BREATHe Dissemination Meeting

Soluble Biomarker Studies

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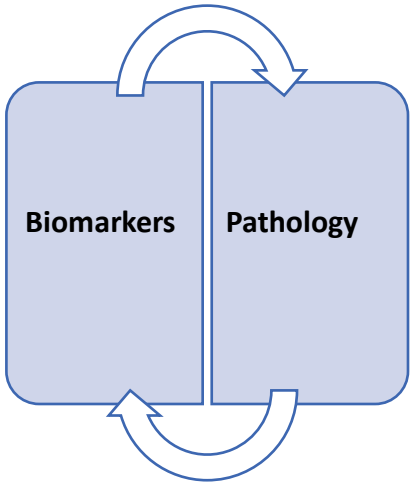
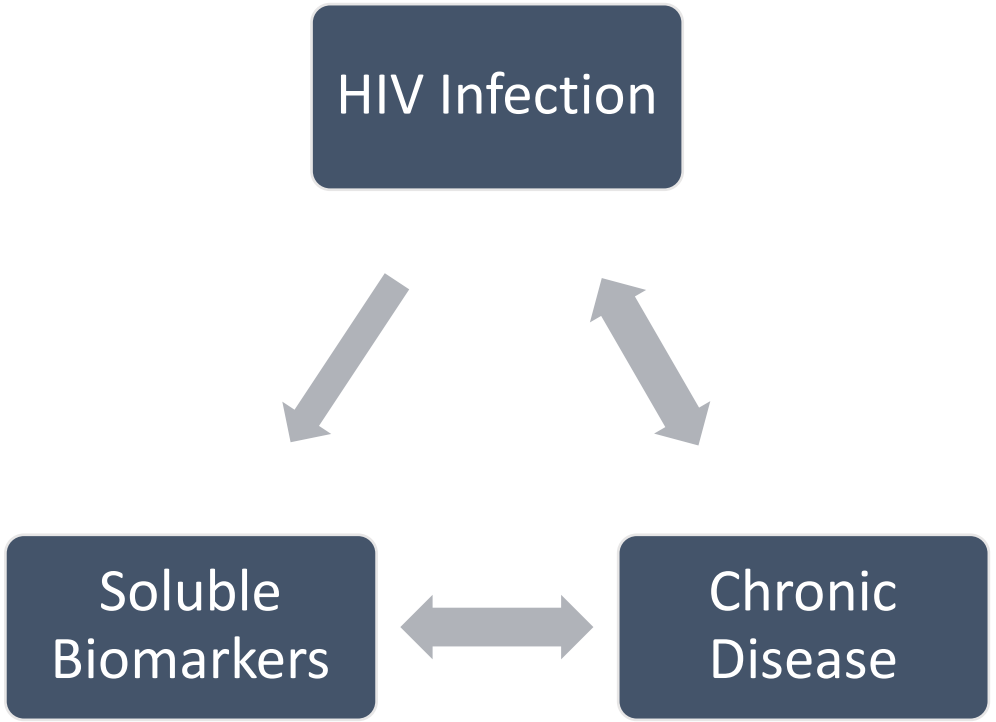
What are soluble Biomarkers and why are we interested in them?

- Chronic diseases are associated with changes in the expression of soluble proteins
- Irrespective of causality, proteins that are altered can be useful in understanding and treating disease

