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New unified nomenclature for genes involved in the oxidation of methanol in Gram-negative bacteria

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Abstract: The system involving the oxidation of methanol to formaldehyde in Gram-negative methylotrophic bacteria is complex. A total of 32 genes have been reported, termed *mox*, for methanol oxidation, and it is possible that more will be identified. Some *mox* genes carrying out completely different functions have been given the same designations by different laboratories and others have been given separate designations that were later discovered to be the same. It is now important to change the *mox* nomenclature to remedy this confusing situation. This communication proposes a new nomenclature for genes involved in methanol oxidation based on currently known linkage groups.

Key words: Methanol oxidation; Methylotrophic bacteria; Methanol dehydrogenase; Pyrroloquinoline quinone; *mox* Gene; *pqq* Gene

Introduction

In the last decade, genes required for the oxidation of methanol to formaldehyde (*mox* genes) have been identified from a number of methylotrophic bacteria. A total of 32 genes have been reported, with the initial isolations coming mainly from work with *Methylobacterium extorquens* AM1, *Methylobacterium organophilum* DSM 760, *Methylobacterium organophilum* XX, and *Paracoccus denitrificans* (see Table 1) [1–17]. Because gene descriptions have involved different laboratories with different strains, in some cases the same gene designations have been given to different genes, while in others, different designations have been given to genes that have turned out to be the same. It is clear that the field of methanol oxidation genetics would benefit from a new, unified nomenclature system that would clear up the current confusion and serve as a rational basis for naming any new genes that are discovered.

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Table 1

Old and new designations for the known methanol oxidation genes in methylotrophic bacteria

Old	New	Function	References [a]
POO synthesis genes			
moxC	*pqqA*	PQQ synthesis	1–5
moxP	*pqqA*	PQQ synthesis	3–5
moxV	*pqqB*	PQQ synthesis	3–5
moxT	*pqqC*	PQQ synthesis	3–5
moxO	*pqqG*	PQQ synthesis	3–5
(none)	*pqqD*	PQQ synthesis	3–5
moxH	*pqqE*	PQQ synthesis	1–5
moxU	*pqqF*	PQQ synthesis	3–5
Mox genes			
Group 1			
moxA / moxA1	*mxaA*	calcium insertion	1, 2, 6
moxK / moxA2	*mxaK*	calcium insertion	1, 2, 6
moxL / moxA3	*mxaL*	calcium insertion	1, 2, 6
moxB	*mxaB*	regulation	1, 2, 7
moxF	*mxaF*	MDH alpha subunit	1, 2
moxJ	*mxaJ*	unknown	8–10
moxG	*mxaG*	cyt c_L	1, 2, 8
moxI	*mxaI*	MDH beta subunit	8, 11
moxR	*mxaR*	unknown	9
moxS	*mxaS*	unknown	12
moxX	*mxaX*	regulation	13
moxY	*mxaY*	regulation	13
moxZ	*mxaZ*	regulation	13
moxW	*mxaW* [b]	regulation	14
Group 2			
moxM	*mxbM*	regulation	14
moxD	*mxbD*	regulation	1, 2, 14, 15
moxN	*mxbN*	regulation	14
cou-6	*mxbA* [c]	unknown	16
Group 3			
moxQ	*mxcQ* [b]	regulation	14
moxE	*mxcE* [b]	regulation	1, 2, 14
moxU	*mxcU* [b]	regulation	14
cou-1	*mxcA* [d]	unknown	16
Group 4			
moxR	*mxdR*	unknown	17
moxS	*mxdS*	unknown	17

[a] References cited include the original full description of the gene in which the old designation was first used, and also in some cases include later descriptions involving functional characterization. In some cases, the gene designation has only been used in reviews, and for those genes the appropriate review is cited.

[b] It is possible that *mxaW*, *mxcQ*, *mxcE* and *mxcU* (identified only in *methylobacterium strains*) are functionally equivalent to *mxaX*, *mxaY* and/or *mxaZ* (identified only in *P. denitrificans*).

[c] It is possible that *mxbA* is equivalent to *mxbM*, *mxbD* or *mxbN*.

[d] It is possible that *mxcA* is equivalent to *mxcQ*, *mxcE* or *mxcU*.

