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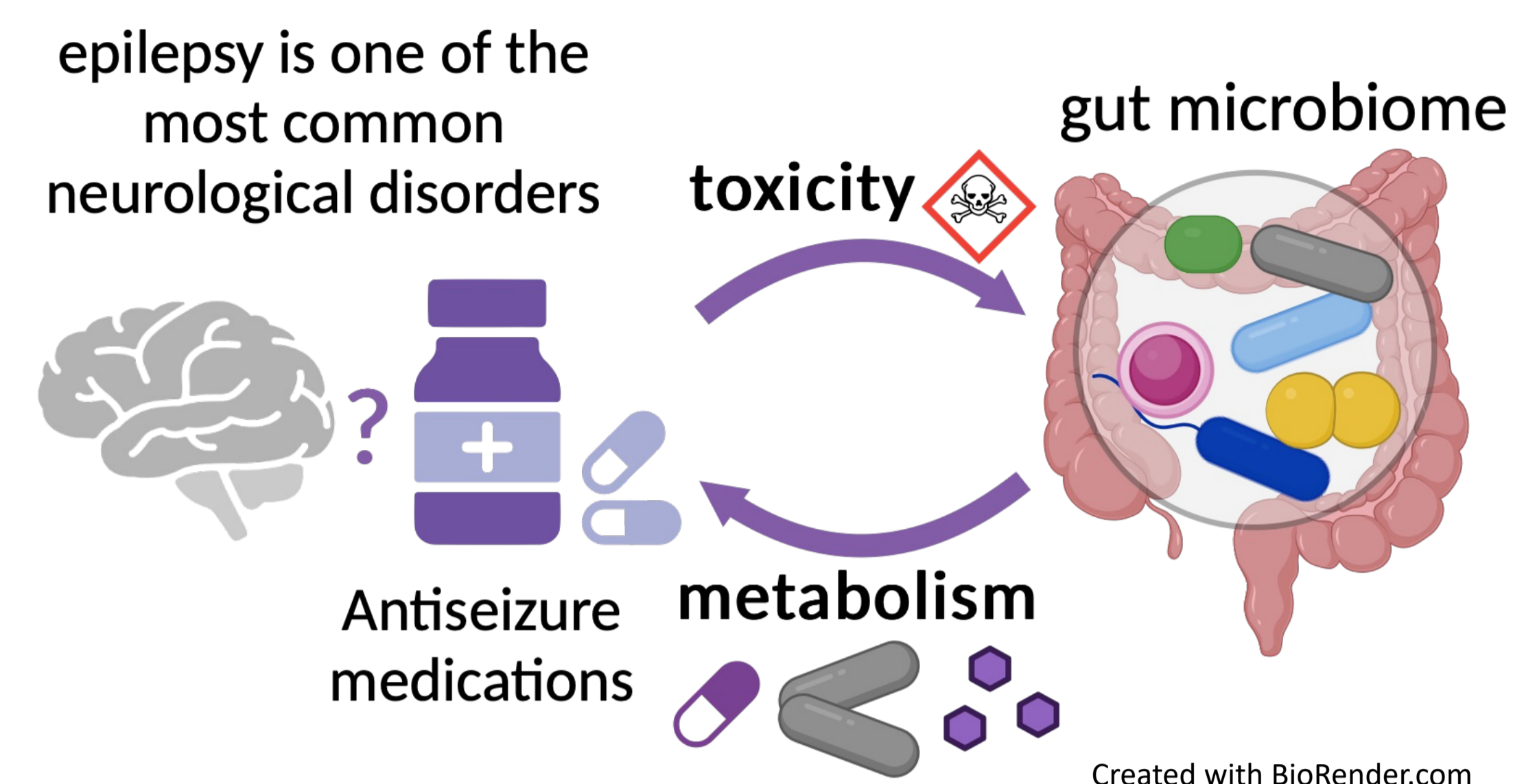
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Members of the gut microbiota modulate the bioavailability of the antiseizure medication lamotrigine

