



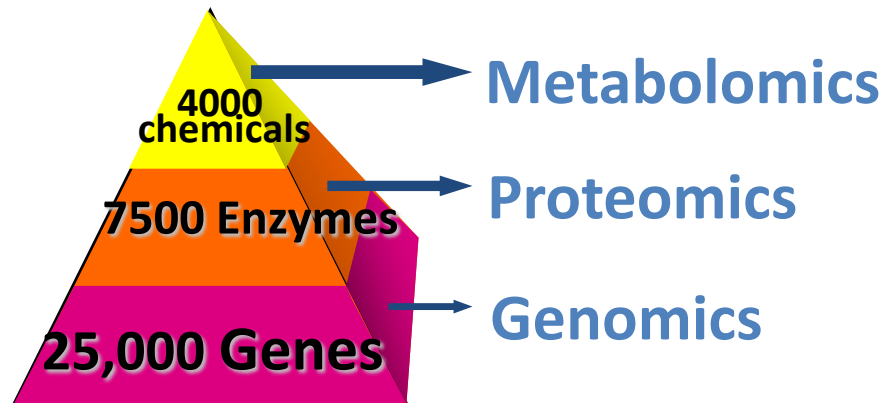
Metabolomics In IBD: A Novel Diagnostic Test – year 0.8

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Background - 1

- Metabolomics
 - The characterization of small molecular weight compounds in biofluids or tissues



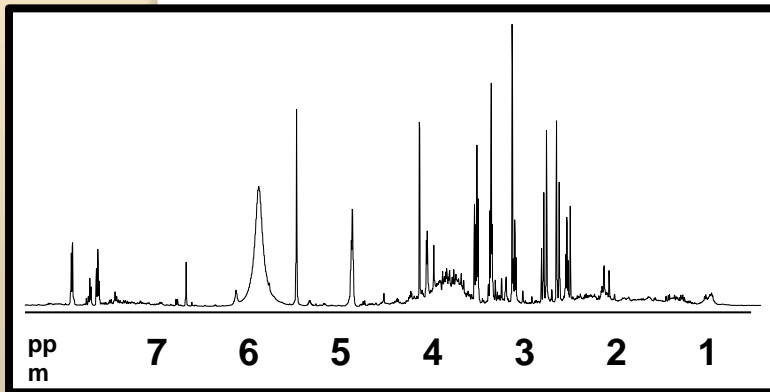
- The urinary metabolomic “fingerprint” reflects the somatic (minor) and luminal bacterial (major) constituency



Metabolomics Workflow



Biofluids or Extracts



Data Analysis



NMR or MS Chemical Analysis

Background - 2

- Altered luminal microflora play a key pathogenic role in IBD
 - Changes in microflora have been shown to markedly alter small molecule metabolites

Hypothesis

- Analysis of urinary metabolite profile (metabolomics) could differentiate individuals with different luminal bacterial profiles



Objective

- In the current study we examined urinary metabolomic profiles to differentiate patients with IBD from those without IBD
 - Develop a biomarker for IBD and a predictor of response to therapy