In order to clearly distinguish the new nomenclature from the old, we feel that it is best to abandon the old system and develop an entirely new system. In this way, any designation used in a paper in the literature will immediately be recognized as using the old or new system. It is not possible to develop a function-based naming system, since some of the genes have unknown functions and since genes that are isolated in the future may be named before their functions are understood. Therefore, we propose a system that is based on linkage groups in the bacteria in which Mox genetics is the best understood, *M. extorquens* AM1, *M. organophilum* DSM 760, *M. organophilum* XX, and *P. denitrificans*. Although we realize that the same linkage groups may not be present in all methylotrophs, this serves as a starting point for a rational naming system that can be immediately applied to all known *mox* genes.

New nomenclature

Genes involved in PQQ synthesis

Some of the *mox* genes are now known to be involved in the synthesis of the prosthetic group, pyrroloquinoline quinone (PQQ) [3–5] and in *M. organophilum* DSM 760, these have been termed *pqq* genes [3]. PQQ is not specific to methanol dehydrogenase, and genes involved in PQQ synthesis in methylotrophs can be distinguished from non-PQQ *mox* genes by testing mutants in these genes for the ability to grow on methanol in the presence of PQQ [3]. Therefore we propose that all PQQ synthesis genes be renamed *pqq*, with appropriate letter extensions (Table 1). Since the first report of *pqq* genes was made in *M. organophilum* DSM 760 [3], we propose to use these designations in the naming of known *pqq*

genes. Other letter designations can be chosen for any new *pqq* genes as appropriate.

Mox genes

All genes that are involved in the oxidation of methanol to formaldehyde that are not involved in PQQ synthesis will be given new names with a base symbol beginning with *mx*, for *m*ethanol o*x*idation. The third letter will be determined by the chromosomal linkage groups known for *M. extorquens* AM1, *M. organophilum* XX, and *P. denitrificans* (see Table 1). Linkage group 1 will be termed *mxa*, linkage group 2 will be termed *mxb*, linkage group 3 will be termed *mxc* and linkage group 4 will be termed *mxd*. Genes are given alphabetical extensions based on previous *mox* designations (for instance, *moxF* now becomes *mxaF*; Table 1). If new genes are identified that are in different linkage groups, they can be designated *mxe*, *mxf*, etc.

Other recommendations

If additional genes are identified in one of the known linkage groups, they should be given a letter other than those noted in Table 1. If genes are reported for which the appropriate linkage group is unknown at the time, it is recommended that *mxu* (for *m*ethanol o*x*idation-*u*nknown linkage) be used until more information is available, and then a more appropriate designation can be chosen. This may temporarily result in the designation of more than one *mxu* group, but authors using this designation should specifically state that the linkage group is unknown. If what was believed to be a single locus turns out to be multiple, the original extension should be used for one of the genes and other letters chosen for the new genes. If two genes given different designations are discovered to be the same, one of the designations should be dropped, but it should not be used again for a different gene.

In order to avoid the simultaneous use of new designations by different laboratories, it is suggested that authors preparing manuscripts describing new genes involved in methanol oxidation clear the designation with M.E. Lidstrom in the U.S. by letter or fax ((818) 395 2940).

We propose that Mox^- should be retained as the abbreviation for the phenotype in which the oxidation of methanol to formaldehyde is impaired. In addition, *mox* should be used as a collective symbol for methanol oxidation genes, regardless of linkage group.

In spoken usage, we recommend that *mxa* be pronounced "em-ex-a", *mxb*, "em-ex-bee", *mxc*, "em-ex-see" and *mxd*, "em-ex-dee".

In those cases in which the same genes from different strains are being discussed, we propose the use of subscript capital letters after the gene, P for *P. denitrificans*, A for *M. extorquens* AM1, X for *M. organophilum* XX and D for *M. organophilum* DSM 760. Other qualifiers can be used for other strains, as appropriate.

Conclusions

The complexity of the methanol oxidation system in Gram-negative methylotrophic bacteria has necessitated a new system of nomenclature for *mox* genes. The nomenclature described here will provide a rational basis for the discussion of these genes and the naming of new genes. It is being incorporated into all new papers by the authors of this proposal, and we strongly urge all other authors to do the same.

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