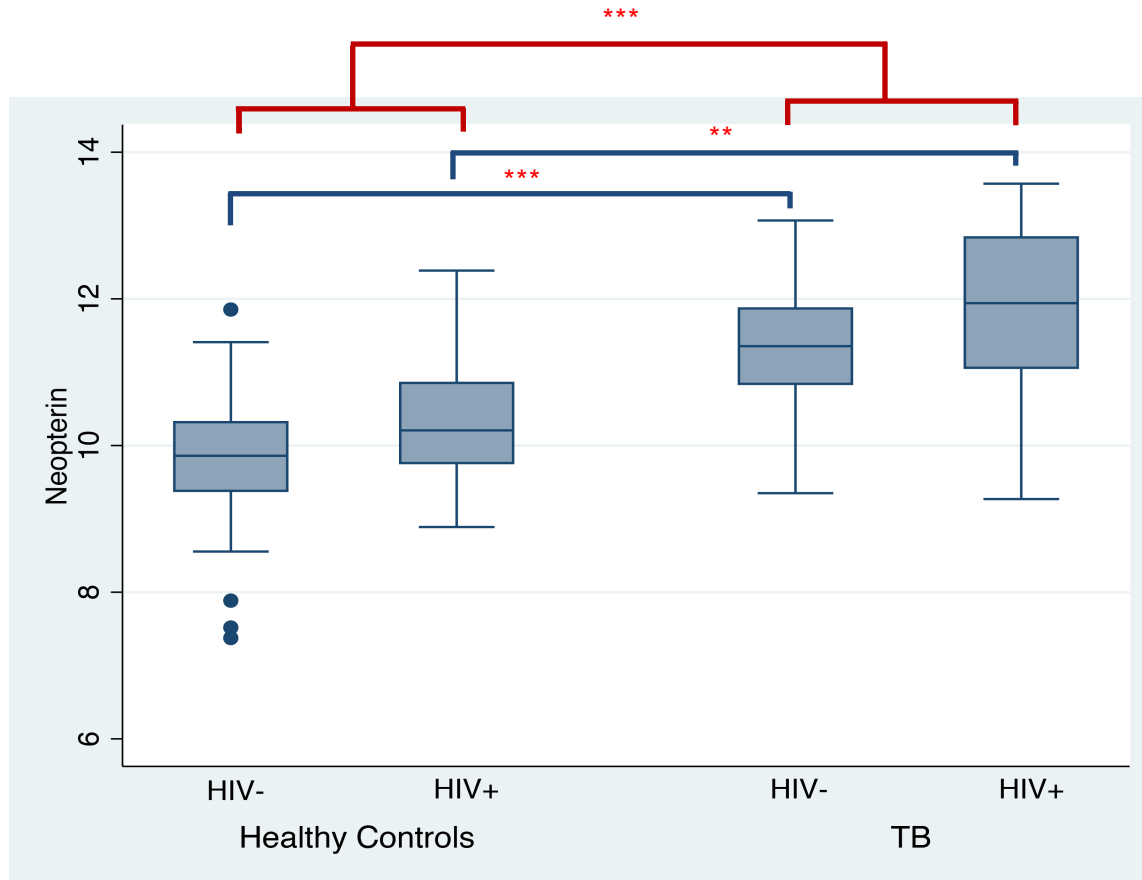