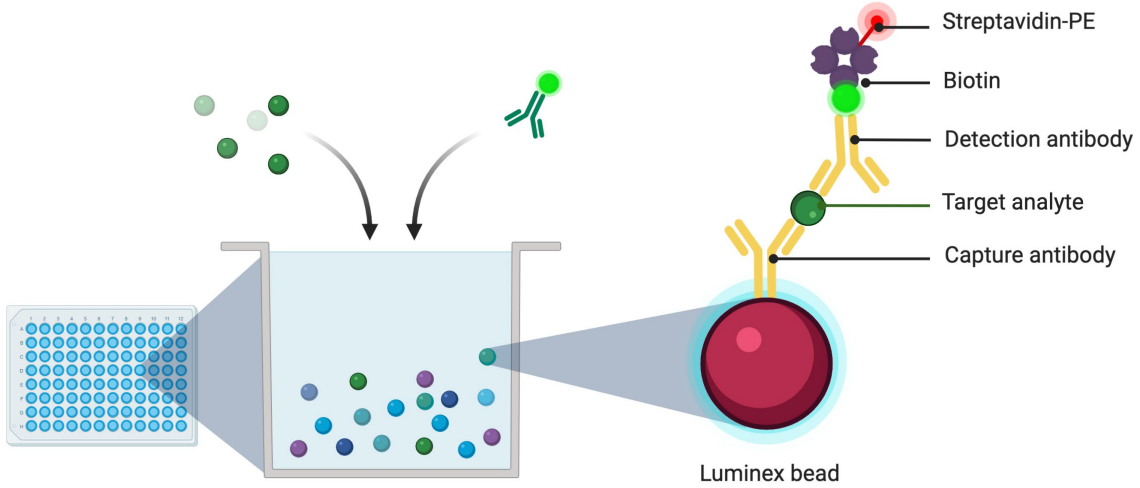


- Systemic Immune Activation
- Monocyte Activation
- T-Cell Activation
- Endothelial Activation
- Cellular Adhesion
- Coagulation
- Apoptosis
- Extracellular matrix degradation



Methods: How do you measure soluble biomarkers?

Luminex Principles:



