

A Review of the Book *Aerobnye metilobakterii* (Aerobic Methylobacteria) by Yu.A. Trotsenko, N.V. Doronina, and M.L. Torgonskaya (Pushchino: ONTI PNC RAN, 2010)

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This book is the first Russian monograph summarizing our knowledge on aerobic methylotrophic bacteria, a metabolically unique group of prokaryotic microorganisms utilizing various oxidized and substituted methane derivatives as carbon and energy sources. This is an ambitious project, since methylotrophic metabolism is widespread among microorganisms. Unlike methanotrophic bacteria, which are highly specialized methane utilizers, methylotrophic prokaryotes utilize a broad spectrum of C_1 substrates (up to 50 compounds of different degrees of reduction). While the metabolic and phylogenetic diversity of the known methylotrophic prokaryotes is considerable, it is only a part of their diversity in nature.

Until recently, the monograph on biology of aerobic methylotrophs (*The Biochemistry of Methylotrophs*, Academic, 1982) by Christopher Anthony was the only book summarizing the data on the transformations of C_1 compounds and the energy metabolism of methylotrophs. Although it is still a valuable source, research of the last decades, employing a new generation of molecular techniques, as well as the emergence of genomics, proteomics, and transcriptomics, resulted in a veritable avalanche of new information that is difficult to navigate even for specialists with some experience in research of methylotrophs, let alone general microbiologists. However, this is no longer a problem, since the authors of the reviewed monograph, who are among the internationally acclaimed leading experts in research on methylotrophs, undertook the task of systematization and rendition of this new knowledge.

The book consists of seven chapters. The first chapter provides a general introduction to methylotrophy as a specialized type of microbial metabolism and describes the milestones in this field, starting from the discovery of the first methylotrophic bacteria by German researchers over a century ago. A reader is introduced to a list of reduced C_1 compounds used by methylotrophs as growth substrates and a brief review of the known pathways of their metabolism among the

various groups of methylotrophic prokaryotes. The main hypotheses are described, which explain the obligate dependence of some methylotrophs on C_1 compounds as carbon and energy sources.

In the second chapter, the information on the diversity of aerobic methylotrophic bacteria is summarized, including their taxonomy and phylogeny, metabolic and genetic organization, physiological, biochemical, and structural characteristics. Numerous electron micrographs of the cells of methylotrophic bacteria provide a comprehensive picture of the diversity of their morphological types. All presently known taxa of methylotrophic bacteria are grouped in the tables according to their pathways of C_1 substrate assimilation, which is a good basis for the subsequent list of the key enzymes and analysis of metabolism of these methylotrophic groups. Special attention is paid to unusual methylotrophic mycobacteria and actinomycetes, as well as to the description of the biodiversity of bacteria utilizing such specific C_1 substrates as halomethanes, methylated sulfur compounds, methyl acetate, and methyl *tert*-butyl ether.

In the third chapter, available information on the genes and enzymes of the primary C_1 metabolism of aerobic methylotrophic bacteria is summarized. This is a field in which significant progress was achieved during the last decades. Although the description is aimed at an advanced reader, numerous illustrations and schematic figures facilitate its understanding. The primary pathways of methanol oxidation are described in detail, as well as the properties of the PQQ- and NAD⁺-dependent methanol dehydrogenases (MDH), N,N'-dimethyl-4-nitrosoaniline oxidoreductase, and the recently discovered alternative MDH form (XoxF). The data on the pathways and enzymes of primary oxidation of methylated amines (di- and trimethylamine monooxygenases, tri- and monomethylamine dehydrogenases, methylamine oxidase) are summarized further, as well as the organization of the recently identified genes of the N-methylglutamate pathway (N-methylglutamate synthase,

γ -glutamylamide synthetase, and N-methylglutamate dehydrogenase) in bacteria from different taxonomic groups. Special attention is paid to the modern concepts of the pathways of the degradation of methylhalides (chloro-, bromo-, and iodomethane and dichloromethane), the key enzymes of these transformations, and organization and distribution of the relevant genes. Biodegradation pathways for methylated sulfur compounds (dimethyl sulfide, dimethyl disulfide, dimethyl sulfoxide, methanethiol, and methanesulfonic acid) involving monooxygenases, methyl transferases, reductases, and oxidases are also described in detail; the relevant enzymes are characterized. Finally, the electron transport chain of aerobic methylotrophic bacteria is discussed, which is responsible for electron transfer from methanol and methylamine dehydrogenases to specific acceptors (cytochrome c_L , cupredoxins), as well as the structure of the unusual cytochromes c_L and c_H . In general, attentive reading of the material in this chapter will provide a higher, principally new level of knowledge of the metabolic basics of methylotrophy.

