

Supplementary Information

***An in vitro* method for the prediction of renal proximal tubular toxicity in humans**

Yao Li, Zay Yar Oo, Shu Yung Chang, Peng Huang, Kim Guan Eng, Jia Liu Zeng, Alicia J. Kaestli, Began Gopalan, Karthikeyan Kandasamy, Farah Tasnim and Daniele Zink*

Institute of Bioengineering and Nanotechnology, 31 Biopolis Way, The Nanos, Singapore 138669, Singapore

* Corresponding author:

Phone: +65 6824 7107, Fax: +65 6478 9080, E-mail addresses: dzink@ibn.a-star.edu.sg

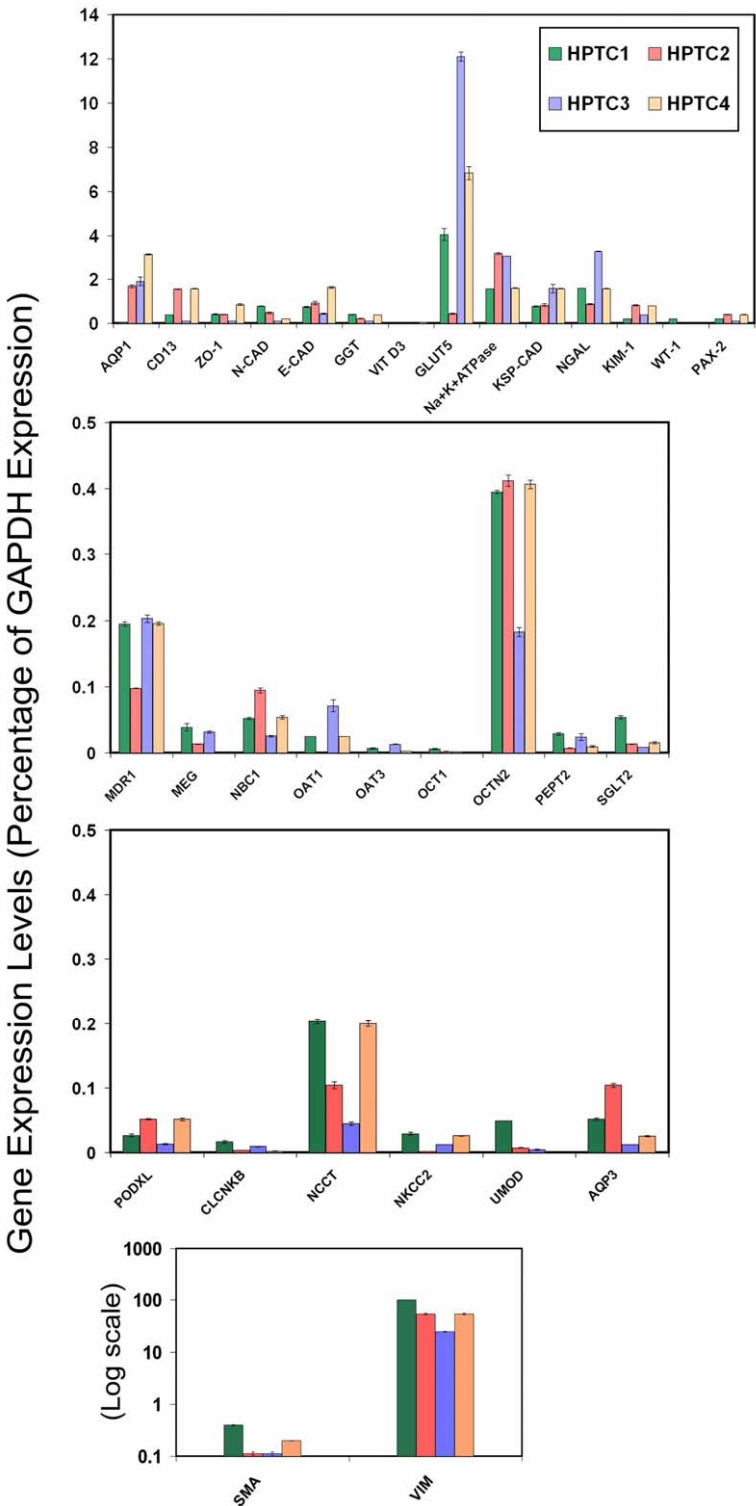


Figure S1: Marker gene expression determined by qPCR in HPTC 1-4. The relative expression levels of the 31 genes indicated (x-axis) are displayed as percentage of

