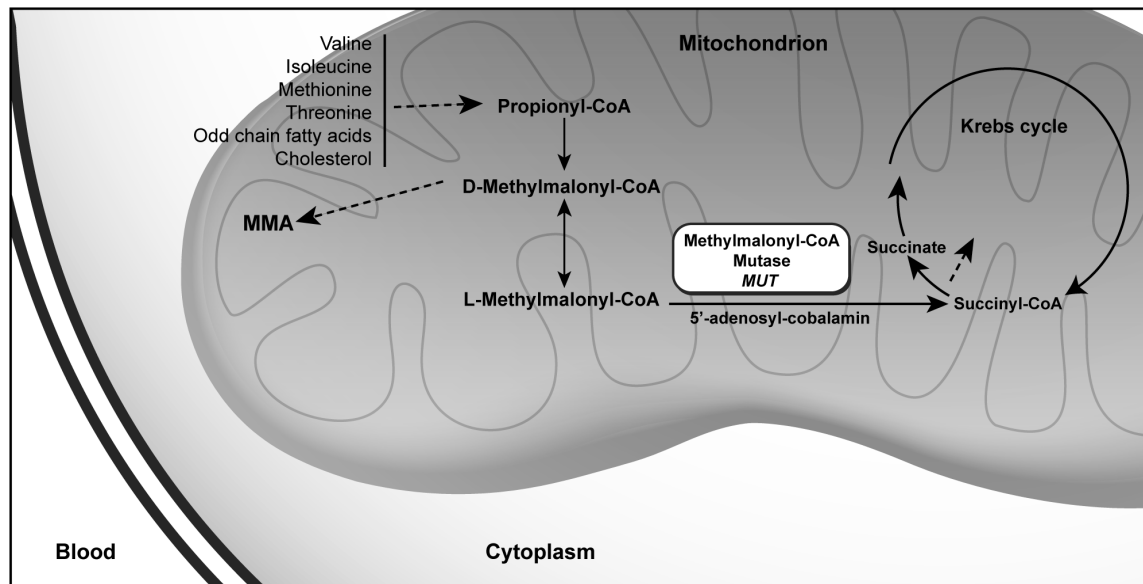


Supplementary Figures



Supplementary Figure S1. Major pathway of methylmalonic acid metabolism. Four amino acids (valine, isoleucine, methionine, threonine), odd chain fatty acids, cholesterol metabolism and propiogenic gut flora generate propionyl-CoA, which is converted to D-methylmalonyl-CoA, and then to L-methylmalonyl-CoA. Isolated MMA is most commonly caused by a block at the isomerization of L-methylmalonyl-CoA into succinyl-CoA due to a complete or partial defect in methylmalonyl-CoA mutase (*mut⁰*, *mut⁻*). Mutations in genes involved in the synthesis, transport and regulation of the MUT cofactor 5'-deoxyadenosylcobalamin are more rare causes of isolated MMA.