Cross-Sectional Study

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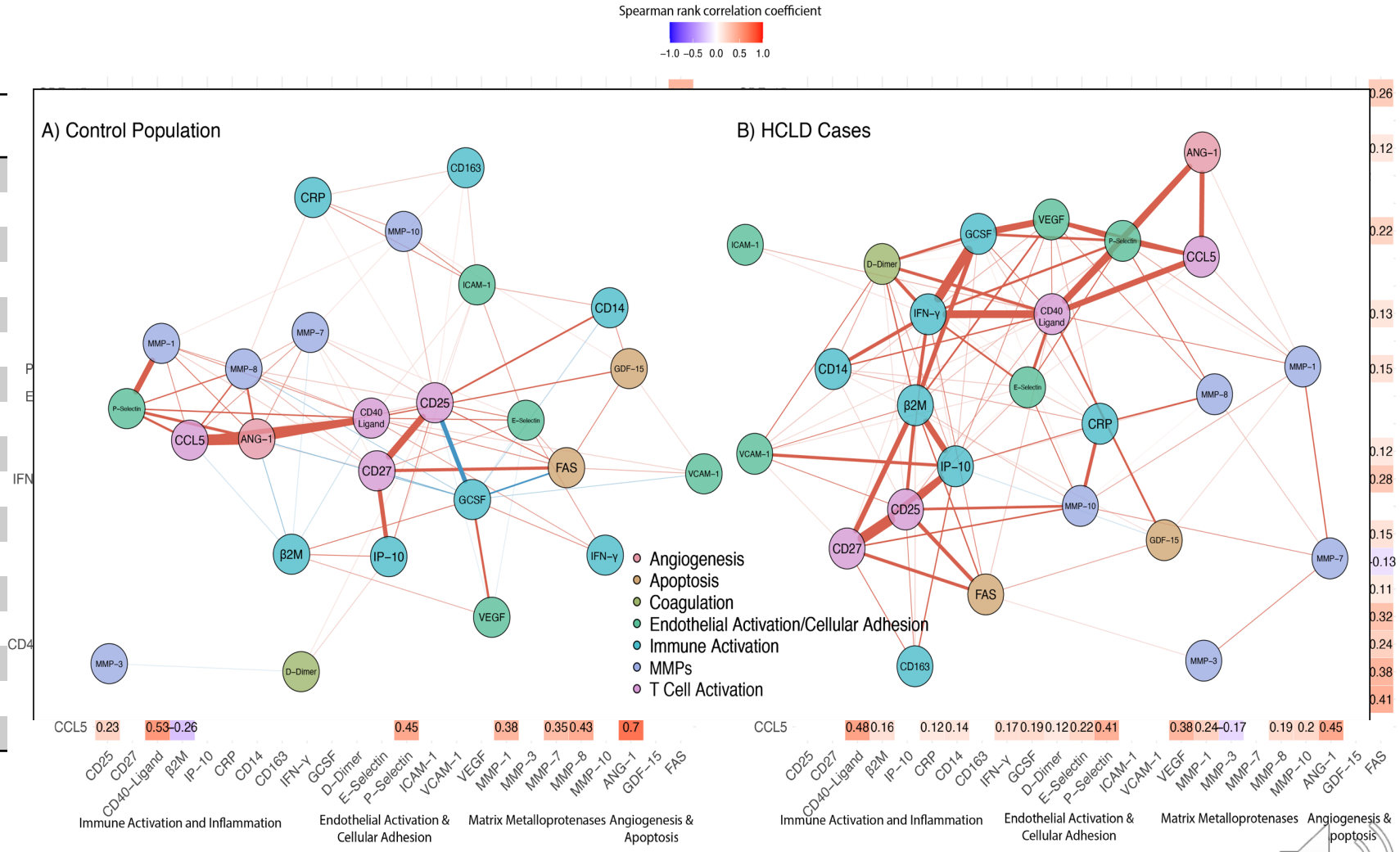
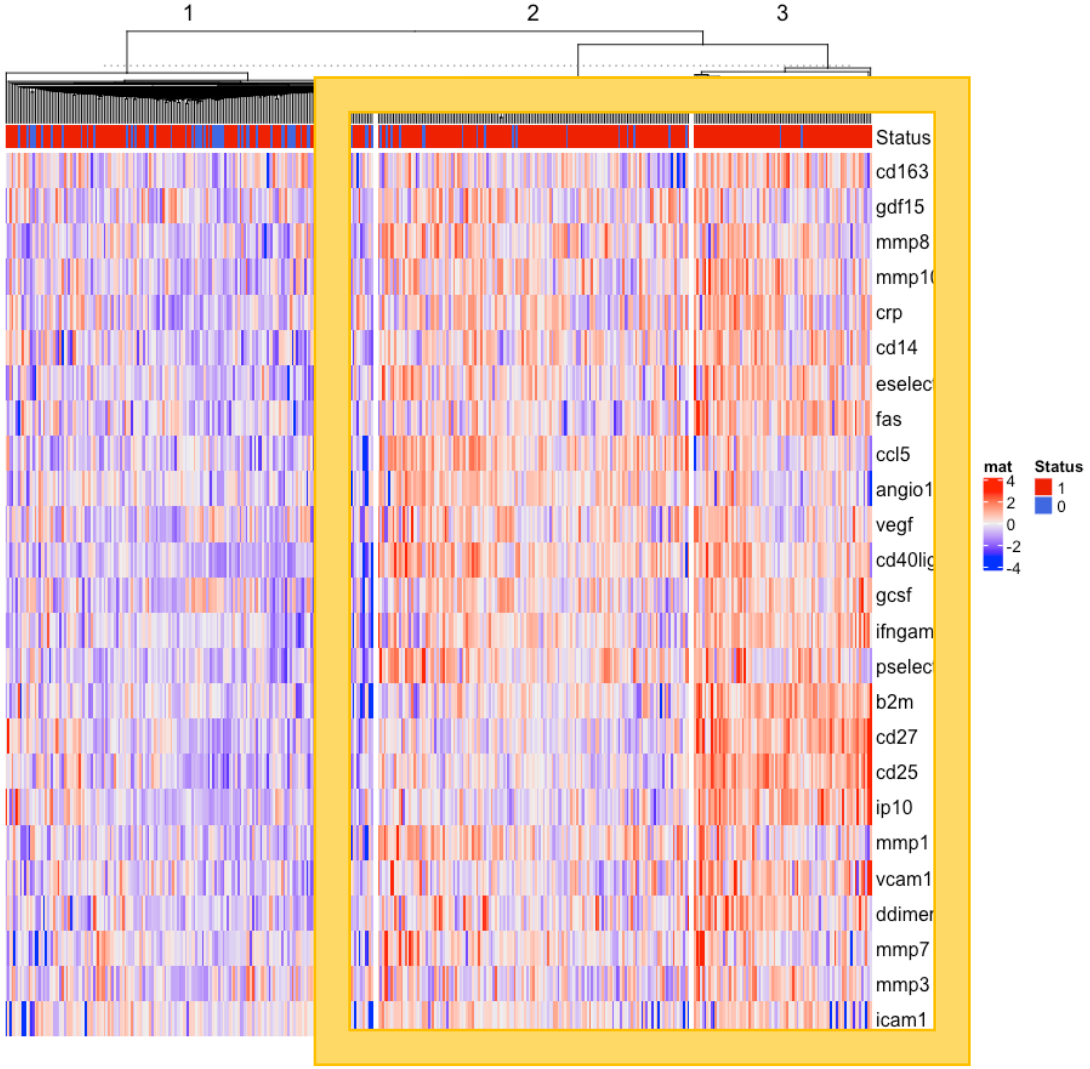
Predominantly T-cell activation biomarkers are associated with chronic lung disease in BREATHE

