Exploring the Effect of Oral Vancomycin on the Pipecolic Acid Synthesis Pathway in Mice

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Pipecolic acid is a lysine metabolite produced by hepatocytes and by the gut microbiome. It is associated with numerous health benefits including anti-inflammatory properties, reduction of fat accumulation, and reduction of oxidative stress. Previous metabolomics data from our lab has shown that oral vancomycin, commonly used to treat Clostridioides difficile infections, corresponds with decreased levels of pipecolic acid in mice. However, the specific metabolic pathway(s) inhibited by vancomycin remain unknown. The purpose of this study was to examine the effect of oral vancomycin on pipecolic acid synthesis by measuring the murine expression of hepatic genes involved in lysine metabolism. Specifically, the present study is focused on genes Aass, Phykpl, Pipox, and Hykk. To investigate the effects of vancomycin on these genes, mice were either given oral vancomycin or phosphate buffer saline (PBS) at 48, 24, or 12 hours before they were sacrificed. Liver samples were obtained from each mouse and RNA was extracted, followed by cDNA synthesis. Real-Time Polymerase Chain Reaction (RT-qPCR) was used to measure hepatic gene expression, and the gene expression ratios were compared between treatment groups. We found that Aass expression was significantly increased in vancomycin-treated mice. There was also a trend in which females had higher gene expression than males across all treatment groups, excluding Phykpl. These results help to uncover the mechanisms behind vancomycin's effect on the abundance of pipecolic acid in the gut microbiome, potentially revealing possible harmful effects and contributing to the development of more effective treatment options.