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Background

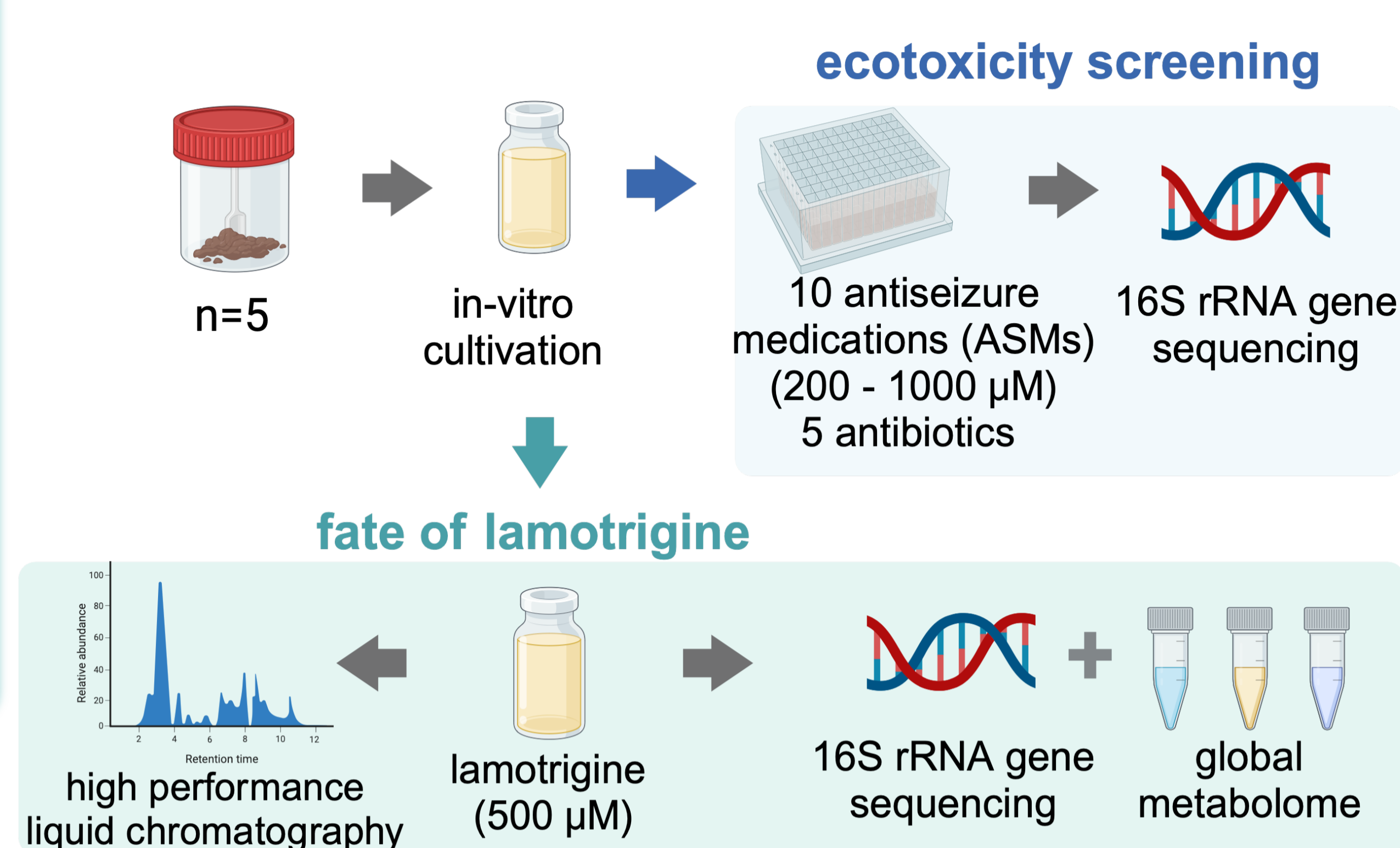


Antiseizure medications are not effective in 1/3 of the pediatric patients.

