode of action has yet to be fully understood. The breakthrough discovery now reported in the journal "Science" shows that a key mechanism of the ParB family proteins is the use of an alternative energy currency within the cell, cytidine triphosphate (CTP).

While the related molecules ATP, GTP and UTP are commonly used as building blocks in the cell together with CTP, only ATP and GTP have thus far been described as major energy carriers. This surprising discovery marks the first instance in which an enzyme uses CTP as source of energy.

The discovery of the utilization of an alternative energy carrier is the first of its kind since the identification of the regulatory GTPases several decades ago, which laid the foundations of a completely novel field of pharmaceutical research. The new finding therefore could have similarly far-reaching implications.

The work shows a core-function of a major DNA organizer that has gone unnoticed for decades. ParB being a critical protein in several bacteria of major concern for global health, such as Pseudomonads, this discovery might be the first step in identifying an antibiotic drug target. It is likely that the use of the alternative cellular energy carrier CTP is not limited to bacteria, but might play a significant role in the regulation of a variety of fundamental cellular processes - possibly even in humans.

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Original Publication

Y.M. Soh, I.F. Davidson, S. Zamuner, J. Basquin, F.P. Bock, M. Taschner, J-W Veening, P. De Los Rios, J-M Peters, S. Gruber, Self-Organization of parS Centromeres by the ParB CTP Hydrolase, Science.

About the DMF of UNIL

The Department of Fundamental Microbiology (DMF) of the University of Lausanne consists of 13 groups that study a broad range of topics from the microbiome of the bee gut to the biochemistry behind protein function. UNIL is located near École polytechnique fédérale de Lausanne, the close proximity promotes collaborative research between the two universities. The DMF is also active in working together with the Lausanne University Hospital (CHUV) combining basic science with research topics that are also interesting for the medical community.

About the IMP at the Vienna BioCenter

The Research Institute of Molecular Pathology (IMP) in Vienna is a basic biomedical research institute largely sponsored by Boehringer Ingelheim. With over 200 scientists from 40 countries, the IMP is committed to scientific discovery of fundamental molecular and cellular mechanisms underlying complex biological phenomena. The IMP is located at the Vienna BioCenter, one of Europe’s most dynamic life science hubs with 1,800 employees from 70 countries in four research institutes, three universities and two dozen biotech companies.