Supplemental Data to:

Regional Differences in Human Intestinal Drug Metabolism

Raditya Iswandana, Marina I. Irianti, Dorenda Oosterhuis, Hendrik S. Hofker, Marjolijn T.

Merema, Marina H. de Jager, Henricus A. M. Mutsaers, and Peter Olinga

Division of Pharmaceutical Technology and Biopharmacy, Department of Pharmacy,

University of Groningen, The Netherlands (R.I., M.I.I., D.O., H.A.M.M., P.O);

Faculty of Pharmacy, Universitas Indonesia, Indonesia (R.I.);

Department of Surgery, University Medical Center Groningen, University of Groningen, The

Netherlands (H.S.H.);

Division of Pharmacokinetics, Toxicology and Targeting, Department of Pharmacy,

University of Groningen, The Netherlands (M.T.M., M.H.J.);

Department of Clinical Medicine, Aarhus University, Denmark (H.A.M.M.)

Drug Metabolism and Disposition

Running Title: Regional differences in human intestinal drug metabolism

Corresponding Author: Peter Olinga, Division of Pharmaceutical Technology and

Biopharmacy, Department of Pharmacy, University of Groningen, Antonius Deusinglaan 1,

9713 AV, Groningen, The Netherlands. Phone: (+31) 50 3638373. Fax: (+31) 50 3632500.

Email: p.olinga@rug.nl

Number of Pages: 8

Number of Supplemental Tables: 2

Number of Supplemental Figures: 4

1

Supplemental Tables

TABLE S1Metabolic rates during 3 h of incubation in small intestinal (ileum) and colon slices (Data are expressed as mean \pm -- SEM, n=5-7)

Metabolite Formed	0-3 hours (pm	Ratio		
	Ileum	Colon	(Ileum/Colon)	
Androstenedione	9.55 ± 2.27	4.34 ± 0.96	2.20	
6β-ТОН	1.78 ± 0.65	$0.42 \pm 0.05*$	4.24	
15α-ΤΟΗ	0.33 ± 0.08	0.48 ± 0.08	0.69	
2β-ТОН	0.24 ± 0.11	0.06 ± 0.01	4.00	
7-HC Glucuronide	27.16 ± 7.27	$59.37 \pm 20.85^{\dagger}$	0.45	
7-HC Sulfate	17.59 ± 6.34	10.29 ± 3.97	1.71	

^{*}Significantly different from ileum with p < 0.05

 $^{^{\}dagger}$ Significantly different from 7-HC Sulfate colon with p < 0.05

TABLE S2Correlations between phase I and phase II metabolite formation in the ileum (all data above the black box) and the colon (all data below the black box); n=5-7

Correlation	Andro	6β-ТОН	15α-ТОН	2β-ТОН	7-HC	7-H C
vs.	Anuro	ор-101	134-1011	2p-10H	Glucuronide	Sulfate
Andro		p=0.13	p=0.99	p=0.27	p=0.34	p=0.32
		r=0.76	r=-0.01	r=0.62	r=0.54	r=0.56
6β-ТОН	p=0.09		p=0.45	p=0.01	p=0.01	p=0.02
ор-1011	r=0.81		r=0.44	r=0.97	r=0.94	r=0.93
15α-ТОН	p=0.74	p=0.54		p=0.50	p=0.26	p=0.39
130-1011	r=0.21	r=0.37		r=0.40	r=0.63	r=0.50
2β-ТОН	p=0.34	p=0.97	p=0.93		p=0.01	p=0.001
2p-1011	r=-0.55	r=0.63	r=0.06		r=0.94	r=0.99
7-HC	p=0.40	p=0.13	p=0.02	p=0.91		p=0.11
Glucuronide	r=0.49	r=0.80	r=0.94	r=0.07		r=0.65
7-HC	p=0.40	p=0.59	p=0.10	p=0.48	p=0.04	
Sulfate	r=0.49	r=0.33	r=0.81	r=-0.42	r=0.77	