OBJECTIVES

- Assess the impact of antiseizure medications on gut microbiome dynamics and function
- Elucidate the role of gut microbiome on bioavailability of lamotrigine

Methods

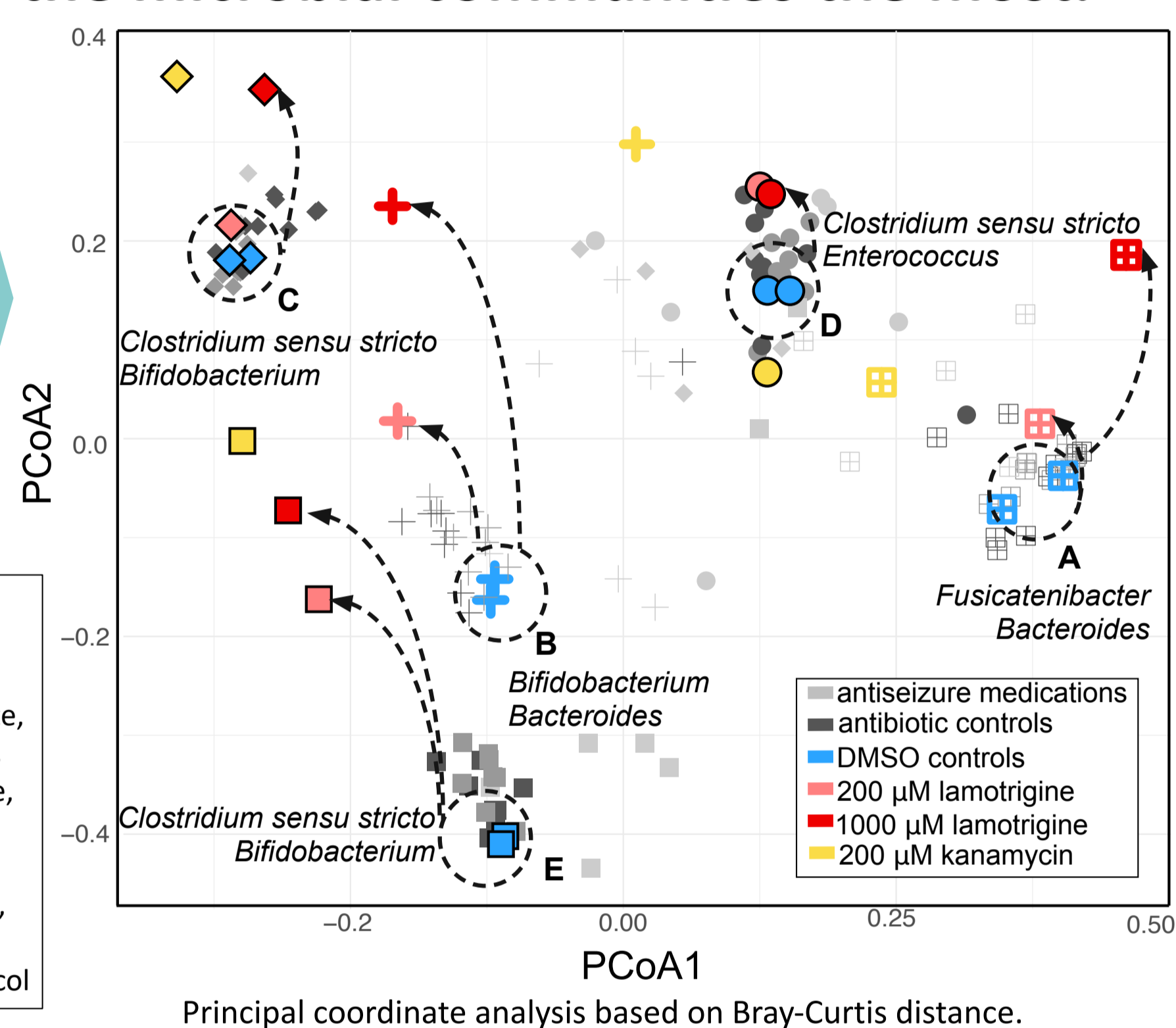