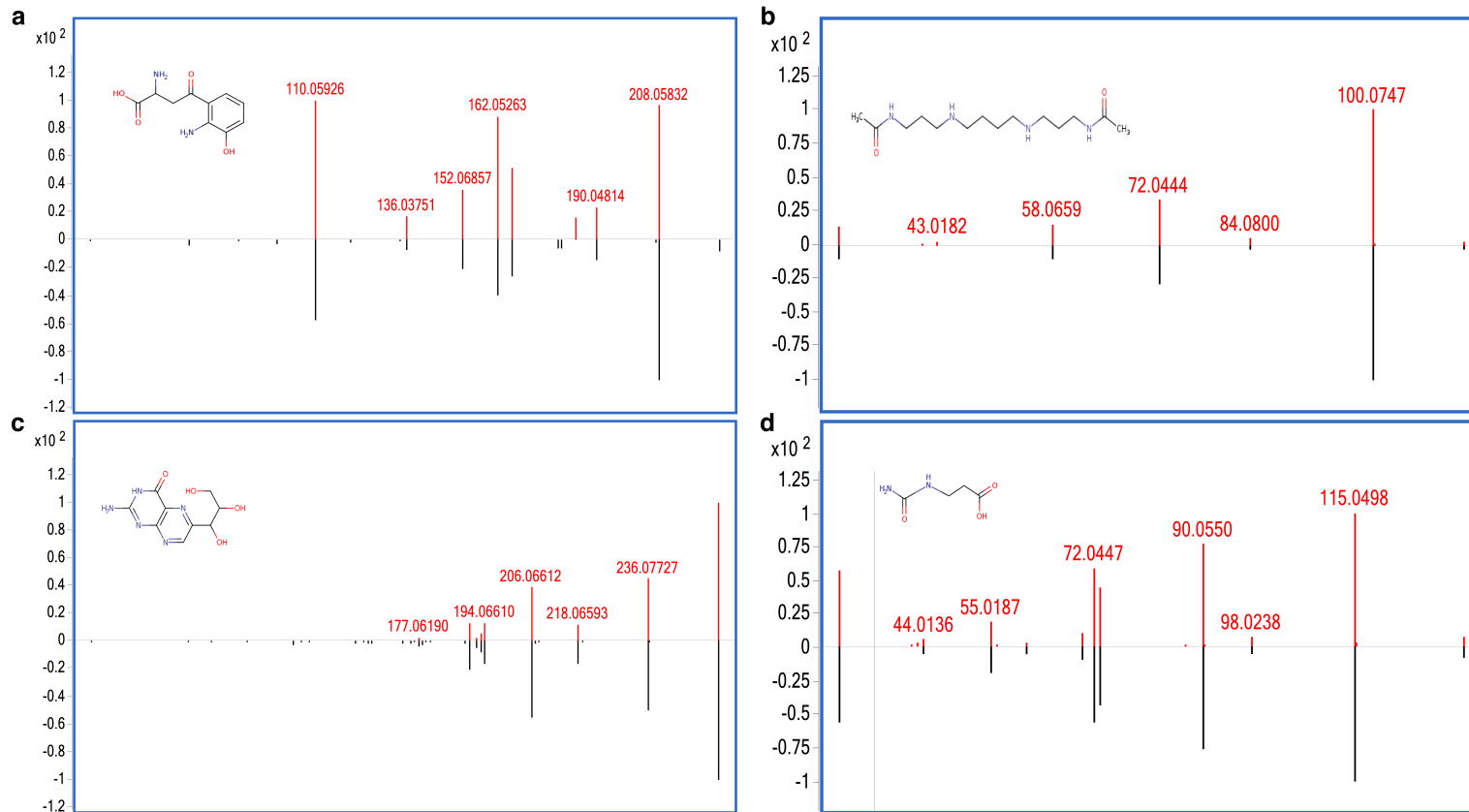


