Title: OPA3-Related 3-Methylglutaconic Aciduria *GeneReview* – Table 3 with Additional Protein Information
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Table 3a. New Classification for Inborn Errors of Metabolism with 3-Methylglutaconic Aciduria as Discriminative Feature

Patho-Mechanism	Disease Name	Former Designation	Additional Hallmarks [1] of Phenotype	Affected Gene / Protein / Subcellular Localization / Proposed Function	Mode of Inheritance
Primary 3-MGA-uria					
Organic aciduria	3-methylglutaconyl-CoA hydratase deficiency (*AUH* defect)	3-MGCA type I (3-MGCA-1)	Adult onset leukoencephalopathy, dementia, progressive spasticity	*AUH* / 3-methylglutaconyl-CoA hydratase / Mitochondrial matrix / Leucine catabolism	AR
Secondary 3-MGA-uria					
Defective phospholipid remodeling	*TAZ* defect (Barth syndrome)	3-MGCA type II (3-MGCA-2)	(Cardio)myopathy, short stature, neutropenia, hypocholesterolemia, cognitive phenotype, mild dysmorphic features, OXPHOS dysfunction	*TAZ* / Tafazzin / (Inner) mitochondrial membrane / Cardiolipin remodeling	XL
	SERAC1 defect (MEGDEL syndrome)	3-MGCA type IV (3-MGCA-4)	Progressive spasticity, dystonia, deafness, Leigh syndrome-like MRI, severe psychomotor retardation, hypocholesterolemia, OXPHOS dysfunction	*SERAC1* / SERAC1 / Mitochondria-associated membranes fraction / Phosphatidylglycerol remodeling, cardiolipin composition	AR
Mitochondrial membrane disorder	*OPA3* defect (Costeff syndrome)	3-MGCA type III (3-MGCA-3)	Ataxia/extrapyramidal dysfunction, optic atrophy	*OPA3* / OPA3 / Outer mitochondrial membrane / ?Protective function for respiratory chain	AR

Patho-Mechanism	Disease Name	Former Designation	Additional Hallmarks [1] of Phenotype	Affected Gene / Protein / Subcellular Localization / Proposed Function	Mode of Inheritance
Mitochondrial membrane disorder (continued)	*TMEM70* defect	3-MGCA type IV (3-MGCA-4)	Broad phenotype, hypertrophic cardiomyopathy, myopathy, dysmorphic features, cataracts, psychomotor retardation, ATPase deficiency, lactic acidosis, hyperammonemia	*TMEM70* / TMEM70 / Inner mitochondrial membrane / ?Complex V assembly and insertion in mitochondrial membrane	AR
	DNAJC19 defect (DCMA syndrome)	3-MGCA type V (3-MGCA-5)	Dilated cardiomyopathy, ECG abnormalities, non-progressive cerebellar ataxia, small atrophic testes, cryptorchidism, growth failure, anemia, steatosis hepatitis (i.e., fatty liver)	*DNAJC19* / DNAJC19 / ?Inner mitochondrial membrane / ?Mitochondrial protein import	AR
Unknown	NOS 3-MGA-uria	3-MGCA type IV (3-MGCA-4)	Variable, mostly progressive neurologic disease	Unknown	Unknown

From Wortmann et al [2013]

OXPHOS = oxidative phosphorylation

DCMA = dilated cardiomyopathy with ataxia

NOS= not otherwise specified

1. In addition to 3-MGA-uria

References

Wortmann SB, Duran M, Anikster Y, Barth PG, Sperl W, Zschocke J, Morava E, Wevers RA. Inborn errors of metabolism with 3-methylglutaconic aciduria as discriminative feature: proper classification and nomenclature. J Inherit Metab Dis. 2013;36:923–8.