Exploring the Metabolome of the IL10$^{-/-}$ Gene Deficient Mouse

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Introduction

The interleukin-10-deficient (IL10$^{-/-}$) mouse is a model for inflammatory bowel disease (IBD).

Biomarkers predictive of intestinal inflammation are sought to non-invasively measure the efficacy of functional foods in reducing intestinal inflammation.

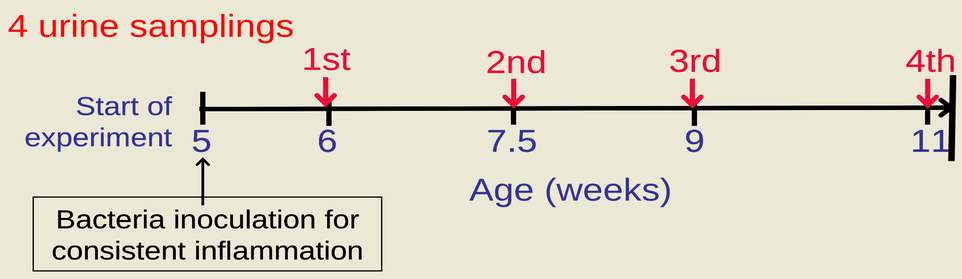
We compare biomarker candidates generated by GC-MS and LC-MS metabolomic analysis of urine from IL10$^{-/-}$ mice.

We distinguish between metabolic differences associated with:

- intestinal inflammation
- genetic differences between mouse strains
- differences in intestinal microflora**.**

Methods

Mouse experiments[1]



GC-MS and Ion Trap LC-MS[2]

Short column (infusion)
Long column LC
UHPLC

Metabolic differences
IL10$^{-/-}$ and WT mice

Validation experiment ± bacterial innoculation[3]
(dosed vs. specific pathogen free (SPF) treatments)

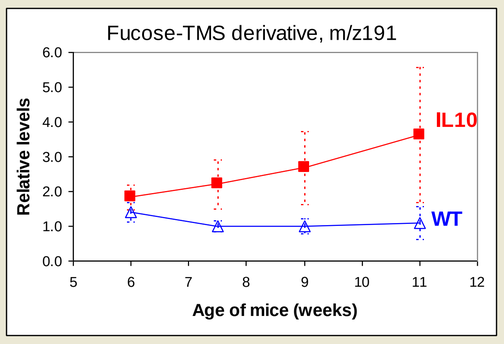
metabolites specifically associated with intestinal inflammation

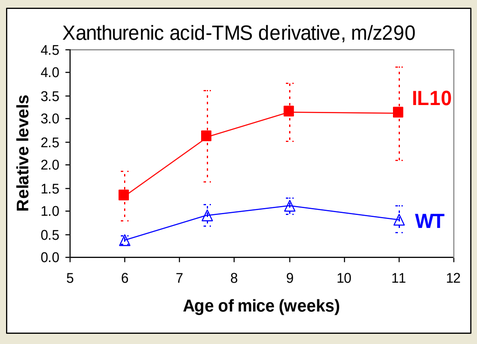
Results

1. Metabolic differences IL10$^{-/-}$ and WT mice

***GC-MS*[1]**

Fucose
Xanthurenic acid
Dicarboxylic Acids:
- Glutarate
- 2-Hydroxyglutarate
- 2-Hydroxyadipate
Hexanoylglycine
Unknowns





***LC-MS*[2]**

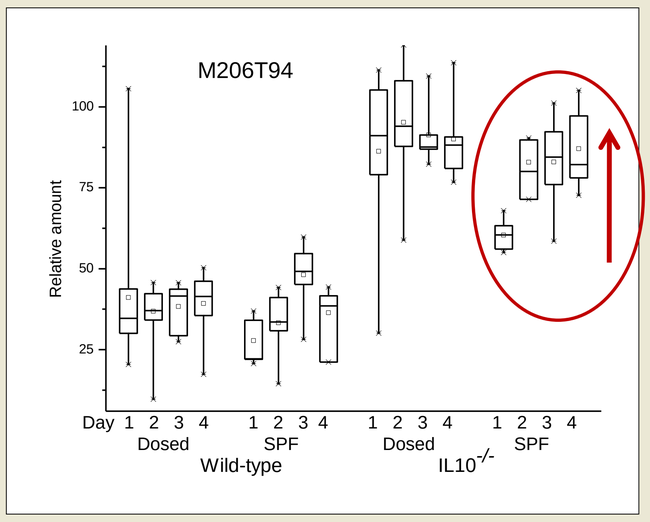
Positive Ions

Short LC	
xcms	wavelet
382	382
151	519
165	285
572	151
252	118
519	
263	

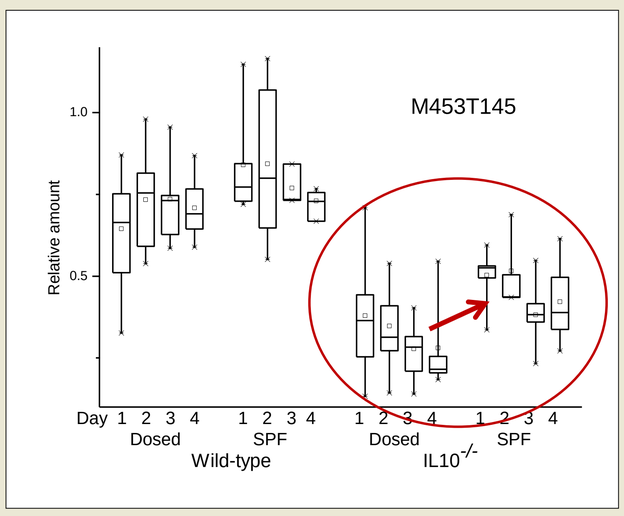
Negative Ions

Short LC	Long LC xcms	UPLC	Short LC wavelet	Hypersorb xcms
609	224	178	160	586
160	202	274	609	587
823	366	224	824	639
418	134	357	823	414
204	179	229	766	412
809	178	466	822	482
752	121	409	204	789
766	276	184	453	575
611	161	180	540	577
597	177	233	110	435
810	676	386	810	481
419	161	204	205	700
205	358	230	840	509
636	160	182	765	684
260	357	177	752	349
308	204	431	610	398
231	532	283	308	559
540	542	369	753	625
495	205	359	233	825
405	282	185	172	282

2. Metabolites associated with inflammation[3]



xanthurenic acid m/z 206^{+}



α-CEHC glucuronide m/z 453^{-}

Summary

Complementary techniques extend coverage of the metabolome.

GCMS identified 4 metabolites and 11 unknowns associated with intestinal inflammation.

LCMS identified xanthurenic acid and α-CEHC glucuronide as associated with intestinal inflammation as well as a number of other positive and negative candidate ions of unknown structure.

References: [1] Lin *et al*. *J. Proteome Res.* 8, 2045, 2009. [2] Otter *et al*. *J. Biomed. Biotech.* 6, 974, 2011. [3] Lin *et al*. *J. Proteome Res.* 9,1965, 2010.