GAPDH expression (y-axis). The bars show the mean $\pm$ standard deviation (s.d.; $n = 3$). Due to differences in expression levels the scales on the y-axes of the different diagrams are different and a log scale has been used with respect to α -smooth muscle actin (SMA) and vimentin (VIM; bottom). In addition to these 2 markers for trans- and de-differentiation, the following epithelial, HPTC-specific, renal, and renal injury-specific markers were included: aquaporin-1 (AQP1), aminopeptidase N (CD13), zonula occludens 1 (ZO-1), N-cadherin (N-CAD), E-cadherin (E-CAD), γ -glutamyl transferase (GGT), 25-hydroxyvitamin D3 1 α -hydroxylase (VIT D3), glucose transporter 5 (GLUT5), Na⁺/K⁺ ATPase, kidney-specific cadherin (KSP-CAD), neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), Wilms' tumor gene 1 (WT1), paired box gene 2 (PAX2), multidrug resistance gene 1 (MDR1), megalin (MEG), Na⁺HCO₃⁻ co-transporter 1 (NBC1), organic anion transporter 1 (OAT1), OAT3, organic cation transporter 1 (OCT1), organic cation/carnitine transporter 2 (OCTN2), proton-coupled peptide transporter 2 (PEPT2), sodium-dependent glucose co-transporter 2 (SGLT2). In addition, the following markers were included that were specific for other parts of the nephron: podocalyxin-like (PODXL, glomerulus), chloride channel Kb (CLCNKB, distal nephron), thiazide-sensitive sodium-chloride co-transporter (NCCT, distal tubule), Na⁺/K⁺/2Cl⁻ co-transporter (NKCC2, thick ascending loop of Henle), uromodulin (UMOD, thick ascending loop of Henle and distal convoluted tubules) and AQP3 (collecting duct). For primers see references 27 and 28 (main text) and Table S11. HPTC were analyzed at passage (P) 1.

The results shown here are in agreement with our previous results obtained with HPTC cultivated up to P 5 (see reference 27, main text). For instance, in agreement with our

previous results obtained with HPTC at higher passage numbers OAT3 and OCT1 were expressed at extremely low levels and HPTC expressed some markers that are *in vivo* expressed in other parts of the nephron/kidney (NCCT and AQP 3) at relatively high levels. Also the finding that VIM is expressed at high levels *in vitro* is in agreement with previous results (references 27 and 46, main text). Some HPTC-specific markers, like GGT, CD13 and ZO-1 are expressed at low levels (~ 0.4% of GAPDH expression in HPTC 1 obtained from ATCC). In case of GGT quantitative PCR data have been published previously ¹, which are in agreement with the low expression levels observed here. Nevertheless, GGT is functional in HPTC obtained from ATCC (references 27 and 28, main text) and CD13 as well as ZO-1 can be detected by immunoblotting and immunostaining (see Figure S2).

