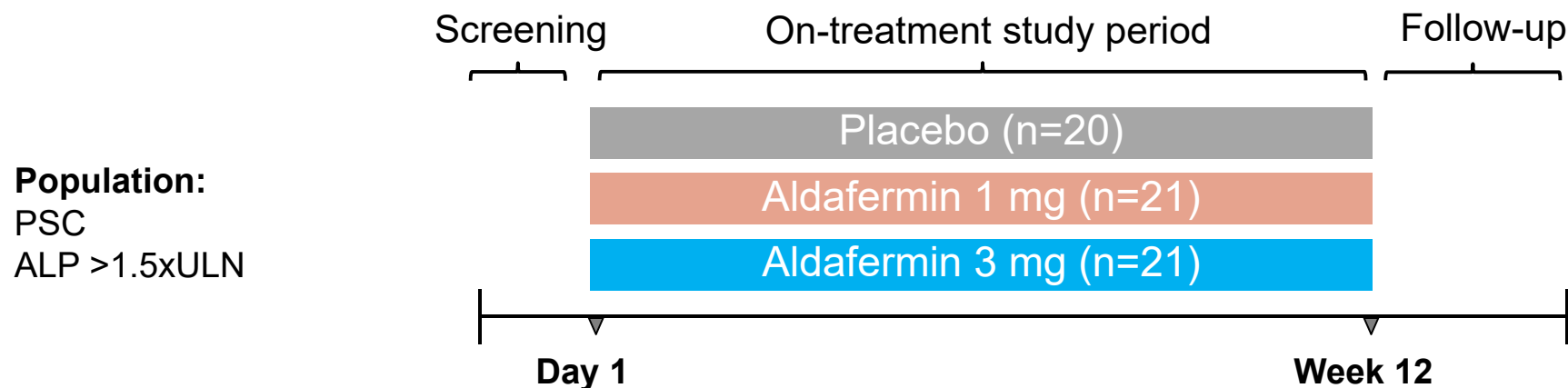


The FGF19 Analogue Aldafermin Enriches the Lactate-Consuming, Bile Acid-Sensitive Commensal Microbe *Veillonella* in Patients with Primary Sclerosing Cholangitis