Results

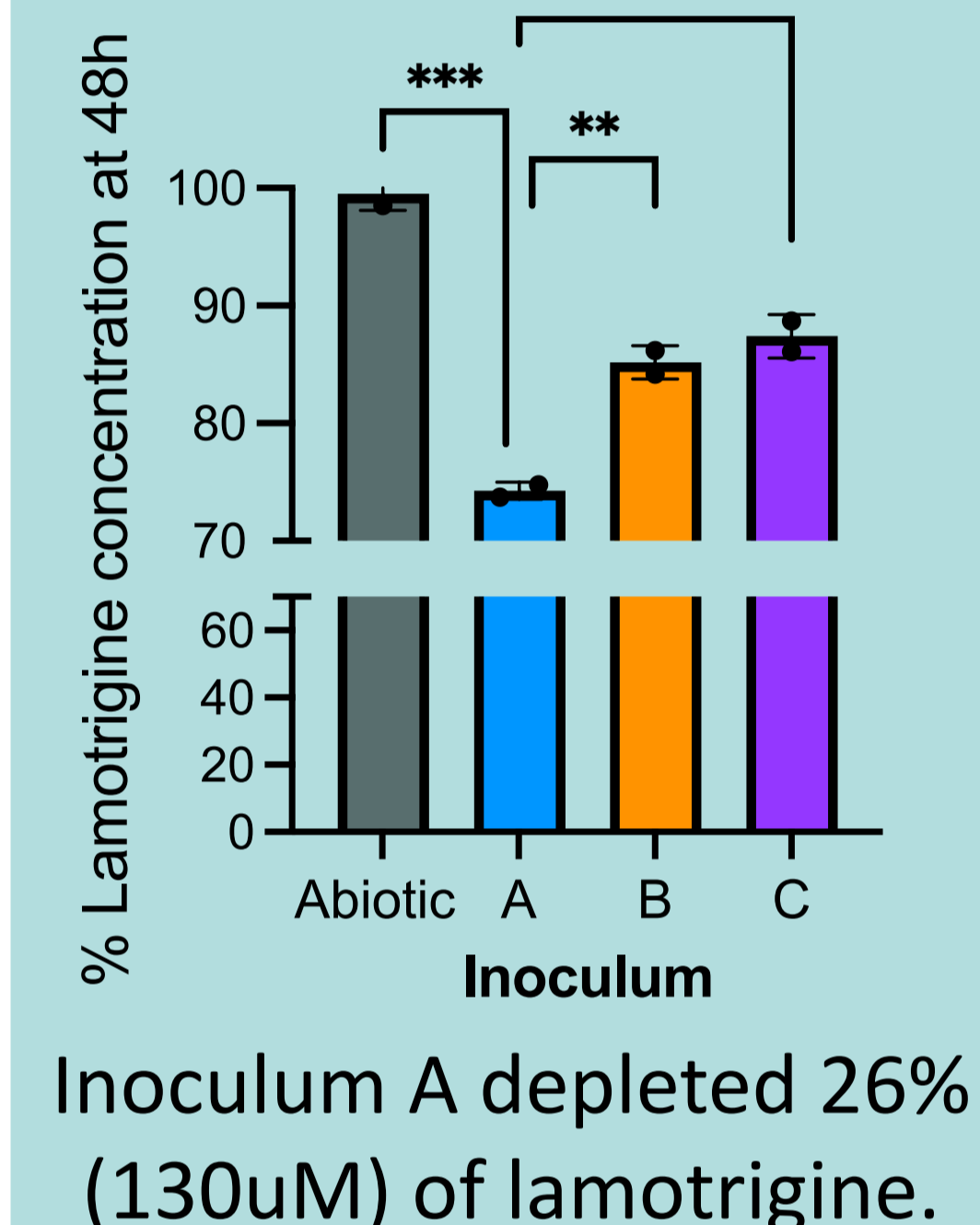
1. Among the 10 antiseizure medications, lamotrigine disturbed the microbial communities the most.

Lamotrigine had an impact similar to kanamycin.

