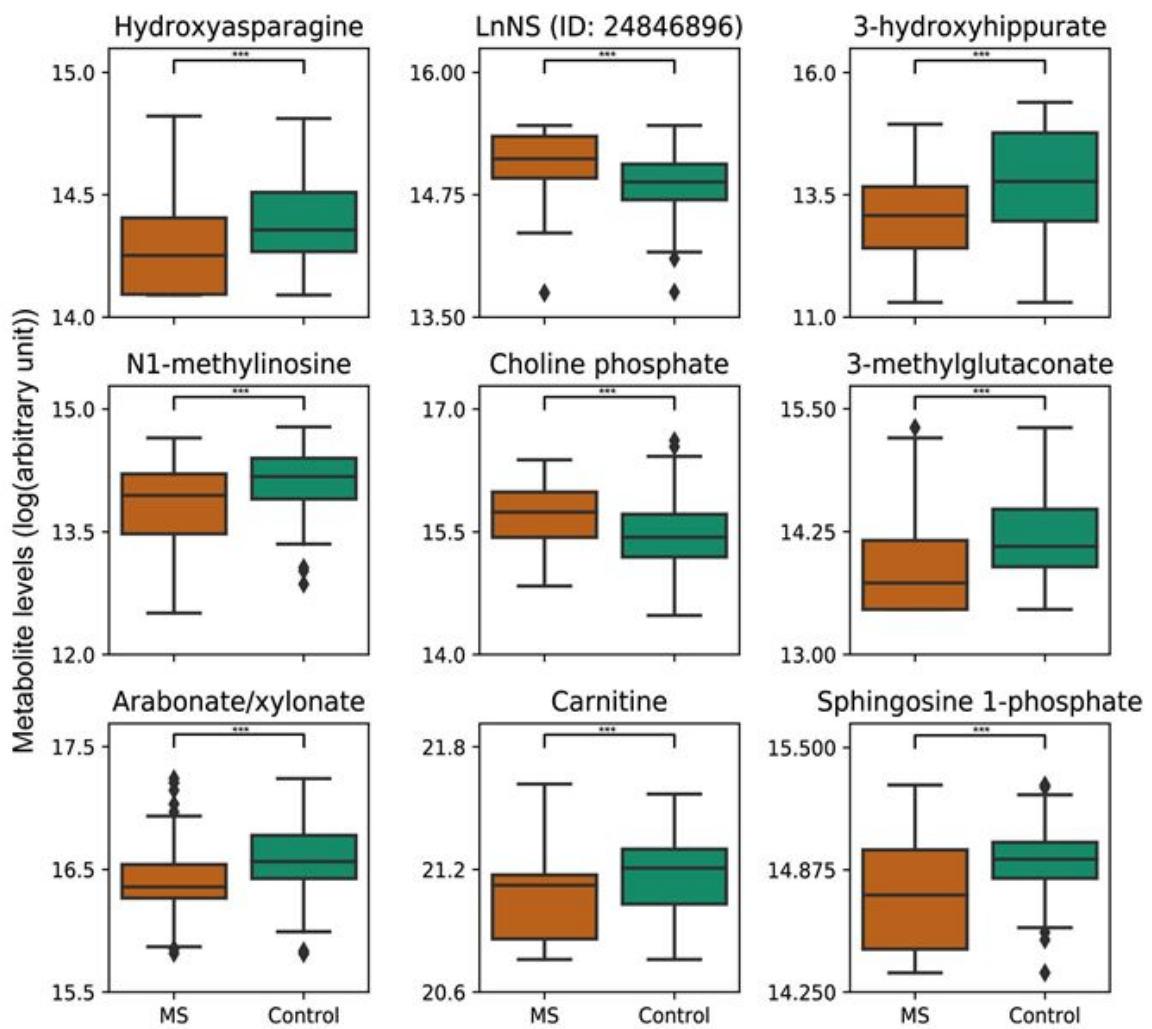


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Supplemental information

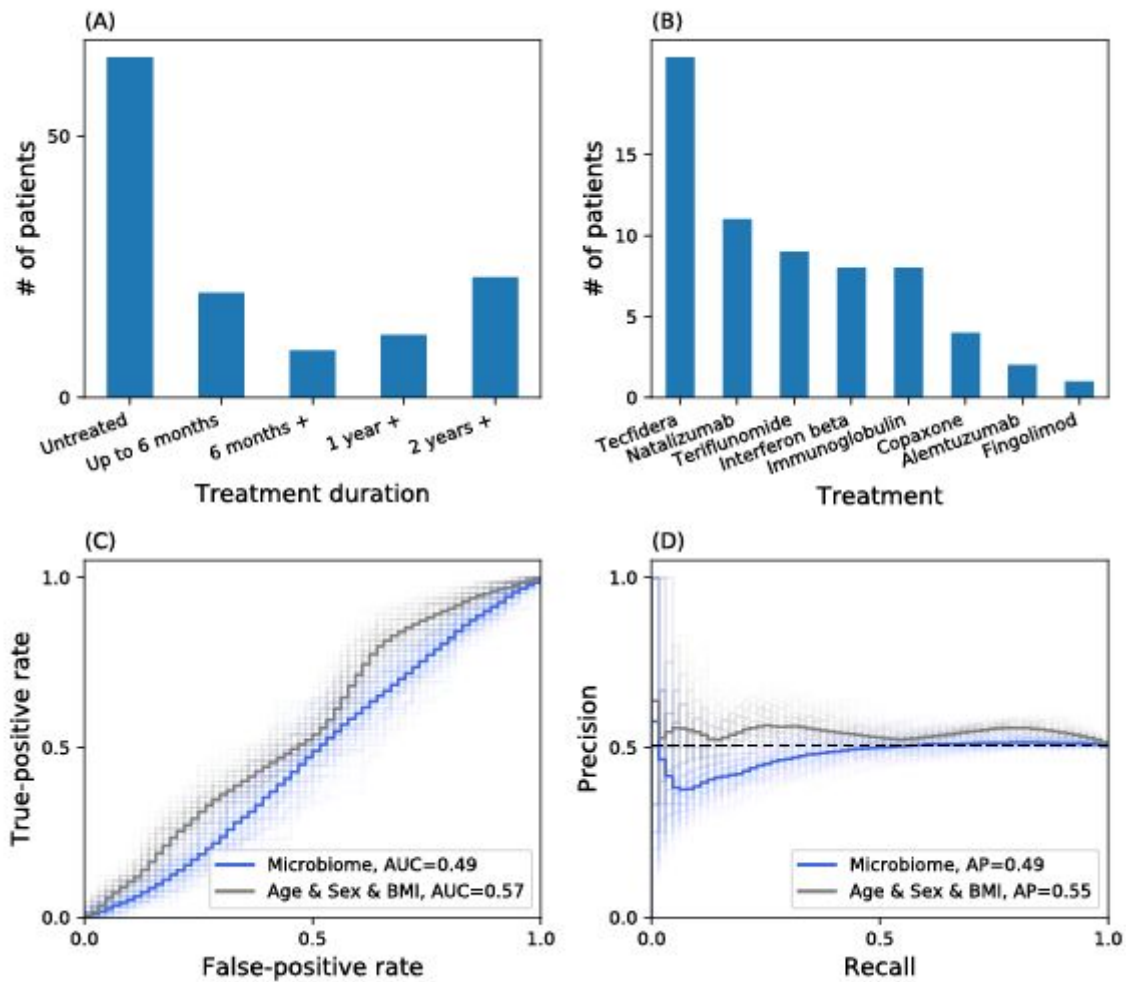
**Potential role of indolelactate and butyrate
in multiple sclerosis revealed by integrated
microbiome-metabolome analysis**

Izhak Levi, Michael Gurevich, Gal Perlman, David Magalashvili, Shay Menascu, Noam Bar, Anastasia Godneva, Liron Zahavi, Danyel Chermon, Noa Kosower, Bat Chen Wolf, Gal Malka, Maya Lotan-Pompan, Adina Weinberger, Erez Yirmiya, Daphna Rothschild, Sigal Leviatan, Avishag Tsur, Maria Didkin, Sapir Dreyer, Hen Eizikovitz, Yamit Titngi, Sue Mayost, Polina Sonis, Mark Dolev, Yael Stern, Anat Achiron, and Eran Segal