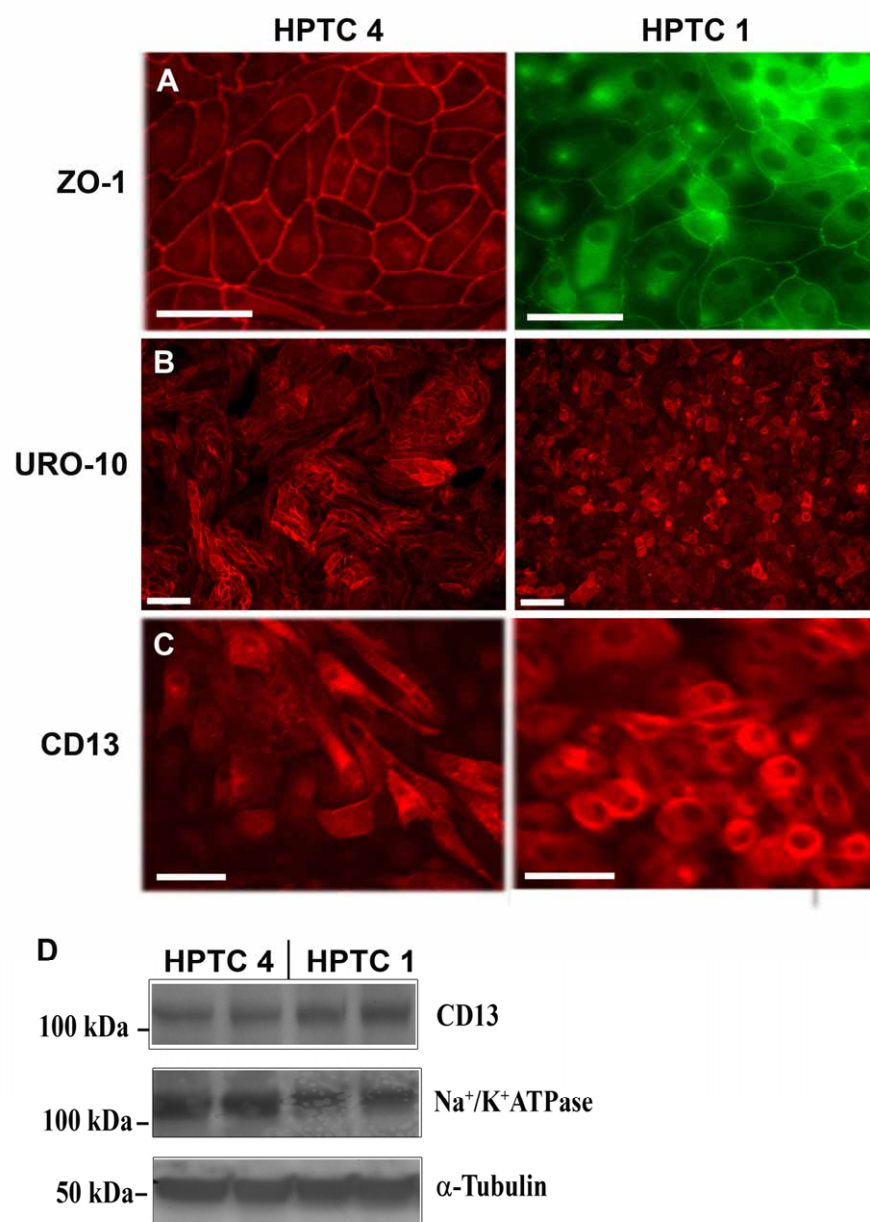


Figure S2: Marker expression determined by immunostaining and immunoblotting in HPTC 1 and 4. (A) ZO-1, (B) URO-10 and (C) CD13 were detected by immunostaining. The tight junctional protein ZO-1 is organized into the characteristic chicken wire-like patterns indicating extensive tight junction formation. Scale bars: 50 μm (A and C) and 100 μm (B). (D) CD13 and the α-subunit of the Na⁺/K⁺ ATPase were detected by immunoblotting. α-tubulin was used as loading control. The positions of the 100 kDa and

50 kDa size marker bands are shown on the left. Antibodies and immunoblotting and immunostaining procedures are described in reference 27 (main text).