The fourth chapter is based on experimental data obtained by the authors of the monograph, who have made a valuable contribution to our knowledge of the biodiversity; occurrence; and cytological, biochemical, ecological, and physiological characteristics of extremophilic/tolerant aerobic methylotrophs. The series of detailed studies on halo(alkali)philic methylotrophic bacteria deserve special attention. This research comprised the complete logical chain of investigation of target organisms, from characterization of their physiology and determination of the mechanisms of their survival under high salinity by accumulation of osmoprotectants (ectoine, glutamate, and sucrose) to determination of the pathways and genes responsible for the biosynthesis of these compounds and the regulatory mechanisms of this biosynthesis. This chapter includes data on the organization of the genes of ectoine biosynthesis in the *ectABC* or *ectABC-ask* clusters in correlation with bacterial salt resistance. Acquisition of halotolerance due to horizontal transfer of the *ect* genes is discussed. A schematic model of the regulation of ectoine biosynthesis at the level of the ectoine operon transcription is proposed, involving the EctR transcriptional regulatory protein discovered by the authors.

The fifth chapter deals with a highly important, although poorly studied until recently, aspect of the functional role of methylotrophic bacteria in natural environments, i.e., their interaction with plants and the metabolic basics of this interaction. Much of the material presented in this chapter has also been obtained by the authors. The data on occurrence and taxonomic diversity of aerobic methylotrophic phyto-

symbionts, their effect on plant growth, and molecular mechanisms of their adaptation to the phyllosphere and rhizosphere conditions are related with exhaustive completeness. Experimental evidence is presented for plant tissue colonization by methylotrophic bacteria, bacterial biosynthesis of phytohormones and biologically active compounds (auxins, cytokinins, vitamin B₁₂, and indole acetic acid) required for plant growth and development, and the ability to decrease ethylene levels in plants due to the activity of 1-aminocyclopropane-1-carboxylate deaminase. In general, this chapter provides a good demonstration of the major aspects of the metabolic dialogue between plants and associated methylotrophs.

The advent of geno-proteomic research and its role in investigation of the genetic determinants of methylotrophy are discussed in the sixth chapter. This is the first generalization of this kind, certainly deserving serious attention. *Methylobacterium extorquens* AM1, the best-studied methylotrophic organism, was used to develop the conceptual scheme of the primary pathways of C₁ metabolism showing the genes of the methylotrophic metabolic modules (gene clusters of methanol and methylamine dehydrogenases, tetrahydromethanopterin pathway of formaldehyde oxidation, ethylmalonate cycle, formate dehydrogenases, etc.). The authors use this scheme as a basis for comparison of the genetic determinants of these metabolic modules in ten members of different taxa of methylotrophic bacteria belonging to the classes *Alpha*-, *Beta*-, and *Gammaproteobacteria*. This comparison makes it possible to detect the evolutionary relations between different groups of methylotrophs and between methylotrophic bacteria and other groups of microorganisms, as well as to predict an organism's capacity for methylotrophy based on the presence of the complete set of important methylotrophy modules in its genome.

The seventh chapter deals with the biotechnological potential of aerobic methylotrophic bacteria and its possible realization in such fields of modern biotechnology as production of biopolymers, enzymes, and bioprotectants (ectoine), bioremediation of the ecosystems from toxic mono- and multicarbon compounds, as well as the economic factors relevant for the biotechnological application of methylotrophs. This analysis establishes beyond doubt that methylotrophic bacteria are indeed an attractive object for the promising fields of modern biotechnology.

The brief conclusion summarizes the main conceptual results of investigations in biology of aerobic methylotrophs and outlines the major directions of further development.

The Appendix describes the major techniques used in research on aerobic methylotrophic bacteria,

including the classical cultural approaches and the modern molecular techniques for detection and identification. The commonly used primer systems and probes are listed, together with the assessment of their specificity. Descriptions of all known genera of aerobic methylotrophic bacteria are included in this section for the reader's convenience. The list of literature (839 references) reflects the major tendencies in the development of methylotrophy as a developing field of knowledge and provides a good guideline for the choice of further reading in specific areas of research.

The monograph is an impeccably complete, logical, and highly professional generalization of the latest advances in biology, metabolism, genetics, and phylogeny of aerobic methylotrophic bacteria. Apart from its educational and summarizing function, it may be used as a reference point for further research. The book is of interest to microbiologists and biochemists, university teachers, students, and graduate students studying various aspects of methylotrophy.

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