Supplementary Figure 1: Discovery Cohort Study Enrollment (Haiti)

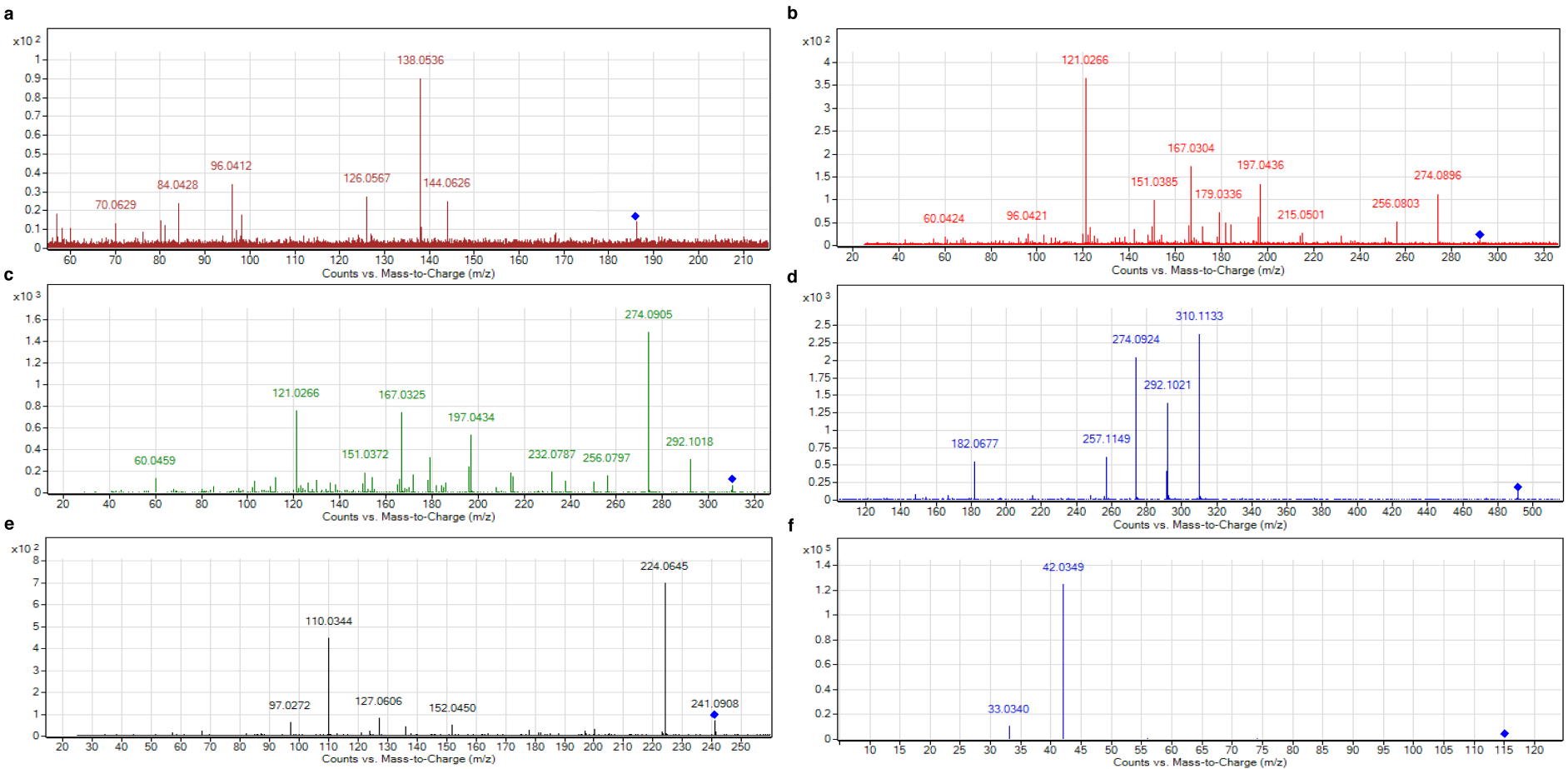


Supplementary Figure 2: Levels of Neopterin in HIV Infected and Uninfected Participants. Box plots showing abundance of neopterin in the discovery cohort when comparing HIV infected (n=31) and HIV uninfected participants (n=173). After adjustment for HIV status neopterin remains significantly increased in active TB. Abundance is shown on Log2 scale. Wilcoxon rank some test. ** p-value <0.001, *** p-value <0.0001.



Supplementary Figure 3: MS/MS Spectra of Identified Metabolites Compared to Pure Chemical Standard.

Mirror plots showing MS/MS spectra of identified metabolites from representative urine sample (red) compared with chemical standard (black). (a) Hydroxykynurenine (m/z 225.0845) (b) Diacetylspermine (m/z 144.1241) (c) Neopterin (m/z 254.0859) (d) Ureidopropionic acid (m/z 133.0600). Parent mass is shown on far right. Chemical structure shown on top left.



Supplementary Figure 4: MS/MS Spectra of Unverified Metabolites. Each metabolite is seen at a collision energy (CE) of 10. (a) N-Acetylhexosamine, (b) Sialic Acid 1, (c) Sialic acid 2, (d) Sialic acid 3, (e) Unknown 1, (f) Unknown 2

a

Discovery Set Not Normalized to Creatinine				
m/z	Obs	AUC	Std. Err.	[95% Conf. Interval]
115.0498	66	0.9449	0.0246	0.89676 - 0.99305
133.0600	66	0.9495	0.0229	0.90455 - 0.99444
144.1241	66	0.9780	0.0137	0.95103 - 1.00000
186.0762	66	0.9660	0.0304	0.90643 - 1.00000
225.0845	66	0.9082	0.0351	0.83940 - 0.97695
241.0903	66	0.8255	0.0523	0.72301 - 0.92804
254.0859	66	0.9725	0.0204	0.93243 - 1.00000
292.0995	66	0.9008	0.0434	0.81578 - 0.98587
310.1148	66	0.9587	0.0315	0.89688 - 1.00000
491.1754	66	0.9458	0.0342	0.87885 - 1.00000