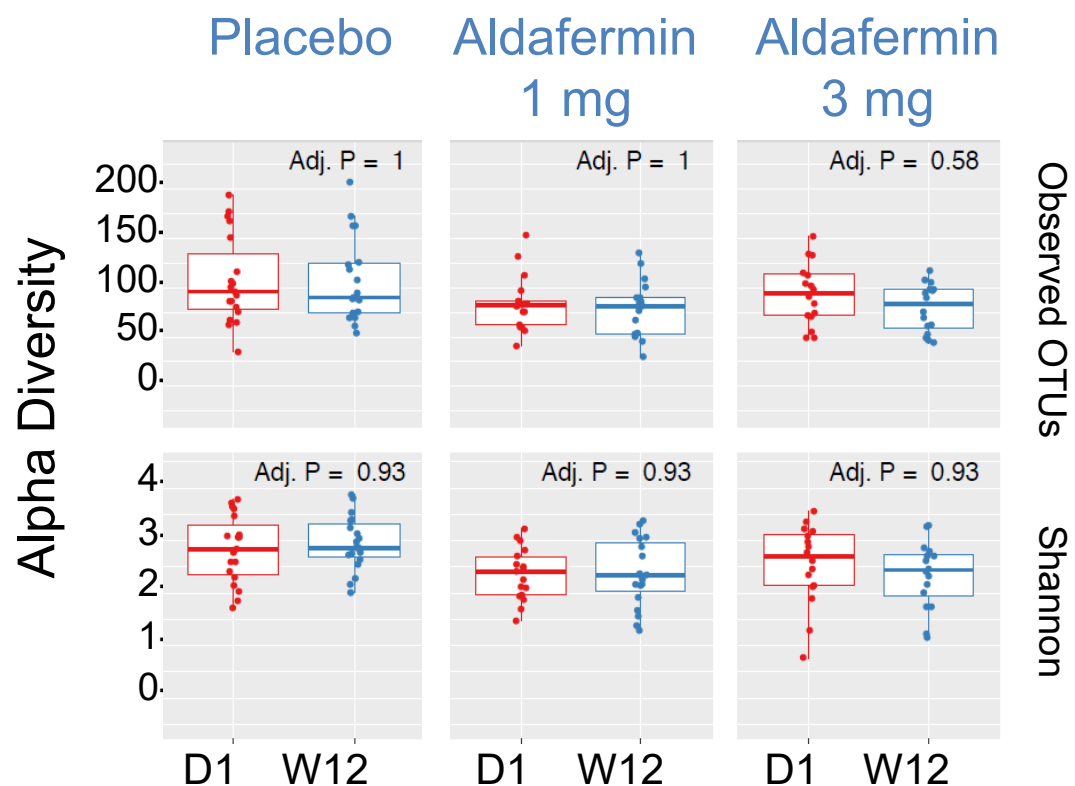


- Primary sclerosing cholangitis (PSC) is a rare, chronic cholestatic liver disease characterized by inflammation and fibrosis of intra- and extra-hepatic bile ducts ¹
- Emerging evidence suggests that alterations in bile acids and the microbiome may contribute to the risk and progression of PSC
- Aldafermin, a non-tumorigenic FGF19 analogue, suppressed bile acid synthesis and decreased hepatic inflammation and fibrosis markers, without affecting alkaline phosphatase levels, in a randomized, double-blind, placebo-controlled phase 2 study in patients with PSC ²
- Here we report results of aldafermin on the gut microbiota from this study