Biomarker (Log_{10} Scaled)	Adjusted Logistic Regression, OR (CI, P) *
MMP-1	1.35 (1.02-1.79, p=0.038)
MMP-7	1.37 (1.03-1.84, p=0.030)
MMP-10	1.57 (1.16-2.15, p=0.004)
Angiopoietin-1	1.50 (1.16-1.95, p=0.002)
sCD14	2.11 (1.58-2.88, p<0.001)
sCD25	2.68 (1.88-3.93, p<0.001)
sCD27	2.08 (1.49-2.99, p<0.001)
sCD40-Ligand	2.82 (2.02-4.05, p<0.001)
CRP	1.62 (1.21-2.21, p=0.002)
IP-10/CXCL10	1.98 (1.41-2.89, p<0.001)
D-Dimer +	1.68 (1.24-2.33, p=0.001)
E-Selectin	2.00 (1.46-2.79, p<0.001)
FAS	1.57 (1.19-2.11, p=0.002)
GCSF	0.72 (0.53-0.97, p=0.033)
IFN-γ	2.81 (1.86-4.46, p<0.001)
VCAM-1	1.56 (1.17-2.11, p=0.003)
VEGF	0.74 (0.56-0.98, p=0.039)

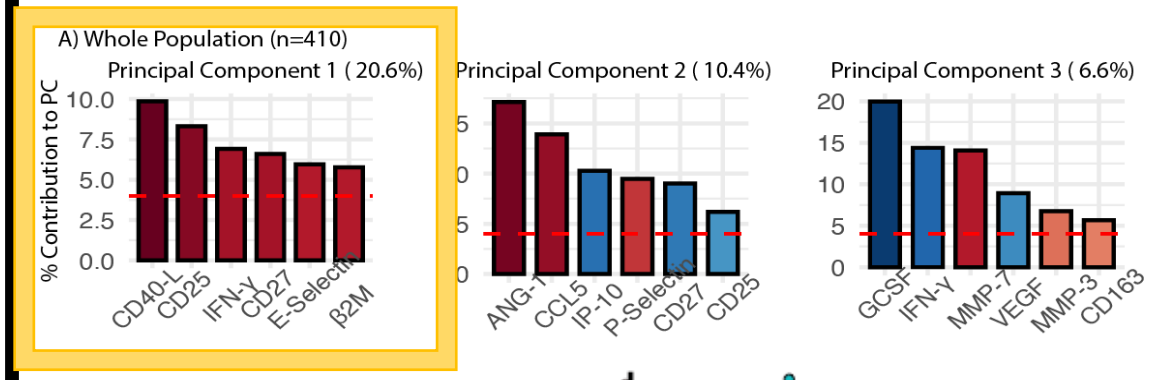


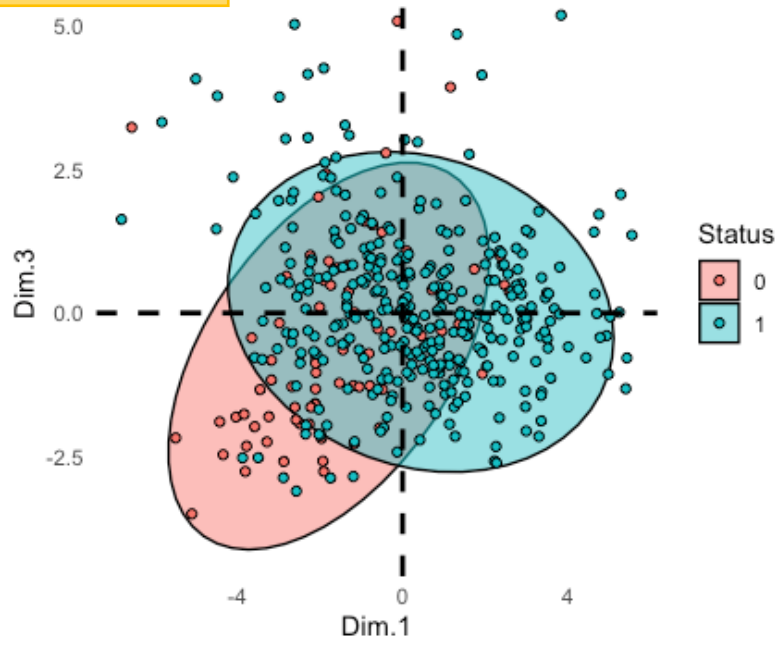
Findings supported by data-reduction techniques, both showing elevated immune activation in the CLD group

