

Metformin-induced alterations in gut microbiome compositions and antibiotic resistance genes

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Metformin is the most commonly prescribed medication for treating type 2 diabetes (T2D). It is known that metformin can alter the gut microbiome, which influences the effectiveness of metformin treatment. We posited that if the gut microbiome, a reservoir of the resistome, is altered, then the resistome should change as well. To test this hypothesis, we reanalyzed microbiome data generated by Wu et al. (Nat. Med. 23(7):850–858, 2017), identifying antibiotic resistance genes (ARGs) and bacterial species. Through read-based analysis, we observed that the abundance of ARGs indeed changed in many samples treated with metformin. Moreover, the altered pattern was sufficiently heterogeneous across individual samples to allow subcategorization. We also found a strong correlation between the abundance of multidrug-resistant ARGs (MDR-ARGs) and the presence of *E. coli*. The contig-based analysis led to the same conclusion: an increase in MDR-ARGs due to metformin was associated with an increase in *E. coli*. In relation to this, we were able to confirm that the majority of MDR-ARGs are likely to originate from *E. coli*. These results suggest that metformin may have the potential side effect of increasing *E. coli* carrying ARGs, particularly MDR-ARGs, which could be a concern in T2D therapy that relies on metformin.