



National Human Genome Research Institute (NHGRI)

Patent-Pending Technology Available for Licensing

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

NHGRI Invention Number:
E-243-2012

Patent Status

PCT Application PCT/US2014/028045
Filed March 14, 2014

Key Words

Methylmalonic Acidemia,
Methylmalonyl-CoA mutase, Gene Therapy

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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

