Title: CLPB Deficiency *GeneReview*: New Classification for Inborn Errors of Metabolism with 3-Methylglutaconic Aciduria as Distinguishing Feature

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Note: The following information is provided by the authors and has not been reviewed by *GeneReviews* staff.

The branched-chain organic acid 3-methylglutaconic acid (3-MGA) is an intermediate of leucine degradation (from *OPA3*-Related 3-Methylgutaconic Aciduria).

The exact source of 3-MGA is known only in 3-methylglutaconyl-CoA hydratase deficiency (or *AUH* defect), the rarest of the five types, caused by primary deficiency of the mitochondrial enzyme 3-methylglutaconyl-CoA hydratase (3-MGH), resulting in a block of leucine catabolism.

In all other types, the origin of the increased 3-MGA excretion is unknown but mitochondrial dysfunction is thought to be the common denominator [Wortmann et al 2009]. Recently it has been postulated, that 3-MGA arises from its CoA-ester which is produced in three enzymatic steps from mitochondrial acetyl CoA [Ikon et al 2016].

Wortmann et al [2013], Table 1 provides a new classification system for inborn errors of metabolism with 3-methylglutaconic aciduria as a discriminating feature.

## References

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