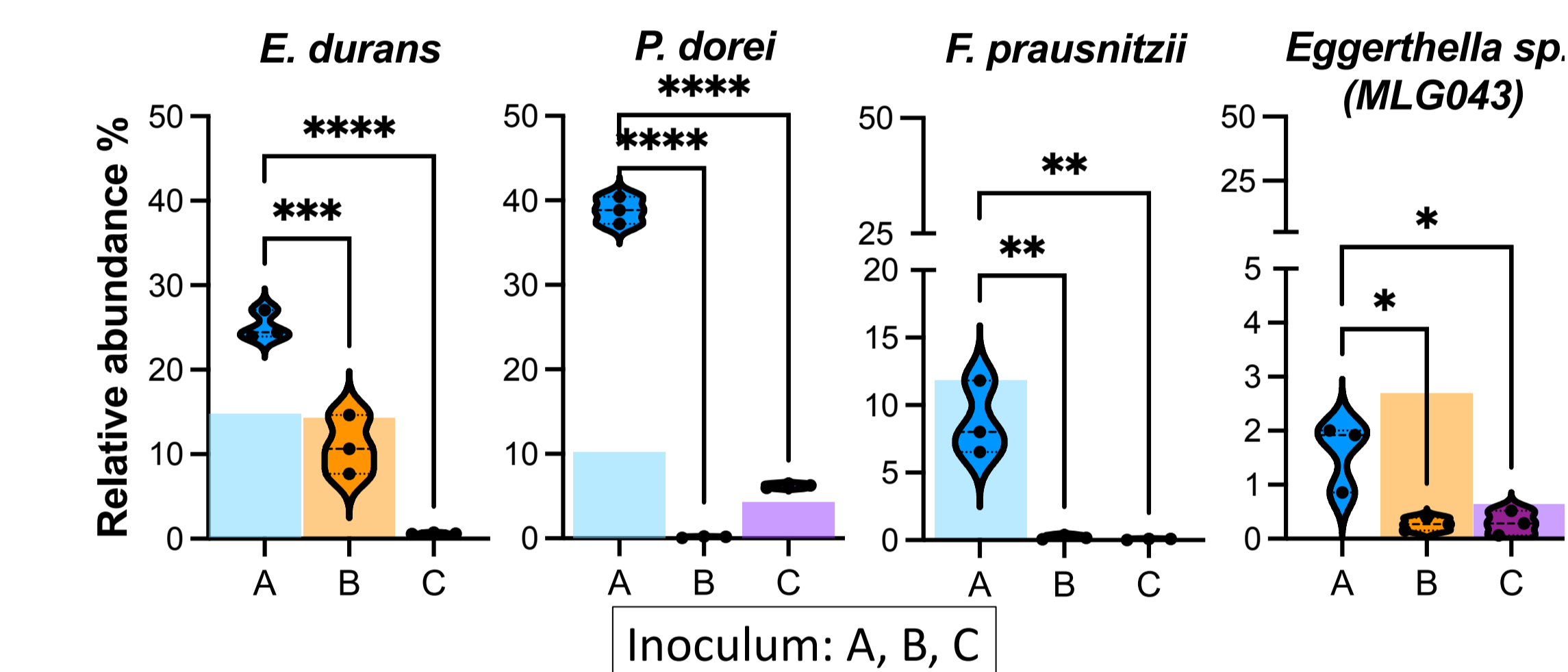
- ASMs:**
valproate, levetiracetam, carbamazepine, topiramate, lamotrigine, gabapentin, ethosuximide, zonisamide, phenytoin.
- Antibiotics:**
kanamycin, ciprofloxacin, azithromycin, vancomycin, chloramphenicol



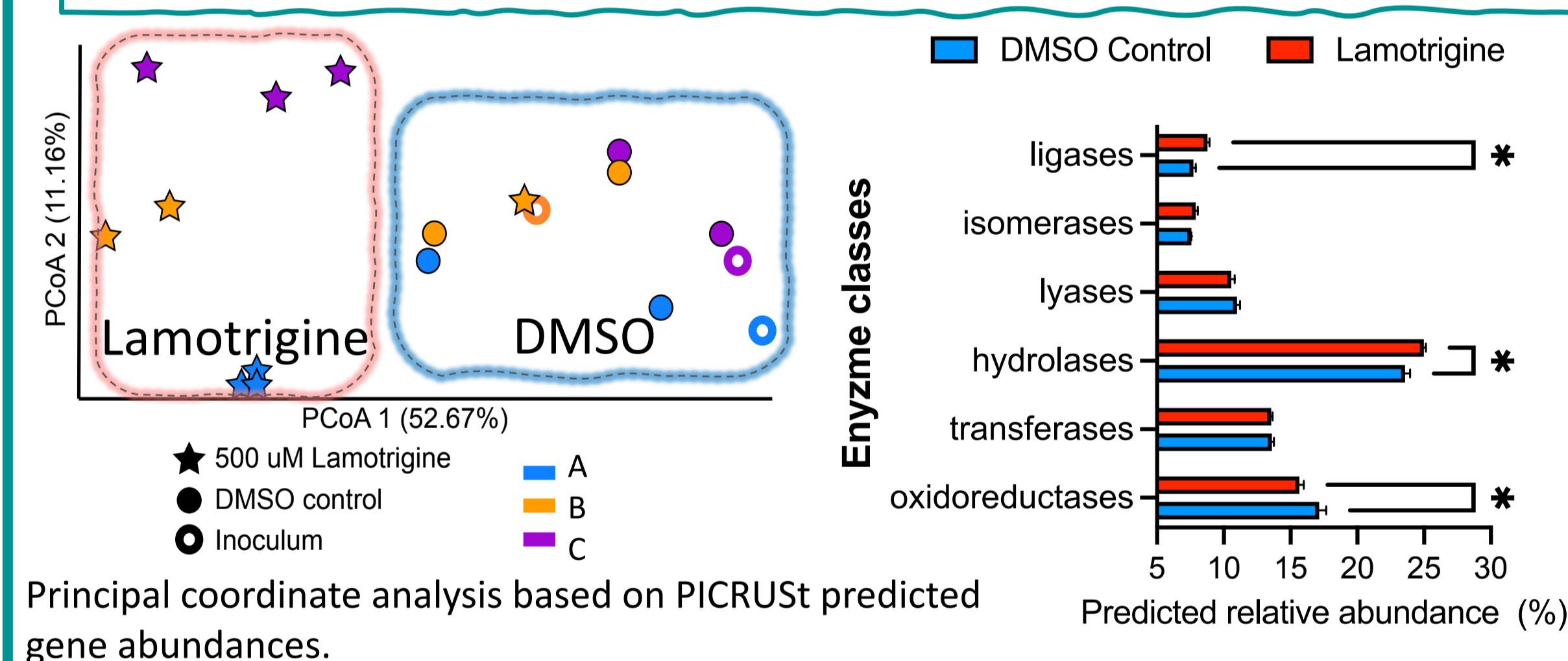
3. Lamotrigine disappearance rate was inoculum specific.