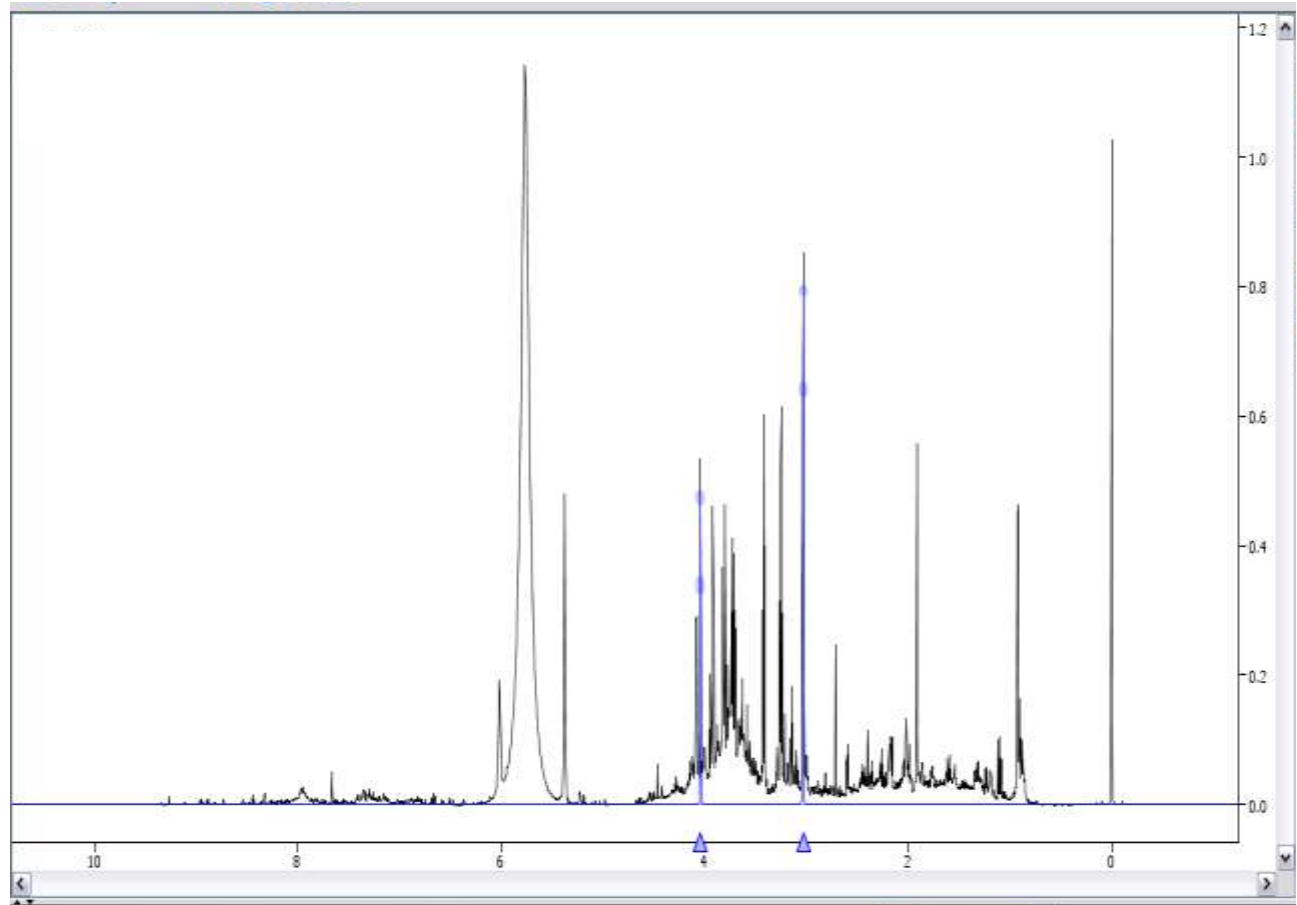
Methods

- Patients with IBD
 - provided a spot urine sample
 - completed a demographics questionnaire,
 - HBI (CD; n=77)
 - modified Mayo Score (UC; n=42)
- Patients with IBS (n=120) were controls
 - Metabolite concentrations were derived from analysis of 600Hz NMR spectra and sorted by *partial least squares discriminate analysis*