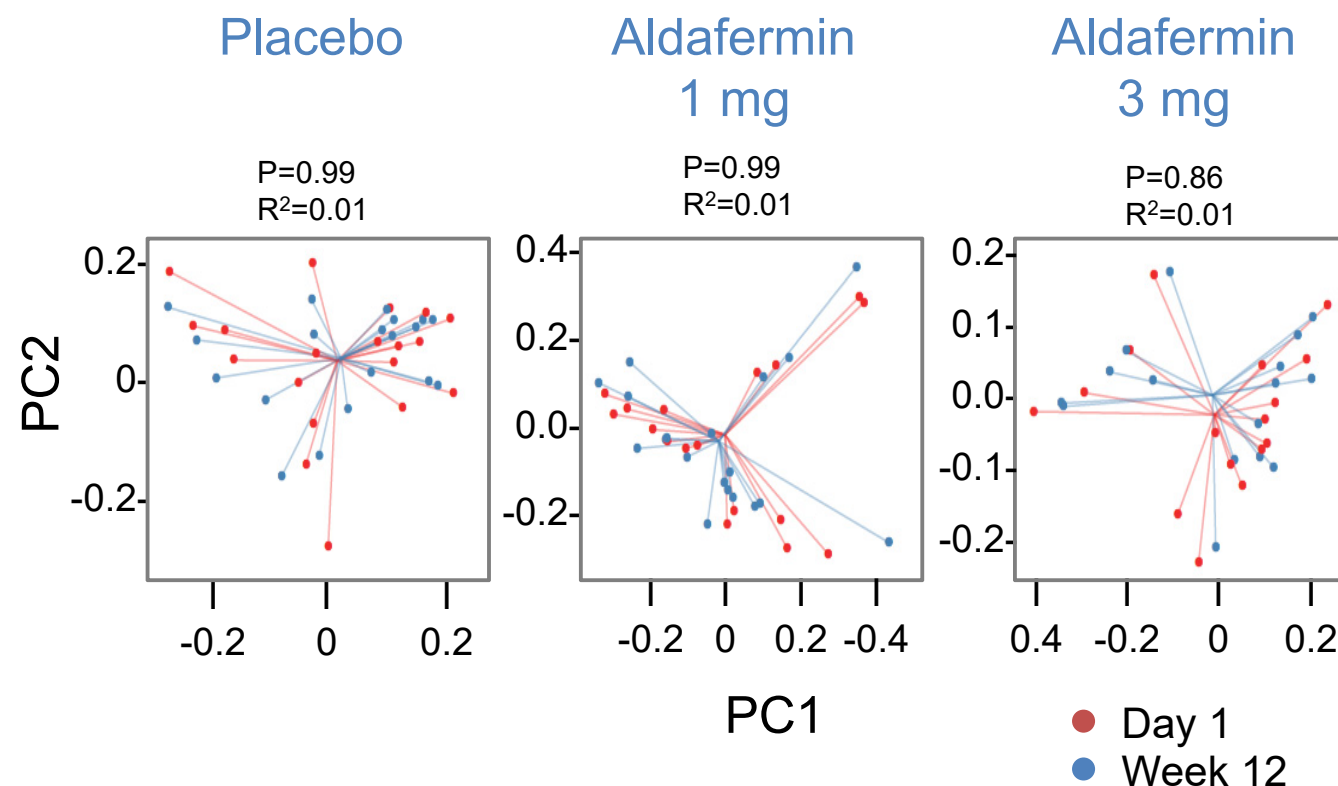


Stable Microbiome in PSC Patients Treated with Adefopurin

Alpha Diversity



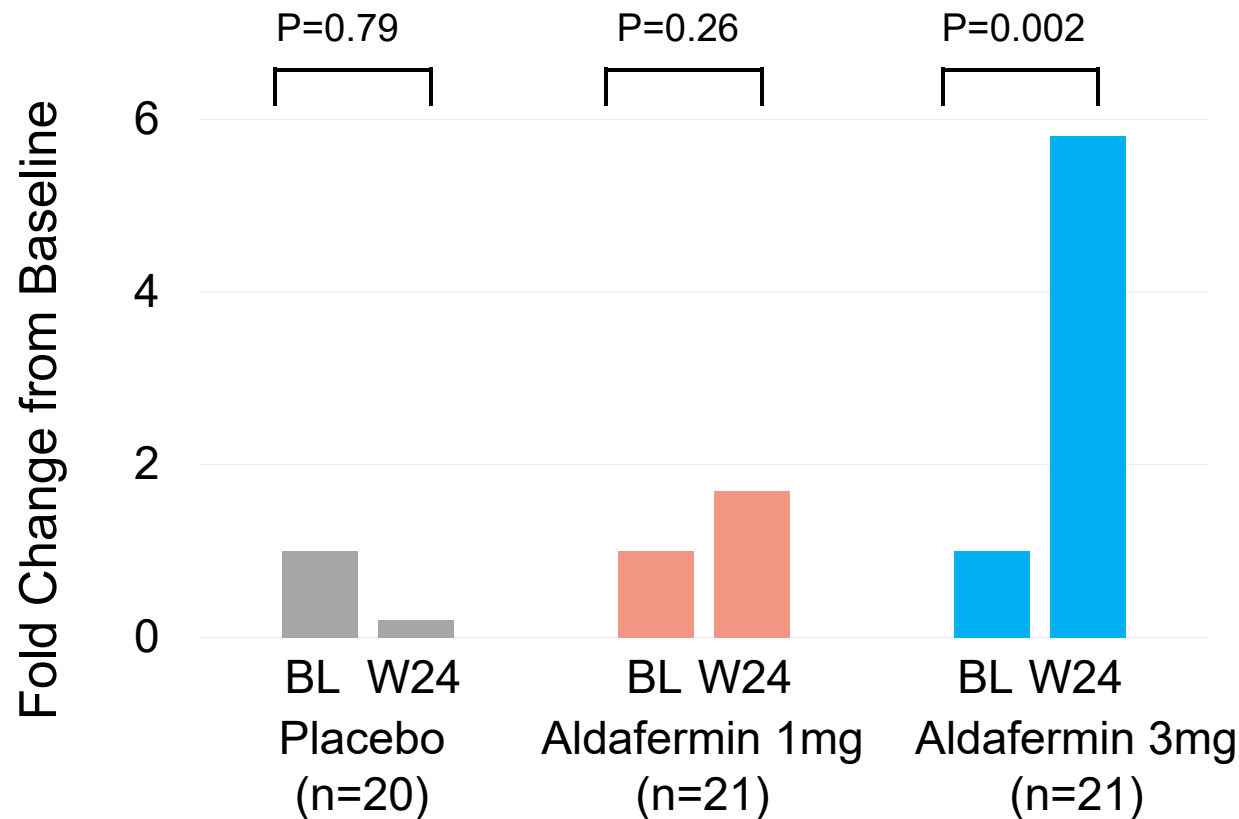
Beta Diversity



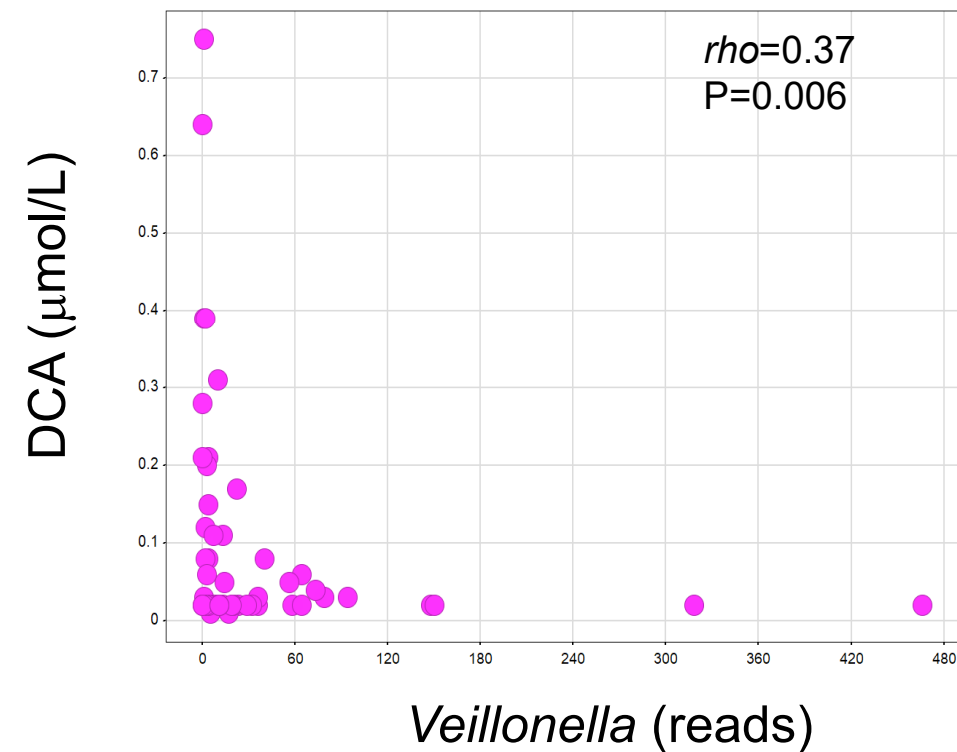
- No changes were observed among all phyla over time or between adefopurin and placebo
- No changes among the top 30 most abundant genera over time or between adefopurin and placebo

Aldafermin Enriched a Rare Genus *Veillonella*

Veillonella Abundance



Correlation Between *Veillonella* and DCA



- The relative abundance of *Veillonella* increased by 1.7- and 5.8-fold in the aldafermin 1 mg and 3 mg groups, respectively, vs no increase in the placebo group
- *Veillonella* inversely correlated with DCA at week 12

Veillonella is a Lactate-Consuming Commensal Microbe Associated with Performance in Athletes