4. Lamotrigine-degrading cultures were enriched in *Enterococcus durans*, *Phocaeicola dorei*, *Eggerthella* sp. and *Faecalibacterium prausnitzii* species.

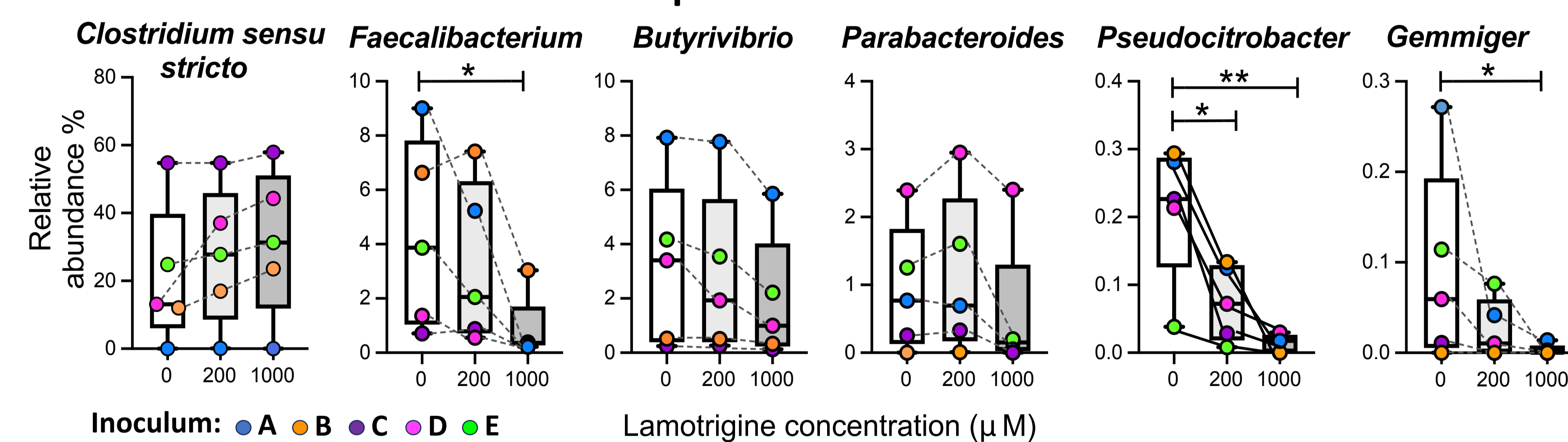


Lamotrigine treatment reduced predicted abundance of oxidoreductases but increased ligases and hydrolases.