Hierarchical Clustering



Principal Component Analysis





Longitudinal Study

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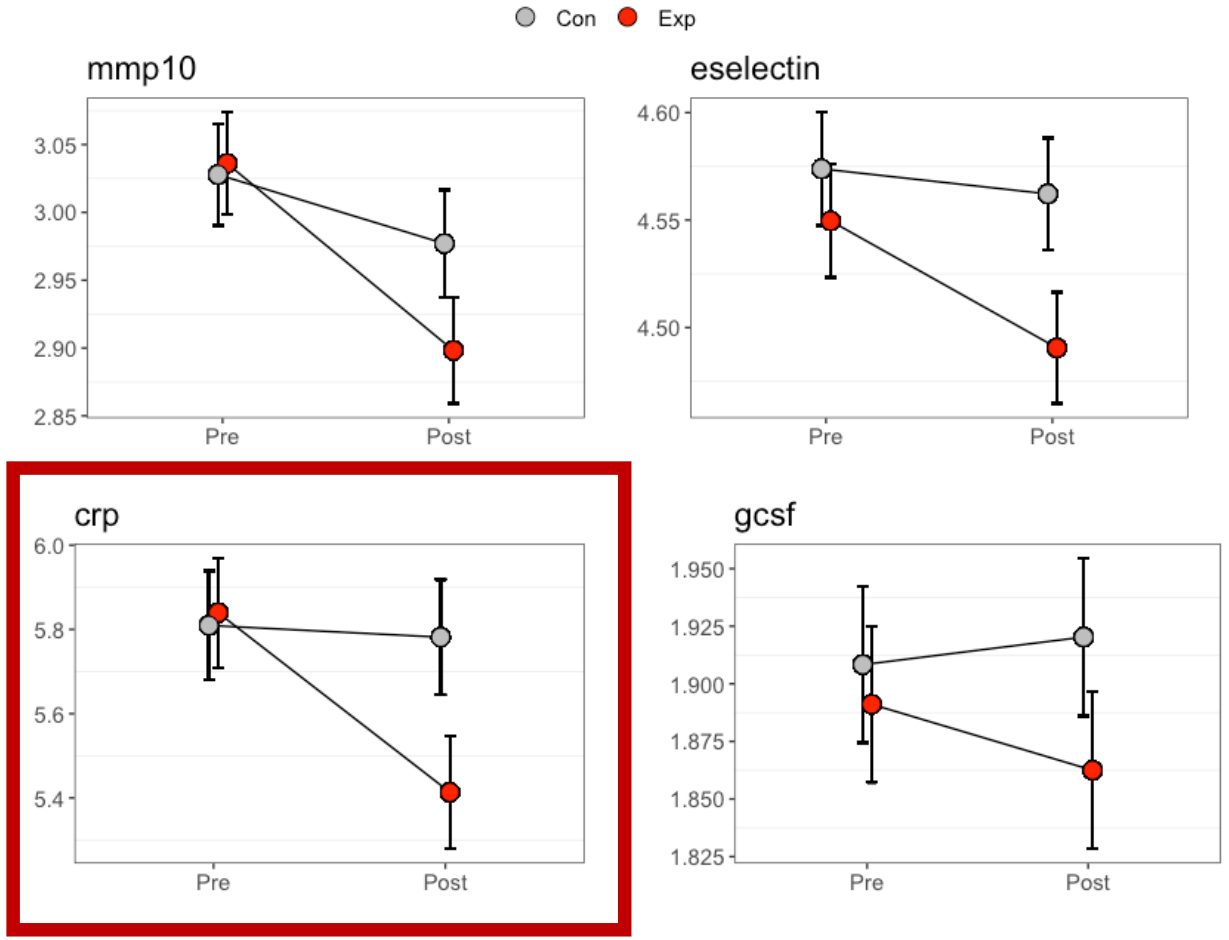
Does 12 month Azithromycin treatment affect levels of soluble biomarker?