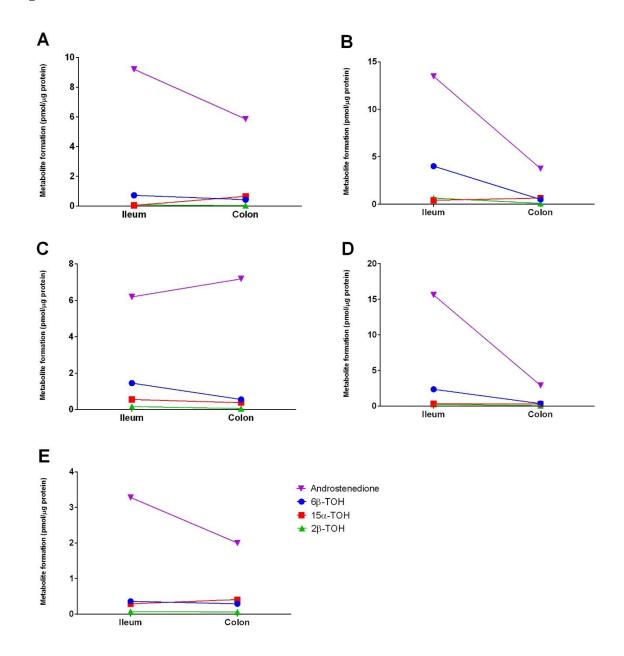
[:] Significantly different and strongly correlated (p<0.05, r>+/-0.5)

Supplemental Figure Legends

- **Fig. S1:** The metabolism rate of phase I in human ileum and colon PCIS: (A) Patient 1; (B) Patient 2; (C) Patient 3; (D) Patient 4; (E) Patient 5 (Each data was obtained triplicates; Zero metabolite formation due to the limit of detection (LOD) of the HPLC).
- **Fig. S2:** The metabolism rate of phase II in human ileum and colon PCIS: (A) Patient 1; (B) Patient 2; (C) Patient 3; (D) Patient 4; (E) Patient 5; (F) Patient 6; Patient 7 (Each data was obtained triplicates; Zero metabolite formation due to the limit of detection (LOD) of the HPLC).
- **Fig. S3:** Correlations of ATP with the phase I metabolite formation in the ileum (A-D) and colon (E-H), n=5.
- **Fig. S4:** Correlations of ATP with the phase II metabolite formation in the ileum (A and B) and colon (C and D), n=7.