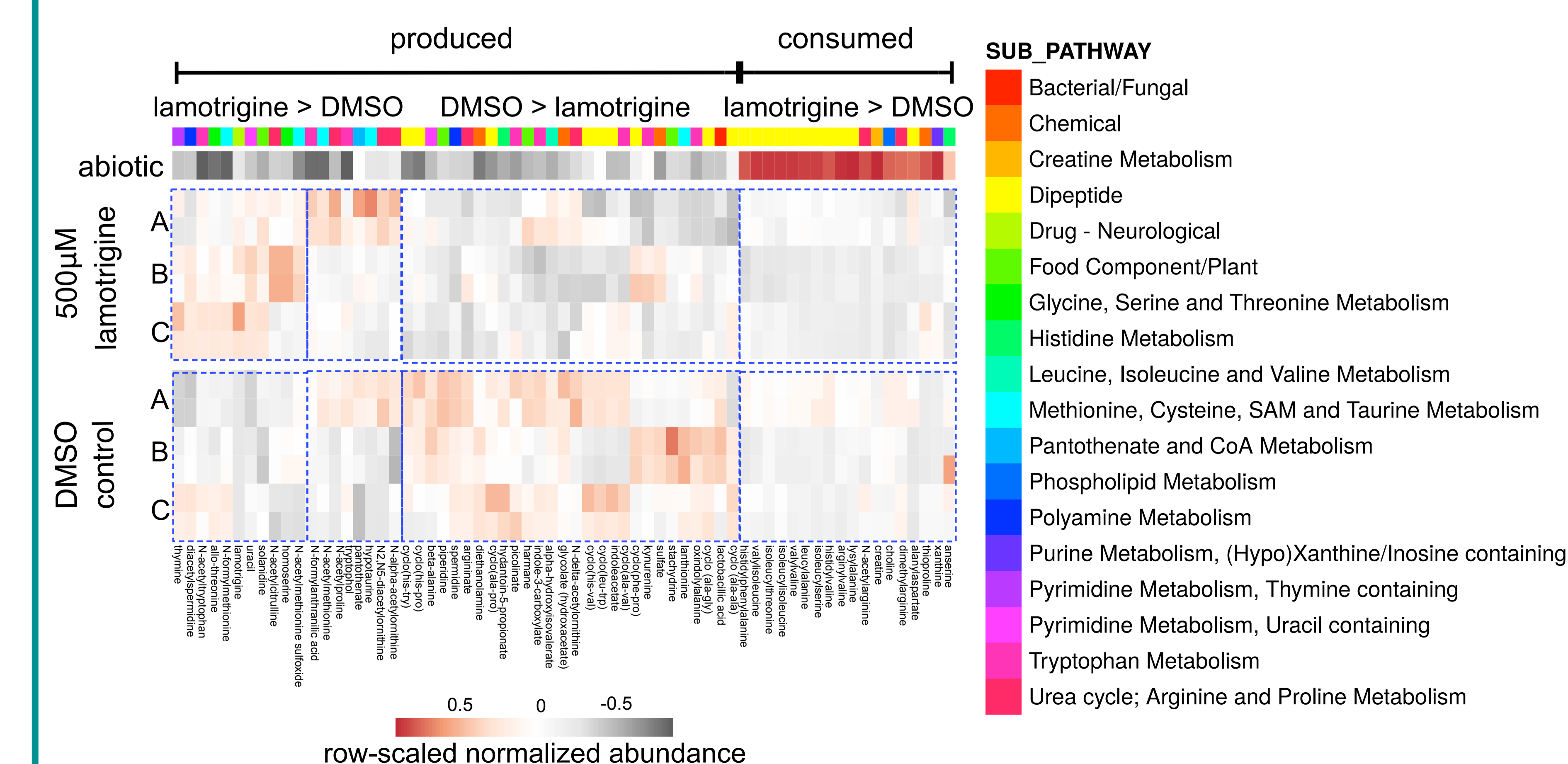


Based on predicted genes, lamotrigine treated and DMSO-control samples formed separate clusters.