b

Validation Set Not Normalized to Creatinine				
m/z	Obs	AUC	Std. Err.	[95% Conf. Interval]
115.0498	88	0.5752	0.0617	0.45430 - 0.69609
133.0600	88	0.6672	0.0577	0.55406 - 0.78031
144.1241	88	0.8052	0.0470	0.71296 - 0.89737
186.0762	88	0.8114	0.0454	0.72236 - 0.90038
225.0845	88	0.6119	0.0607	0.49287 - 0.73090
241.0903	88	0.6925	0.0576	0.57952 - 0.80550
254.0859	88	0.7871	0.0472	0.69454 - 0.87962
292.0995	88	0.7773	0.0500	0.67928 - 0.87524
310.1148	88	0.7313	0.0536	0.62614 - 0.83639
491.1754	87	0.7762	0.0504	0.67750 - 0.87488

c

Discovery Set Normalized to Creatinine				
m/z	Obs	AUC	Std. Err.	[95% Conf. Interval]
115.0498	66	0.9440	0.0255	0.89398 - 0.99399
133.0600	66	0.9486	0.0260	0.89753 - 0.99962
144.1241	66	0.9697	0.0166	0.93710 - 1.00000
186.0762	66	0.9559	0.0317	0.89377 - 1.00000
225.0845	66	0.9229	0.0313	0.86153 - 0.98420
241.0903	66	0.8457	0.0478	0.75205 - 0.93941
254.0859	66	0.9761	0.0180	0.94082 - 1.00000
292.0995	66	0.8705	0.0467	0.77890 - 0.96215
310.1148	66	0.9568	0.0310	0.89600 - 1.00000
491.1754	66	0.9412	0.0359	0.87092 - 1.00000

d

Validation Set Normalized to Creatinine				
m/z	Obs	AUC	Std. Err.	[95% Conf. Interval]
115.0498	88	0.5829	0.0616	0.46229 - 0.70360
133.0600	88	0.6501	0.0589	0.53462 - 0.76564
144.1241	88	0.8026	0.0480	0.70844 - 0.89672
186.0762	88	0.7974	0.0484	0.70259 - 0.89224
225.0845	88	0.5897	0.0612	0.46975 - 0.70957
241.0903	88	0.6739	0.0589	0.55850 - 0.78930
254.0859	88	0.7850	0.0480	0.69100 - 0.87903
292.0995	88	0.7447	0.0526	0.64152 - 0.84789
310.1148	88	0.7085	0.0562	0.59837 - 0.81868
491.1754	88	0.7540	0.0522	0.65163 - 0.85638

Supplementary Table 1: Effect of Creatinine Normalization on AUC in Randomly Selected Subset of Urine samples from Discovery (Haiti) and Validation (Vietnam) Cohorts. AUC of molecules in randomly selected subset of 66 participant urine samples prior to (a) and after (c) normalization to creatinine concentration in discovery cohort. AUC of randomly selected subset of 88 participant urine samples prior to (b) and after (d) creatinine normalization in validation cohort.

AUC= area under receiver operator characteristic curve, Obs= number of samples used in calculation (samples excluded if molecule ion counts below limit of detection).

**Supplementary Table 2:
List of Molecules Found to be
Significantly Different in TB
Cases (n=102) versus Matched
Controls (n=102) in Discovery
(Haitian) Cohort.** Analysis was
performed as described in methods
section. Molecules were declared
significant if p-value <0.0001 after
adjustment for false discovery rate
and if posterior non-null probability
>0.9. Molecules listed as neutral
mass.

RT=retention time, ROC=receiver
operator curve, Obs= number of
samples used in calculation
(samples excluded if molecule ion
counts below limit of detection).
Area= molecule abundance. Std
Err=standard error.