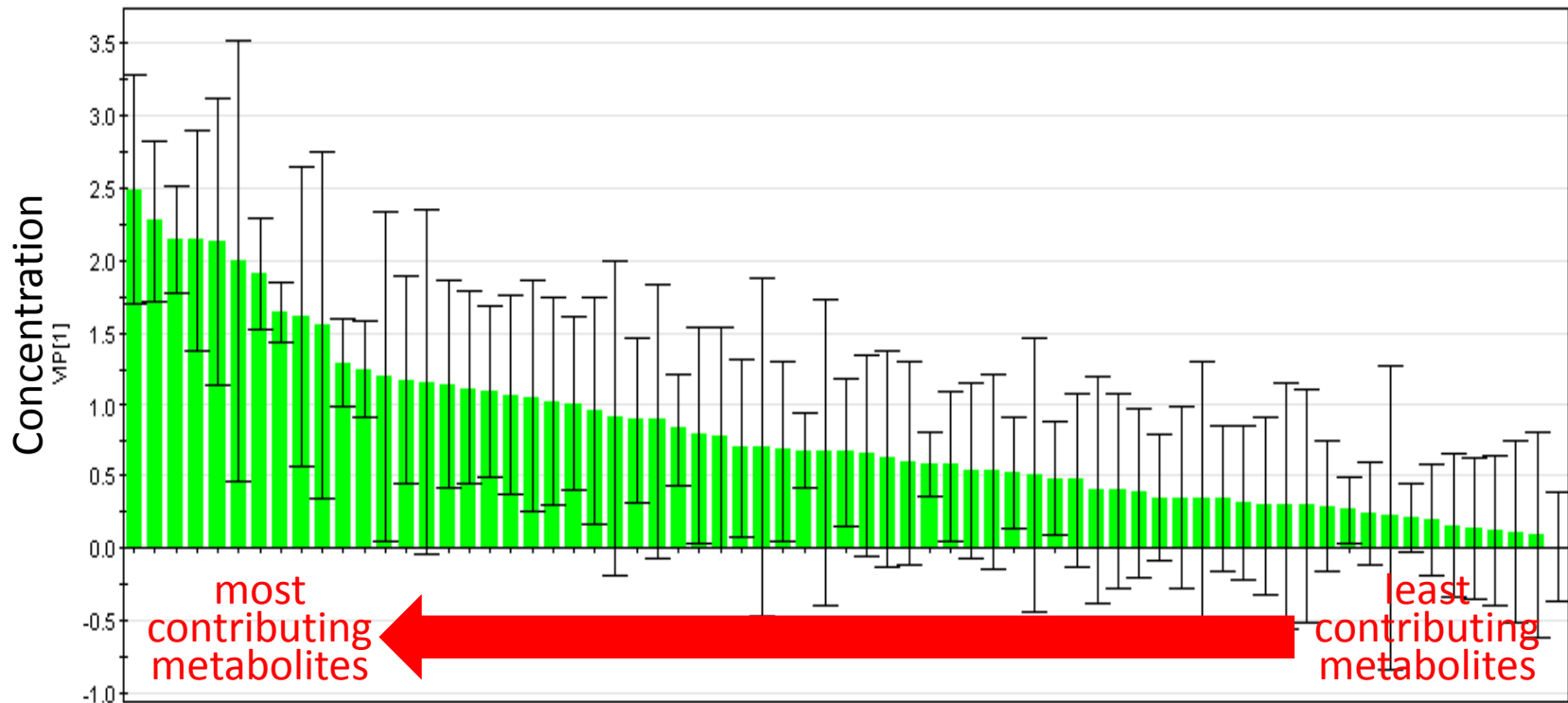
Urine Metabolomics

NMR spectra analysis defines 69 metabolites (Chenomx[®]NMRSuite v7.0)



Urine Metabolomics

*Partial least square discriminate analysis defines
“very important metabolites” and their concentrations*