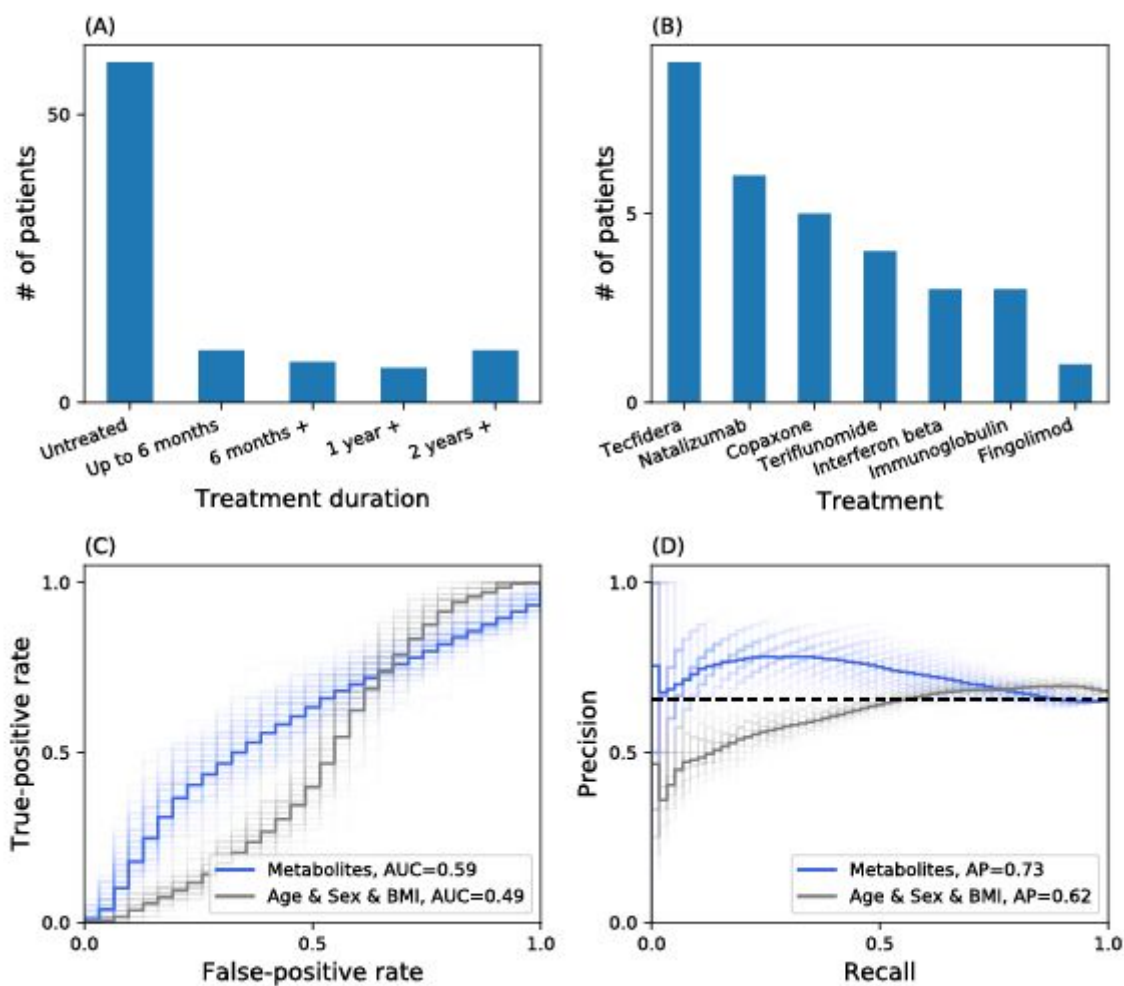
Supplementary Figure 1 | Most significantly different metabolites between MS and controls; Related to Figure 3A.

Box plots (center, median; box, interquartile range (IQR); whiskers, $1.5 \times$ IQR) showing metabolites levels for 90 MS patients and 90 controls, for the 9 most significantly different metabolites (out of 42 significantly different metabolites).



Supplementary Figure 2 | A machine learning model based on microbiome data was not able to separate the MS treated patients from the MS untreated patients; Related to STAR Methods - MS treatment effects.

(A) Treatment duration and (B) treatment type in MS cohort with microbiome data. (C) Receiver operating characteristic curve and (D) Precision recall curve for prediction of treatment group (MS treated vs. MS untreated) using XGBoost model, average of 100 models. The light lines represent results of each model, the dark lines represent the mean of 100 models. Grey curve represents baseline prediction with age, gender, and BMI features. (Area-under-curve=0.567, 95% CI = [0.563, 0.571], average precision=0.552, 95% CI = [0.547, 0.556]). Blue line represents prediction results using microbial features. (Area-under-curve=0.486, 95% CI = [0.480, 0.491], average precision=0.488, 95% CI = [0.484, 0.493]). The XGBoost model with microbial features was not able to separate the two groups.



Supplementary Figure 3 | A machine learning model based on metabolomics data yielded only a moderate separation between MS treated patients and MS untreated patients; Related to STAR Methods.

(A) Treatment duration and (B) treatment type in MS cohort with metabolomics data. (C) Receiver operating characteristic curve and (D) Precision recall curve for prediction of treatment group (MS treated vs. MS untreated) using XGBoost model, average of 100 models. The light lines represent results of each model, the dark lines represent the mean of 100 models. Grey curve represents baseline prediction with possible covariates (age, gender and BMI) as the features. (Area-under-curve=0.493, 95% CI = [0.488, 0.499], average precision=0.622, 95% CI = [0.619, 0.626]). Blue line represents prediction results using metabolites levels as the features. (Area-under-curve=0.593, 95% CI = [0.588, 0.599], average precision=0.731, 95% CI = [0.727, 0.735]). The XGBoost model with metabolomics as features separated moderately the two groups.