2. Lamotrigine influenced the relative abundance of key genera in a dose-dependent manner.

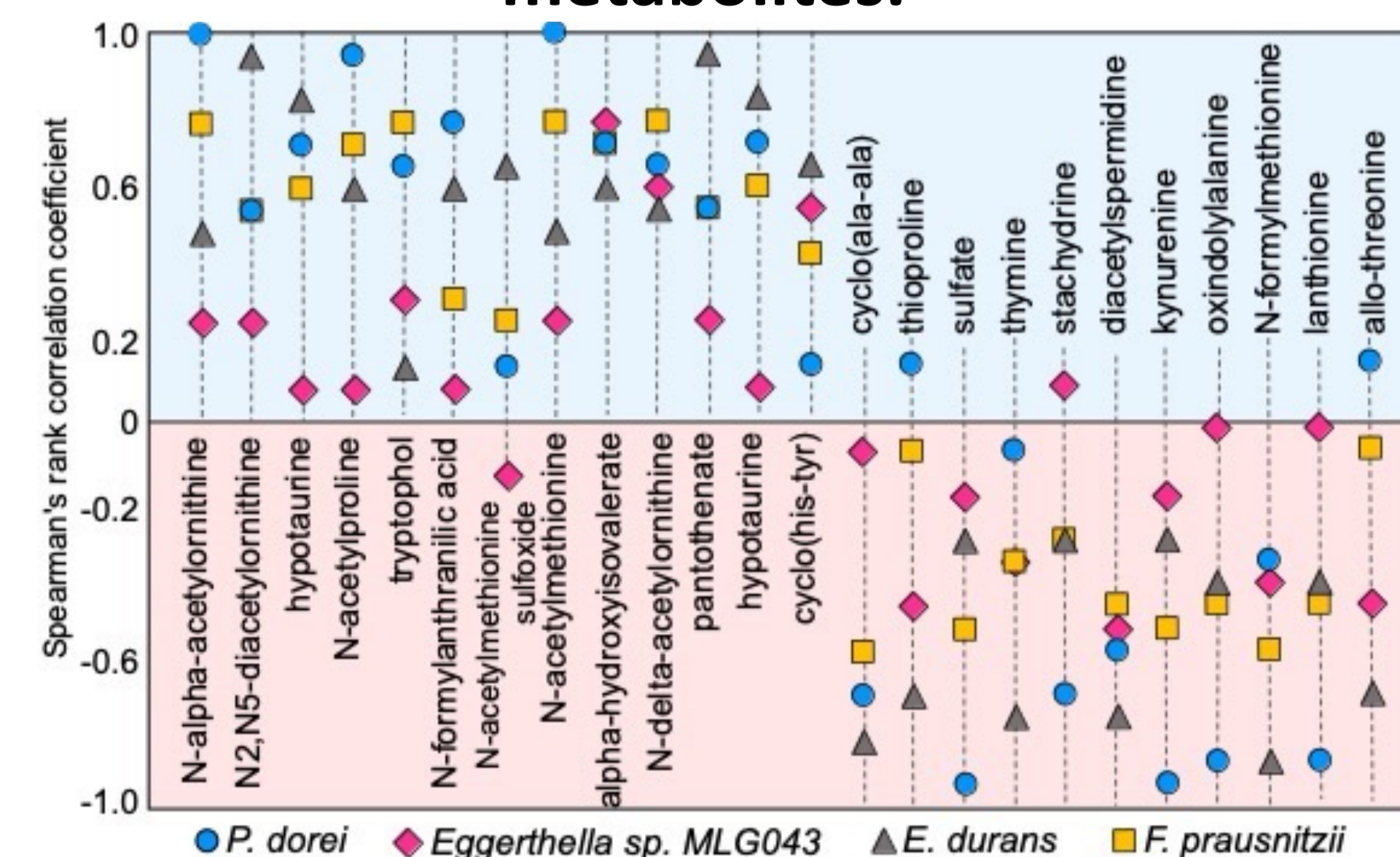


5. Lamotrigine impacted microbiome function more than its composition: altered the production and consumption of 114 metabolites.



Production of several amino acid metabolites were reduced and catabolism of dipeptides were enriched in lamotrigine treated cultures.

6. Genera in lamotrigine-degrading cultures positively correlated with methionine and urea metabolites.



Summary

- Lamotrigine disturbed microbial community dynamics.
- Microbial communities dominated by *E. durans*, *P. dorei*, *Eggerthella* sp. and *F. prausnitzii* reduced bioavailability of lamotrigine.
- Dipeptide consumption and production of several amino acid metabolites increased in lamotrigine treated microbial communities.