N= 69 metabolites in order of
contribution to separation of group A from group B

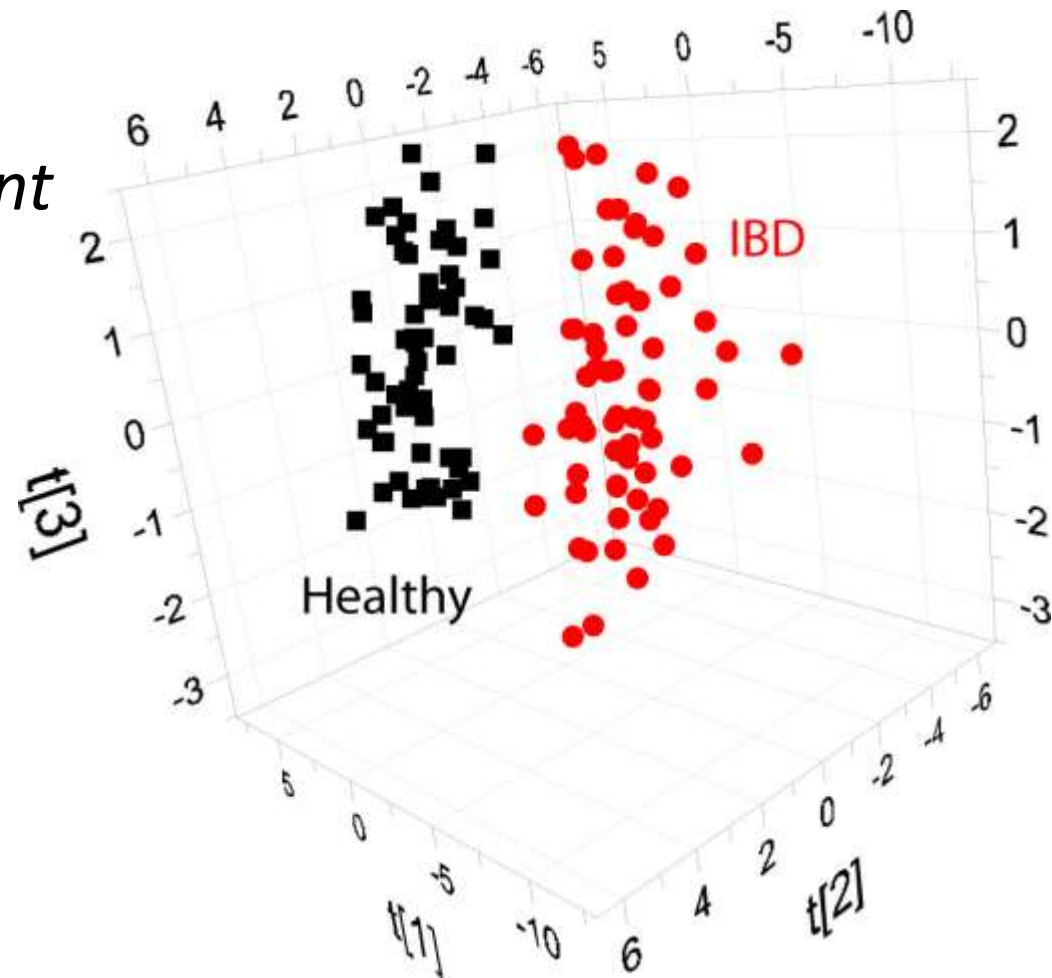


Results – IBD vs Control

Principle component analysis used 69 metabolites to separate each group

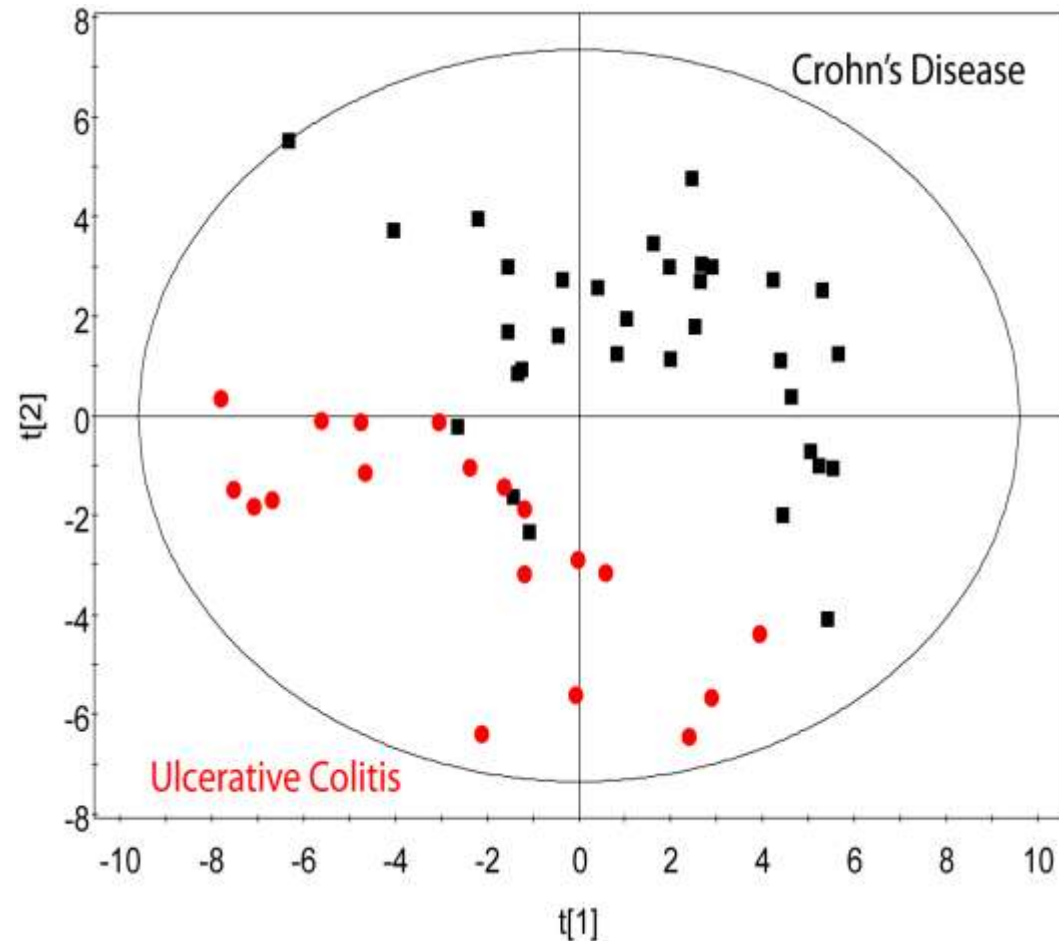
Sensitivity = 78%

Specificity = 89%



Results – Active CD vs Active UC

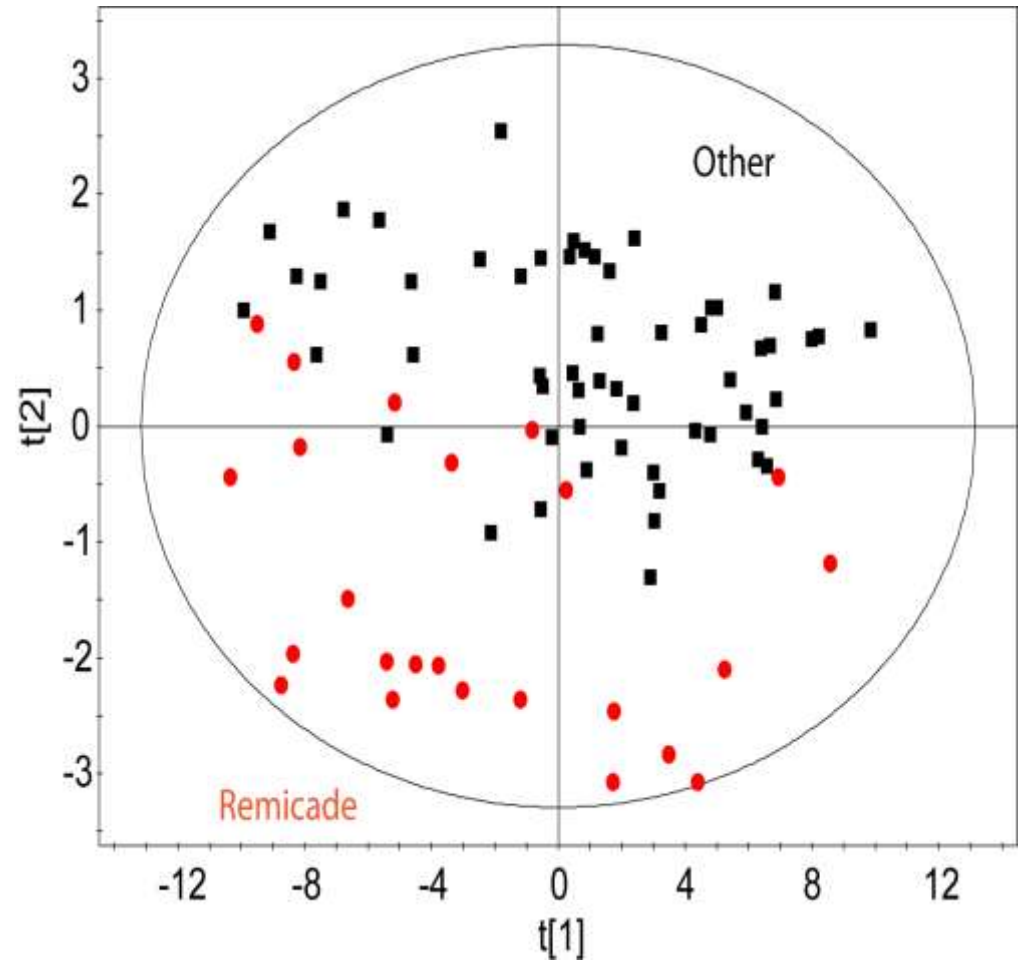
Separation of
patients with
active CD
vs active UC



Results – CD In Remission Infliximab vs Other Rx



Separation of
CD patients with
influxiamb-induced
vs other
medication-induced
remission



Change in Urinary Metabolites

Metabolite	Crohn's Disease	Ulcerative Colitis
Levogluconan*	↑	↓
Sucrose	↑	
Hippurate	↓	
Fucose*		↑
Creatine		↓
TMAO*	↑	
DMA*	↑	

* of bacterial origin



Summary

- Urinary metabolomics can separate “diagnose”:
 - patients with IBD from patients with IBS
 - patients with CD from UC
- Year 2
 - recruit 150 patients in each group
 - Identify predictors of response to therapy
 - Immunosuppressants
 - Biologics
 - insight into origin of the metabolites