		<i>In vivo</i> (Clinical Data)	
		+	-
<i>In vitro</i> (Marker Gene Expression)	+	True positive (TP)	False positive (FP)
	-	False negative (FN)	True negative (TN)

Sensitivity = $TP / (TP + FN)$

Specificity = $TN / (FP + TN)$

Concordance = $(TP + TN) / (TP + FP + FN + TN)$

Balanced Accuracy = $(\text{Sensitivity} + \text{Specificity}) / 2$

Positive Predictive Value (PPV) = $TP / (TP + FP)$

Negative Predictive Value (NPV) = $TN / (TN + FN)$

Figure S3: Terms and definitions. The matrix illustrates the definitions of true positives (TP), false positives (FP), false negatives (FN) and true negatives (TN) in relation to positive (+) and negative (-) clinical and *in vitro* results. Definitions of performance metrics are provided.

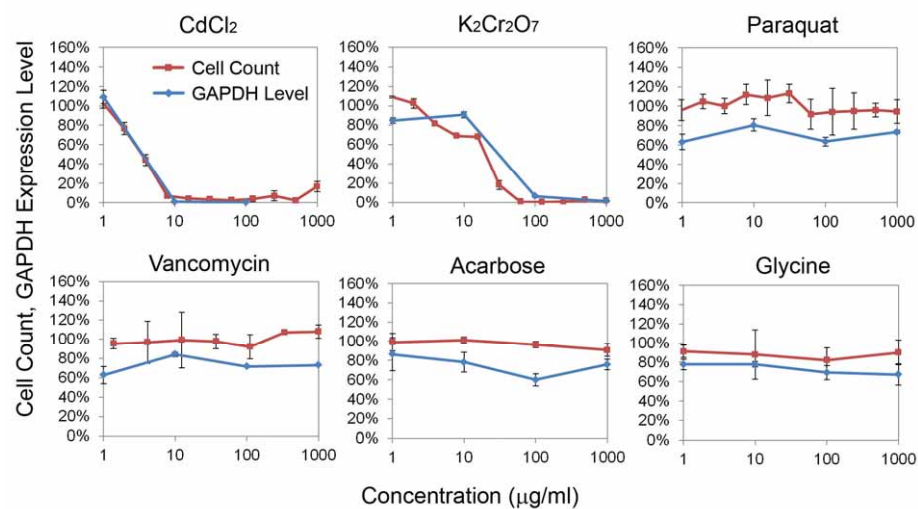


Figure S4: GAPDH levels and cell numbers. GAPDH levels (blue graphs) were determined by qPCR and cell numbers (red graphs) were counted by HCS. The graphs show the values (mean $\pm$ s.d., n = 3) determined at different concentrations (x-axis) of the indicated compounds. All values are expressed as percentage of the vehicle control. The results were obtained with HPTC 1.

Tables S1 – S10

Expression levels of IL-6 and IL-8. Three different batches of HPTC (1-3) as well as HK-2 and LLC-PK1 cells were exposed to the 41 test compounds at concentrations of 1 µg/ml, 10 µg/ml, 100 µg/ml and 1000 µg/ml (vehicle control: 0 µg/ml drug concentration). The vehicle control contained the respective vehicle for the drug tested (see Materials and Methods). The tables list the levels of IL-6 or IL-8 expression determined by qPCR. The numbers show the mean fold expression $\pm$ s.d. (n = 3) relative to the vehicle control. In some cases the expression levels were not determined (ND) due to massive cell death. The highest levels of IL-6 or IL-8 expression that were determined for a given drug and cell type/batch combination when the whole range of drug concentrations was tested (1 µg – 1000 µg) are highlighted (bold). These highest expression values obtained with a specific drug and cell type/batch combination were entered into Tables 1 and 2.