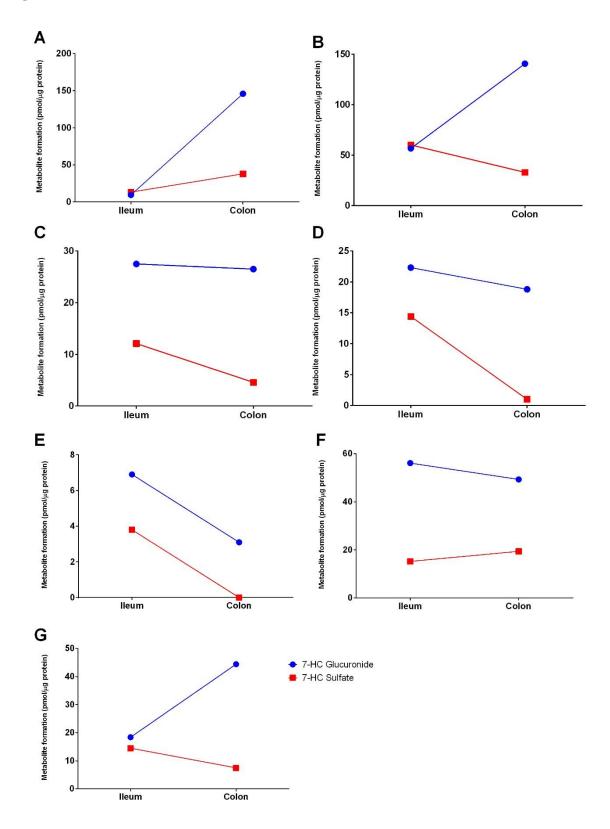
Supplemental Figures

Figure S1



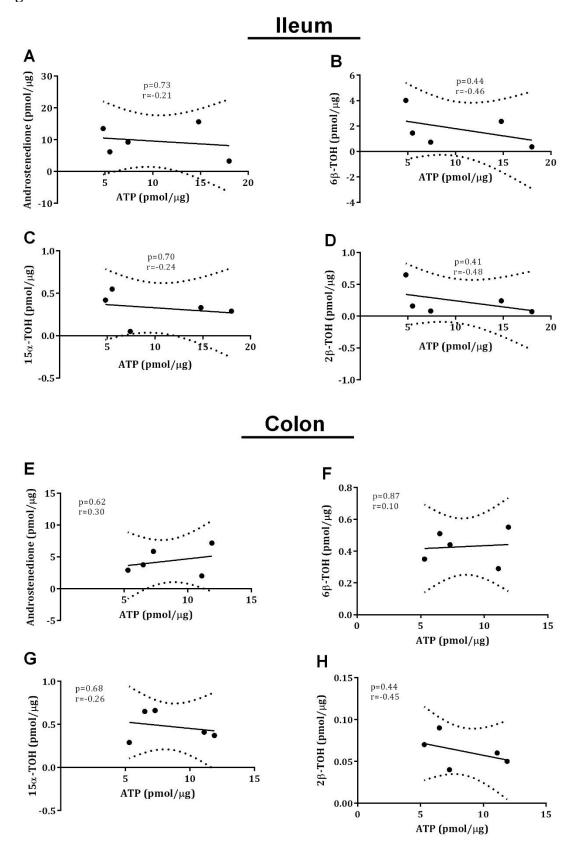
The metabolism rate of phase I in human ileum and colon PCIS: (A) Patient 1; (B) Patient 2; (C) Patient 3; (D) Patient 4; (E) Patient 5 (Each data was obtained triplicates; Zero metabolite formation due to the limit of detection (LOD) of the HPLC).

Figure S2



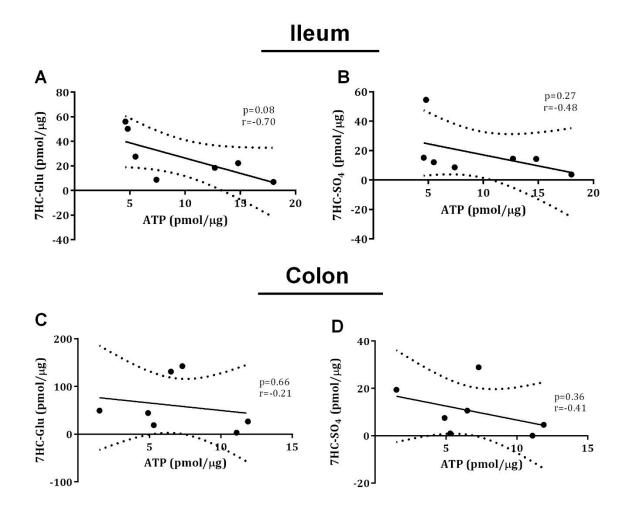
The metabolism rate of phase II in human ileum and colon PCIS: (A) Patient 1; (B) Patient 2; (C) Patient 3; (D) Patient 4; (E) Patient 5; (F) Patient 6; Patient 7 (Each data was obtained triplicates; Zero metabolite formation due to the limit of detection (LOD) of the HPLC).

Figure S3



Correlations of ATP with the phase I metabolite formation in the ileum (A-D) and colon (E-H), n=5.

Figure S4



Correlations of ATP with the phase II metabolite formation in the ileum (A and B) and colon (C and D), n=7.