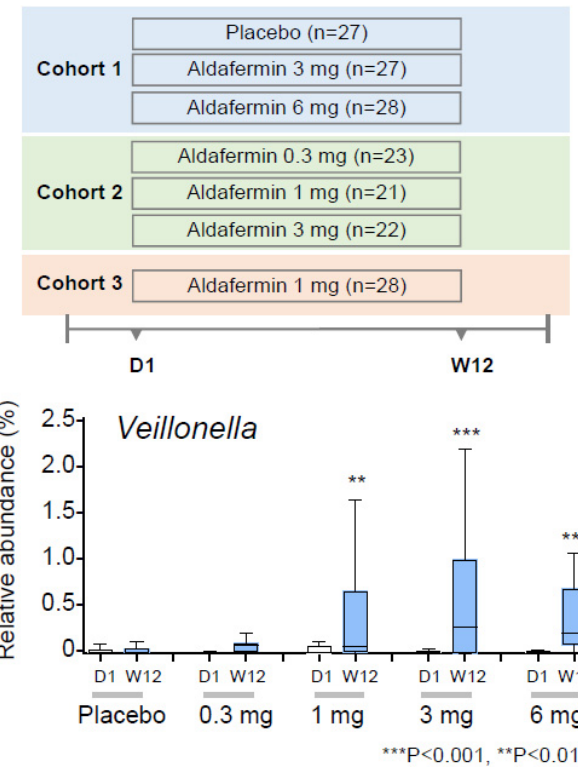
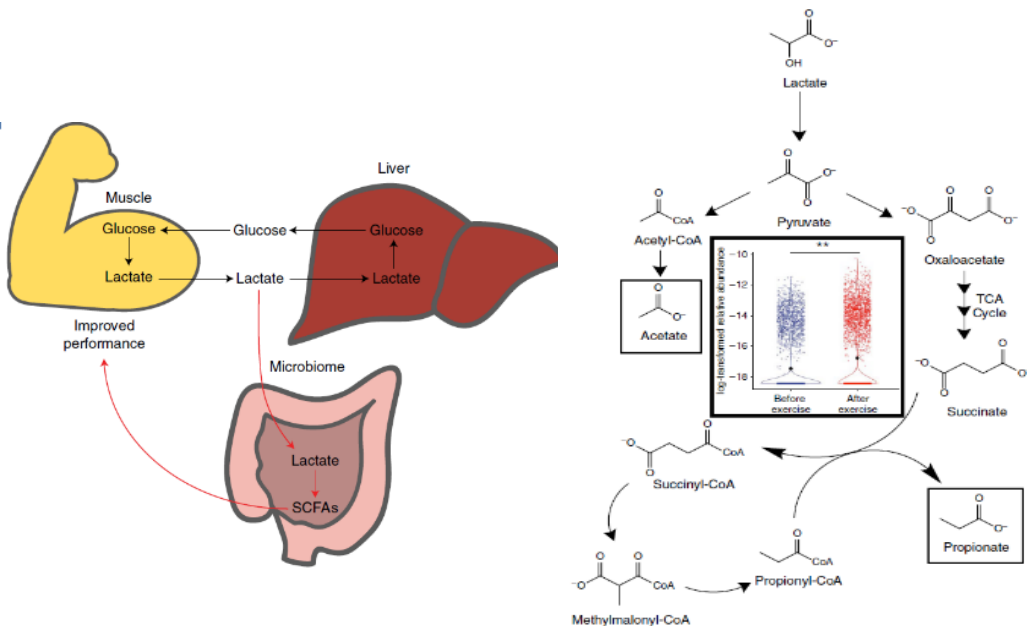
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<https://doi.org/10.1038/s41591-019-0485-4>

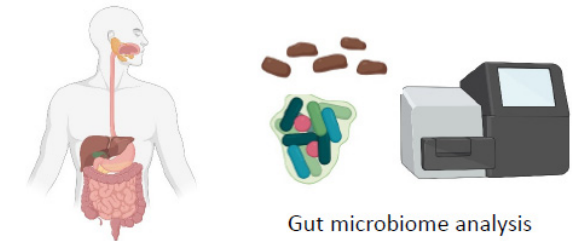
nature
medicine

Meta-omics analysis of elite athletes identifies a performance-enhancing microbe that functions via lactate metabolism

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Patients with NASH



FGF19 analog (Aldafermin)
↓ Bile acids ↑ Veillonella



- Previous studies in non-alcoholic steatohepatitis also revealed an enrichment in *Veillonella* with aldafermin

Conclusion



- PSC patients treated with aldafermin had stable gut microbial composition and diversity
- No taxonomic differences were observed except for an increase in the rare genus *Veillonella*, a commensal microbe known to have lactate-degrading and performance-enhancing properties
- These results echo our previous findings in non-alcoholic steatohepatitis, suggesting that *Veillonella* may serve as a microbiome-based marker for response to aldafermin irrespective of disease etiology

Acknowledgment

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