Mass	RT	Obs	Area	Std. Err.	ROC	
					[95% Conf. Interval]	
71.074	15.03	202	0.5553	0.0406	0.47570	0.63489
75.032	8.56	202	0.4733	0.0409	0.39317	0.55350
88.001	14.05	202	0.7657	0.0340	0.69901	0.83236
99.068	2.19	187	0.3844	0.0425	0.30106	0.46780
103.099	12.98	202	0.6827	0.0373	0.60960	0.75589
105.038	8.03	188	0.5259	0.0424	0.44269	0.60903
114.042	1.55	202	0.9125	0.0196	0.87413	0.95097
114.083	7.29	202	0.7506	0.0341	0.68382	0.81735
117.078	11.31	202	0.4718	0.0408	0.39173	0.55180
119.058	7.62	202	0.5739	0.0404	0.49467	0.65318
130.109	12.33	202	0.6840	0.0371	0.61128	0.75676
131.057	1.48	201	0.5243	0.0411	0.44372	0.60480
132.077	1.56	201	0.9347	0.0155	0.90429	0.96519
136.018	1.68	201	0.6888	0.0373	0.61558	0.76192
136.062	12.86	202	0.6121	0.0394	0.53479	0.68933
137.047	11.08	202	0.5167	0.0411	0.43614	0.59719
137.073	11.08	202	0.5150	0.0411	0.43450	0.59550
143.116	14.92	202	0.9095	0.0213	0.86770	0.95132
143.120	11.78	202	0.6639	0.0381	0.58931	0.73853
146.068	9.63	202	0.6056	0.0398	0.52757	0.68360
146.094	9.63	202	0.5966	0.0400	0.51819	0.67495
155.095	13.83	202	0.4062	0.0401	0.32766	0.48469
159.099	2.18	201	0.3253	0.0391	0.24866	0.40197
165.077	6.29	201	0.6652	0.0379	0.59094	0.73943
169.083	14.26	202	0.5847	0.0402	0.50592	0.66350
169.112	14.26	202	0.5674	0.0405	0.48804	0.64667
185.068	2.08	201	0.9324	0.0191	0.89492	0.96981
187.093	6.64	202	0.6526	0.0383	0.57751	0.72778
190.057	7.20	201	0.7076	0.0370	0.63514	0.77999
199.010	0.58	201	0.7833	0.0323	0.72001	0.84664
199.106	3.09	201	0.7880	0.0316	0.72614	0.84982
201.145	11.76	202	0.7019	0.0366	0.63010	0.77363
217.136	2.14	201	0.4099	0.0405	0.33045	0.48932
220.082	5.98	201	0.8316	0.0279	0.77687	0.88643
224.078	6.22	202	0.8650	0.0255	0.81511	0.91489
228.178	11.61	202	0.6250	0.0392	0.54809	0.70191
240.084	1.77	201	0.8596	0.0254	0.80984	0.90932
240.145	12.02	203	0.6529	0.0382	0.57796	0.72780
245.114	2.90	201	0.7248	0.0359	0.65437	0.79523
253.078	3.32	201	0.9175	0.0201	0.87814	0.95687
258.094	3.11	201	0.8174	0.0291	0.76038	0.87440
258.128	3.11	201	0.8180	0.0290	0.76110	0.87487
278.120	1.57	199	0.7864	0.0333	0.72122	0.85162
287.315	2.82	202	0.5842	0.0410	0.50383	0.66460
291.092	2.10	201	0.9049	0.0219	0.86200	0.94786
297.104	2.44	201	0.7768	0.0324	0.71327	0.84030
309.106	2.56	201	0.9416	0.0164	0.90945	0.97369
324.189	14.09	201	0.7900	0.0315	0.72830	0.85162
490.162	2.51	194	0.9208	0.0209	0.87979	0.96183

Supplementary Table 3: Characteristics of 20 Participants with Pulmonary Tuberculosis Followed Longitudinally (Discovery Cohort). All participants had positive sputum AFB at enrollment. Urine samples were taken prior to initiation of anti-tuberculosis therapy and at day 60 of treatment. Participants were followed for 6 months to ensure sustained treatment response.

*One participant was HIV positive, CD4 count was 538 at the time of enrollment.

Patient Characteristics	Mean (range or percentile)
Age (range)	36 (19-57)
Sex (% male)	M 10 (50%)
Average Weight (range)	115.8 lbs (79-172)
HIV positive*	1 (5%)
Symptoms	
Fever	12 (60%)
Night sweats	12 (60%)
Cough	19 (95%)
Weight loss	17 (85%)
Dyspnea	2 (10%)
Hemoptysis	1 (5%)