Table S1

Compound	HPTC 1, IL-6 Expression				
	0	1	10	100	1000
1	1.0 ± 0.0	1.0 ± 0.0	1.2 ± 0.0	2.9 ± 0.1	16.9 ± 0.2
2	1.0 ± 0.2	1.3 ± 0.1	1.5 ± 0.1	1.8 ± 0.3	8.0 ± 0.9
3	1.0 ± 0.2	3.2 ± 0.5	3.1 ± 0.2	1.7 ± 0.9	38.9 ± 3.0
4	1.0 ± 0.0	1.1 ± 0.1	1.4 ± 0.9	6.3 ± 0.7	1.0 ± 0.1
5	1.0 ± 0.1	1.0 ± 0.1	8.5 ± 1.0	5.0 ± 0.4	6.8 ± 1.3
6	1.0 ± 0.2	0.9 ± 0.0	1.0 ± 0.0	0.7 ± 0.1	3.9 ± 0.1
7	1.0 ± 0.1	1.4 ± 0.2	1.7 ± 0.3	2.6 ± 0.1	3.6 ± 0.8
8	1.0 ± 0.1	2.9 ± 0.6	3.8 ± 0.6	1.0 ± 0.2	ND
9	1.0 ± 0.1	1.5 ± 0.1	1.7 ± 0.2	1.6 ± 0.1	0.8 ± 0.1
10	1.0 ± 0.3	2.0 ± 0.5	2.4 ± 0.2	3.1 ± 0.7	2.4 ± 0.5
11	1.0 ± 0.1	1.1 ± 0.1	0.8 ± 0.1	0.4 ± 0.0	3.0 ± 0.1
12	1.0 ± 0.1	1.1 ± 0.3	1.1 ± 0.2	1.0 ± 0.4	ND
13	1.0 ± 0.1	1.5 ± 0.1	6.6 ± 0.5	2.9 ± 1.5	ND
14	1.0 ± 0.3	1.2 ± 0.2	1.4 ± 0.4	0.9 ± 0.1	10.4 ± 2.9
15	1.0 ± 0.1	0.8 ± 0.1	1.0 ± 0.4	1.2 ± 0.0	1.7 ± 0.5
16	1.0 ± 0.1	1.0 ± 0.1	1.7 ± 0.3	0.8 ± 0.1	10.0 ± 1.3
17	1.0 ± 0.1	1.4 ± 0.3	1.8 ± 0.6	2.4 ± 0.3	3.5 ± 0.4
18	1.0 ± 0.2	0.0 ± 0.0	0.3 ± 0.1	0.6 ± 0.1	1.7 ± 0.2
19	1.1 ± 0.6	7.7 ± 1.6	7.7 ± 0.4	11.7 ± 3.5	24.6 ± 5.7
20	1.0 ± 0.1	0.9 ± 0.2	1.1 ± 0.2	0.9 ± 0.1	0.6 ± 0.2
21	1.0 ± 0.1	1.1 ± 0.3	1.1 ± 0.1	0.6 ± 0.1	3.9 ± 0.7
22	1.0 ± 0.0	1.5 ± 0.2	1.6 ± 0.1	1.5 ± 0.1	0.8 ± 0.0
23	1.0 ± 0.2	1.3 ± 0.0	1.4 ± 0.2	1.3 ± 0.3	0.8 ± 0.2
24	1.0 ± 0.3	1.1 ± 0.2	1.2 ± 0.1	1.1 ± 0.2	0.1 ± 0.0
25	1.0 ± 0.1	1.2 ± 0.1	1.3 ± 0.0	1.0 ± 0.1	0.2 ± 0.0
26	1.1 ± 0.3	0.5 ± 0.1	0.8 ± 0.1	0.9 ± 0.1	2.6 ± 0.8
27	1.1 ± 0.5	0.3 ± 0.0	0.4 ± 0.0	0.2 ± 0.0	1.7 ± 0.4
28	1.0 ± 0.0	0.7 ± 0.1	0.4 ± 0.2	0.4 ± 0.0	0.1 ± 0.0
29	1.0 ± 0.2	0.9 ± 0.0	1.0 ± 0.3	1.0 ± 0.2	0.4 ± 0.0
30	1.0 ± 0.2	0.9 ± 0.1	1.0 ± 0.2	1.0 ± 0.1	0.7 ± 0.1
31	1.0 ± 0.1	1.3 ± 0.1	1.7 ± 0.4	1.1 ± 0.1	0.7 ± 0.3
32	1.0 ± 0.2	1.3 ± 0.1	1.1 ± 0.1	1.0 ± 0.0	0.9 ± 0.1
33	1.0 ± 0.1	1.6 ± 0.2	1.4 ± 0.2	2.3 ± 0.2	4.7 ± 0.6
34	1.1 ± 0.2	1.5 ± 0.1	0.9 ± 0.1	0.3 ± 0.0	0.3 ± 0.0
35	1.0 ± 0.1	1.5 ± 0.1	1.6 ± 0.2	1.7 ± 0.2	1.4 ± 0.1
36	1.0 ± 0.1	0.9 ± 0.0	0.8 ± 0.0	0.9 ± 0.1	0.8 ± 0.1
37	1.0 ± 0.0	1.2 ± 0.1	1.0 ± 0.0	0.8 ± 0.0	0.1 ± 0.0
38	1.1 ± 0.3	1.1 ± 0.1	1.8 ± 0.0	0.4 ± 0.0	0.3 ± 0.1

