

# Host Lipidomic Profile Associated With Adverse Tuberculosis Treatment Outcomes

On behalf of the CTRIUMPH team:

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## Background

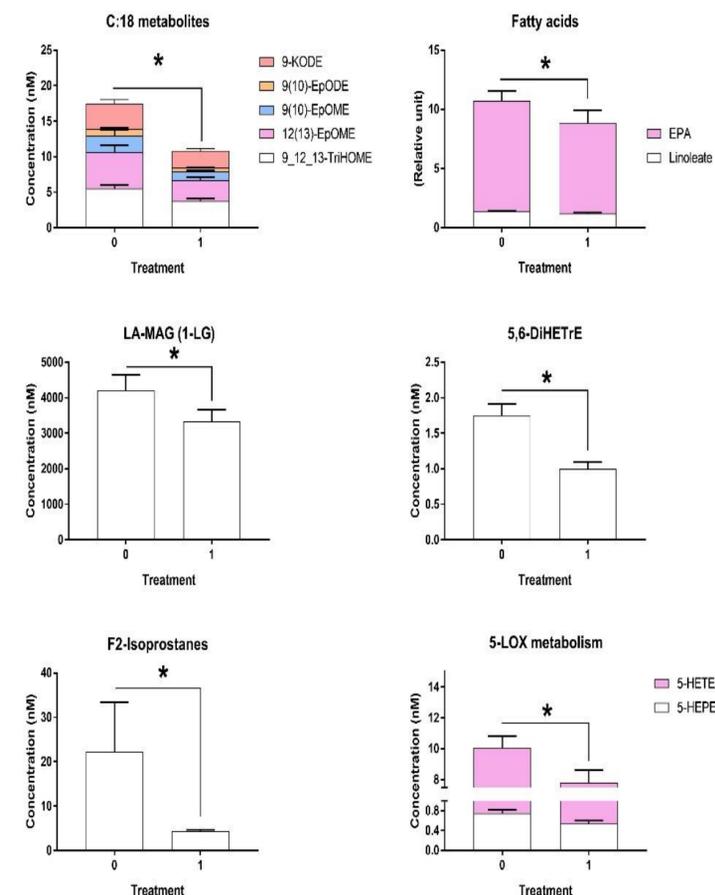
- 'Omics' approaches are increasingly used to identify biomarkers for disease outcomes
- In the field of TB – major focus on host transcriptomics
- Host lipids also play significant role in inflammation and disease outcomes, but studies are lacking on the following topics:
  - Characterization of the host lipidome in those with TB disease
  - Determine profile of host lipidome that may be associated with treatment outcomes such as:
    - TB treatment failure
    - TB recurrence
    - TB-related death
- RePORT biorepository provides an opportunity to utilize bio-banked plasma samples to assess host lipidome and link it with TB treatment outcomes
  - Utilized samples from individuals with TB disease in Pune and Chennai from the CTRIUMPH study

## Study Population Characteristics

	All N=289	Cases N=104	Controls N=185	p-value
<b>Age (median (IQR))</b>	35 (23-48)	33 (22.5-33)	35 (24-48)	0.54
<b>Male Gender (%)</b>	63%	63%	63%	0.90
<b>BMI (median (IQR))</b>	17.3 (15.6-19.9)	16.3 (14.7-18.7)	17.9 (15.8-20.3)	0.001
<b>Diabetic (%)</b>	25%	25%	25%	0.99
<b>HIV+ (%)</b>	5%	3.9%	6.0%	0.58
<b>Current Smokers (%)</b>	13%	16.4%	10.8%	0.20
<b>Alcohol Consumers (%)</b>	40%	45.2%	38.4%	0.27

**Table 1.** Used ranksum test (continuous variables) and chi-squared test to assess differences in covariates by case-control status

## Results



**Figure 1.** Differences in level of oxylipins, fatty acids and monoacyl glycerols between the treatments. All the data are significant with the p-value < 0.05. Error bars represent the standard error of the mean.

## METHODS

- A case-control study (N=289) nested within the CTRIUMPH cohort
  - Cases (n=104): Those with a composite outcome of adverse TB treatment outcomes
    - TB treatment failure
    - TB recurrence
    - TB-related death
  - Controls (n=185): Age and gender matched
- Studied association of baseline (pre-treatment) host plasma lipidome with outcomes
- Two panels assessed by LC-MS/MS:
  - Complex lipids: Untargeted approach
  - Oxylipins: Targeted approach
- Statistical analysis: Analysis of variance

## CONCLUSIONS AND FUTURE DIRECTIONS

- From the targeted panel, we identified 12 lipids that were significantly different between cases and controls:
  - Various 18-carbon metabolites derived from linoleic acid and  $\alpha$ -linolenic acid
  - Baseline levels of linoleic acid, eicosapentaenoic acid, F2-isoprostanes, 5-hydroxyeicosatetraenoic acid (5-HETE) and 5-hydroxyeicosapenta-enoic acid (5-HEPE) were lower in cases compared to controls
- These lipids could predict future adverse treatment outcomes
  - Future studies are needed to determine function
  - Those directly contributing to adverse outcomes could serve as therapeutic targets
- Future Directions:
  - Analysis ongoing that combines both the targeted and untargeted panels
  - Will also do analysis on individual outcomes:
    - Treatment failure only
    - Treatment failure + death within 6 months
    - TB recurrence only
    - Death Only
  - Future studies can validate in other cohorts (e.g. RePORT-wide) and other questions (TB incidence)