The bacterial specific enzyme 5’-methylthioadenosine/5’-adenosylhomocysteine (MTA/SAH) nucleosidase (MTN) is essential for production of the quorum sensing signal autoinducer 2 (AI-2). AI-2 is known to influence biofilm formation and virulence in bacteria. This enzyme serves as a target for development of new antibiotics. In an E. coli MTN gene knockout (MTN KO) strain, we found alteration to growth and biofilm formation. We found biofilm formation in the MTN KO strain could be improved by supplementation with AI-2. However, planktonic growth was independent of AI-2. MTN KO culture growth was improved by the addition of adenine, biotin, methionine, spermidine, and thiamine; all products that could be traced back to proper MTN function. The results of our studies indicate that the inability to break down MTA, SAH or 5’-deoxynucleosides has the potential to affect a wide array of metabolic pathways. These findings suggest the one of the primary mechanisms of action of MTN inhibitors will be to prevent AI-2 synthesis and reduce rates of vitamin dependent enzymes in central carbon metabolism.

**Background Information**

MTN enzyme deficiency alters growth, biofilm formation, and drug resistance through autoinducer-2 dependent and independent mechanisms.

**Experimental: MTN KO Strain Shows Altered Pyruvate Metabolism**

A supplement mixture (Mix 1) containing methionine (10 μM), adenine (1 μM), spermidine (10 μM), biotin (10 μM), and thiamine (0.1 μM) largely corrects the MTN KO growth defect.

**What does this data suggest?**

- The MTN KO strain shows growth defects due to loss of methionine and purine salvage from SAM metabolism.
- The MTN KO strain shows growth defects due to reduced polyamine synthesis.
- The MTN KO strain shows growth defects due to reduced vitamin synthesis resulting from radical SAM reactions.

**Experimental: MTN KO Pyruvate Metabolism is Altered**

Thiamine improves MTN KO growth.

**For the Future**

- Study effect of MTN deficiency on additional pyruvate metabolic enzyme activity.
- Determine metabolite and proteome adaptations to MTN deficiency as a way to explore this pathway as a target for antibiotic development.
- Study MTN inhibitor treatment of WT cells to determine if similar effects are seen to the MTN KO strain.

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