39	1.0 ± 0.2	1.2 ± 0.1	0.9 ± 0.1	0.4 ± 0.1	3.4 ± 1.0
40	1.0 ± 0.4	1.6 ± 0.2	1.0 ± 0.1	0.9 ± 0.1	0.9 ± 0.0
41	1.0 ± 0.2	1.0 ± 0.3	0.5 ± 0.1	0.7 ± 0.2	ND

Table S2

Compound	HPTC 1, IL-8 Expression				
	0	1	10	100	1000
1	1.0 ± 0.3	0.9 ± 0.0	0.8 ± 0.1	0.7 ± 0.0	8.6 ± 1.3
2	1.0 ± 0.2	1.2 ± 0.1	1.2 ± 0.1	1.5 ± 0.3	8.9 ± 1.2
3	1.0 ± 0.4	6.9 ± 1.0	6.0 ± 0.7	4.1 ± 1.4	110.8 ± 39.0
4	1.0 ± 0.0	0.9 ± 0.0	1.2 ± 0.1	1.5 ± 0.1	0.8 ± 0.0
5	1.0 ± 0.0	0.3 ± 0.0	9.5 ± 0.6	8.8 ± 0.9	4.8 ± 0.5
6	1.0 ± 0.3	0.9 ± 0.1	1.0 ± 0.1	2.2 ± 1.1	2.3 ± 0.2
7	1.0 ± 0.0	1.2 ± 0.2	1.2 ± 0.2	2.4 ± 0.2	2.2 ± 0.4
8	1.0 ± 0.1	13.6 ± 2.0	20.1 ± 2.2	13.4 ± 3.2	ND
9	1.0 ± 0.1	1.4 ± 0.1	1.5 ± 0.2	1.5 ± 0.1	0.9 ± 0.2
10	1.0 ± 0.2	2.6 ± 1.7	2.3 ± 0.1	5.9 ± 0.8	16.3 ± 4.6
11	1.0 ± 0.0	1.1 ± 0.1	1.6 ± 0.2	0.8 ± 0.0	6.0 ± 0.1
12	1.0 ± 0.0	1.6 ± 0.3	6.1 ± 0.5	11.9 ± 6.2	ND
13	1.0 ± 0.0	1.9 ± 0.1	2.4 ± 0.1	9.7 ± 2.5	ND
14	1.0 ± 0.2	1.4 ± 0.2	1.7 ± 0.4	3.6 ± 0.3	7.5 ± 4.4
15	1.0 ± 0.2	0.8 ± 0.1	1.4 ± 0.3	1.5 ± 0.1	2.9 ± 1.7
16	1.0 ± 0.0	0.8 ± 0.0	2.2 ± 0.7	1.4 ± 0.4	0.5 ± 0.1
17	1.0 ± 0.1	1.2 ± 0.3	1.5 ± 0.2	2.6 ± 0.4	3.3 ± 0.1
18	1.1 ± 0.5	0.5 ± 0.1	3.8 ± 1.0	2.2 ± 0.4	1.3 ± 0.4
19	1.1 ± 0.4	3.5 ± 0.8	2.8 ± 0.2	3.9 ± 1.3	2.7 ± 1.1
20	1.0 ± 0.0	1.0 ± 0.2	1.1 ± 0.2	2.6 ± 1.9	5.6 ± 1.3
21	1.0 ± 0.1	1.3 ± 0.4	1.1 ± 0.2	0.7 ± 0.1	2.3 ± 0.7
