



National Human Genome Research Institute

# Synthetic Methylmalonyl-CoA Mutase Transgene for the Treatment of Mut Class Methylmalonic Acidemia (MMA)

## NHGRI INVENTION:

Number: E-243-2012

## PATENT STATUS

U.S. Patent 9,719,080 issued August 1, 2017  
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## KEY WORDS

Methylmalonic Acidemia, Methylmalonyl-CoA mutase, Gene Therapy

## LEAD INVENTOR

Charles P. Venditti, M.D., Ph.D.  
Senior Investigator, Medical Genomics and Metabolic Genetics Branch, Head of Organic Acid Research Section, NHGRI, NIH

## NHGRI CONTACT

NHGRI Technology Transfer Office [nhgrittoffice@mail.nih.gov](mailto:nhgrittoffice@mail.nih.gov)

## PATENT-PENDING TECHNOLOGY AVAILABLE FOR LICENSING

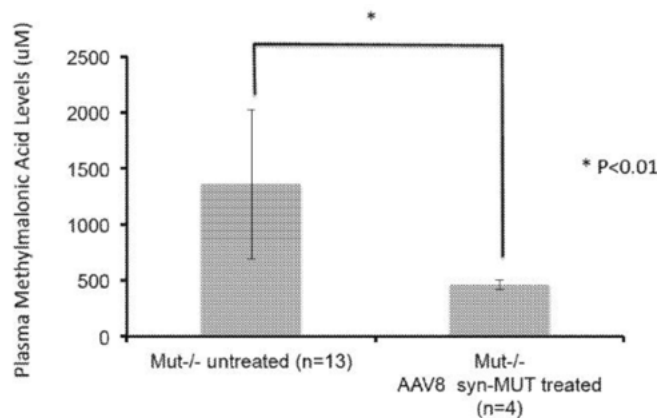
### SUMMARY

Methylmalonic acidemia (MMA) is an autosomal recessive disorder caused by defects in the mitochondria-localized enzyme methylmalonyl-CoA mutase (MUT). MUT deficiency, the most common cause of MMA, is characterized by the accumulation of methylmalonic acid and other disease-related metabolites. The disease is managed with dietary restrictions but lacks definitive therapy. MMA can lead to metabolic instability, seizures, strokes, and kidney failure, and can be lethal even when patients are being properly managed.

In order to develop potential therapy for MMA, investigators at NHGRI engineered a synthetic codon-optimized human MUT gene (co-MUT) encoding human MUT protein. This synthetic gene is translated more efficiently than its naturally-occurring counterpart. The construct was also used to generate a series of novel gene therapy vectors and treat MMA mice. The treatment rescued the MMA mouse model from neonatal lethality, improved their growth, and lowered the levels of plasma methylmalonic acid in the blood.

### POTENTIAL COMMERCIAL APPLICATIONS

The co-MUT transgene could be used as a drug, via viral or non-viral mediated gene delivery, to restore MUT function in MMA patients, prevent metabolic instability and ameliorate disease progression. In addition, it could be used for in vitro production of MUT for use in enzyme replacement therapy for MMA.



Reduction in circulating metabolites in MMA mice after treatment with AAV-synthetic MUT construct.

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