=> ?

- Immunomodulatory effects of macrolides:

- ↓ Cytokine Production
- ↓ Chemotaxis
- ↓ ROS production
- ↓ Adhesion molecules

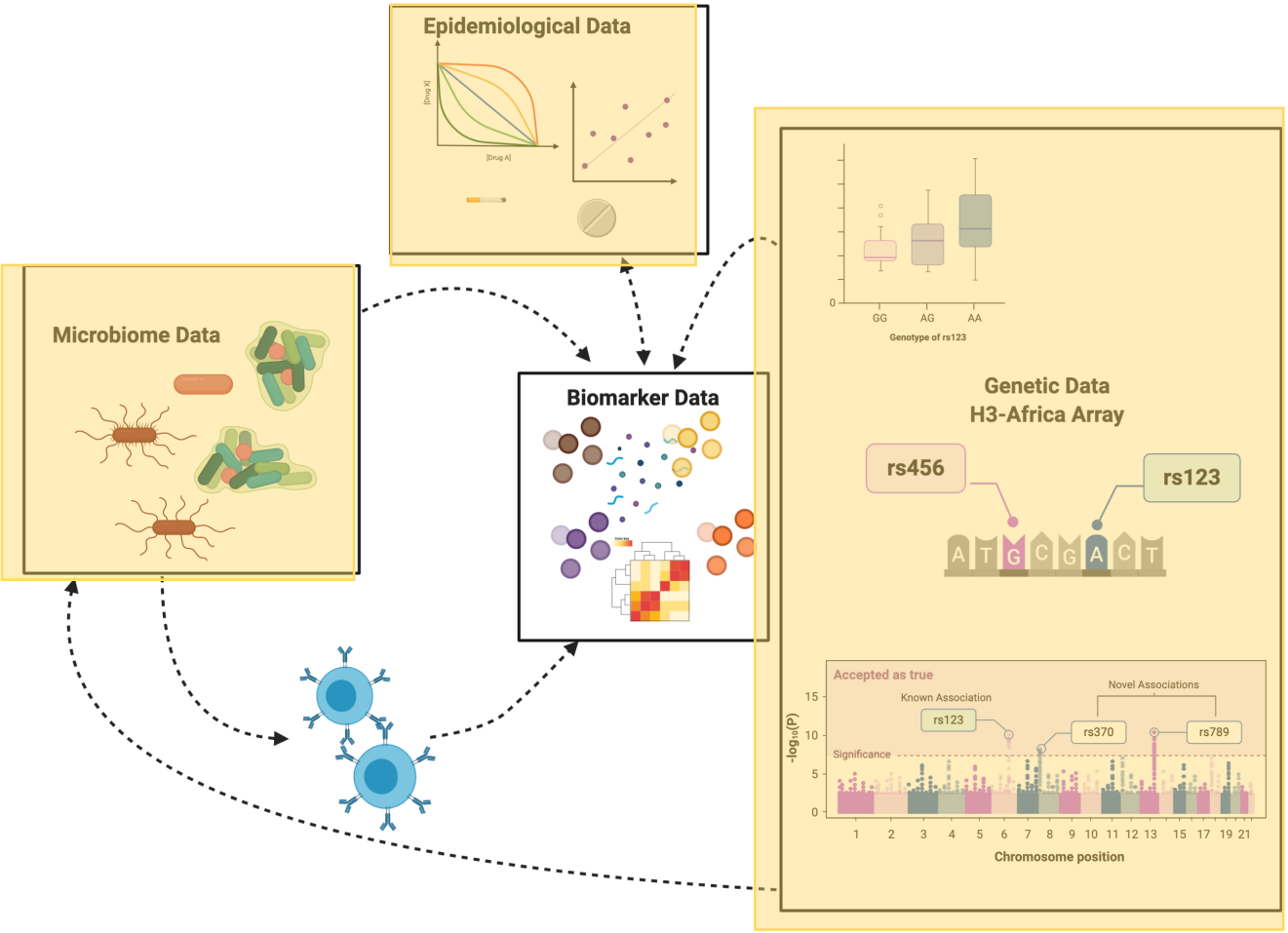
- Linear mixed model for each participant
- Four Biomarkers significantly different after treatment



Further Remarks

Future Plans:

- Biomarker data & epidemiology
- Biomarker data & microbiome
- Genetic understanding of biomarkers



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