

Cologne Evolution Colloquium

Filipe Cabreiro

London Institute of Medical Sciences

CRC 1310 Predictability in Evolution

The metformin *E. coli* resistome regulates host metabolism and lifespan

Development of drug resistance by bacteria is the key prevalent mechanism reducing the effectiveness of antibiotics in treating disease. Recent studies revealed that the anti-diabetic effects of metformin are greatly mediated through the gut microbiota with a special focus on the role played by *E. coli*. But how the development of resistance by the microbiota to non-antibiotic drugs such as metformin regulates drug effects on host physiology is unknown. Using a combination of model organisms, high-throughput screening methods, in vitro evolution experiments and multi-omics approaches, we now identify the molecular mechanisms underlying *E. coli* sensitivity to metformin. Our data shows that development of metformin resistance in *E. coli* involves both private and shared mechanisms with other antibiotics. Importantly, using a novel microbe-drug-host GWAS approach we show that the mechanisms previously identified are conserved at the *E. coli* pan-genome level and mediate metformin effects on host lipid metabolism and lifespan. Overall, our findings provide new insights on the unique action of host-targeted drugs on microbial physiology and its relevance to host physiology.

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Institute for Biological Physics & MPI for Biology of Ageing

Online via Zoom

Hosted by Dario Valenzano