22	1.0 ± 0.1	4.1 ± 1.0	4.3 ± 0.4	4.0 ± 0.5	1.3 ± 0.0
23	1.0 ± 0.3	1.3 ± 1.0	1.5 ± 0.3	1.6 ± 0.3	1.1 ± 0.2
24	1.0 ± 0.1	1.2 ± 0.1	1.3 ± 0.1	1.0 ± 0.2	0.0 ± 0.0
25	1.0 ± 0.1	1.4 ± 0.2	1.5 ± 0.1	1.1 ± 0.1	0.4 ± 0.1
26	1.0 ± 0.2	0.3 ± 0.0	0.5 ± 0.1	0.2 ± 0.0	3.1 ± 1.4
27	1.1 ± 0.4	0.5 ± 0.0	0.4 ± 0.0	0.2 ± 0.0	1.9 ± 0.5
28	1.0 ± 0.0	0.5 ± 0.1	0.5 ± 0.1	0.2 ± 0.0	0.2 ± 0.0
29	1.0 ± 0.3	1.0 ± 0.1	1.1 ± 0.3	1.1 ± 0.4	0.7 ± 0.1
30	1.0 ± 0.2	1.1 ± 0.1	1.0 ± 0.2	0.9 ± 0.0	1.0 ± 0.2
31	1.0 ± 0.1	1.3 ± 0.1	1.2 ± 0.0	1.2 ± 0.1	1.1 ± 0.1
32	1.0 ± 0.1	1.2 ± 0.0	1.0 ± 0.0	0.9 ± 0.0	0.8 ± 0.0
33	1.0 ± 0.3	1.5 ± 0.2	0.9 ± 0.1	0.6 ± 0.1	5.3 ± 1.1
34	1.0 ± 0.1	1.4 ± 0.1	0.9 ± 0.0	0.6 ± 0.1	0.4 ± 0.0
35	1.0 ± 0.2	1.9 ± 0.1	1.7 ± 0.1	2.0 ± 0.1	2.0 ± 0.1
36	1.0 ± 0.0	0.7 ± 0.1	0.8 ± 0.1	1.0 ± 0.0	1.1 ± 0.1
37	1.0 ± 0.0	1.5 ± 0.3	1.3 ± 0.1	0.7 ± 0.0	0.0 ± 0.0
38	1.1 ± 0.3	0.8 ± 0.0	1.3 ± 0.1	1.3 ± 0.1	0.3 ± 0.0

39	1.0 ± 0.1	1.8 ± 0.1	1.3 ± 0.0	0.9 ± 0.1	1.6 ± 0.5
40	1.0 ± 0.0	1.5 ± 0.1	0.8 ± 0.0	0.8 ± 0.1	0.7 ± 0.1
41	1.0 ± 0.1	1.2 ± 0.3	0.6 ± 0.1	3.6 ± 1.2	ND

Table S3

Compound	HPTC 2, IL-6 Expression				
	0	1	10	100	1000
1	1.0 ± 0.0	0.9 ± 0.0	1.0 ± 0.0	1.0 ± 0.0	1.7 ± 0.1
2	1.0 ± 0.0	1.1 ± 0.1	0.9 ± 0.0	1.2 ± 0.1	1.4 ± 0.0
3	1.0 ± 0.1	1.7 ± 0.2	1.8 ± 0.1	1.2 ± 0.0	3.6 ± 0.7
4	1.0 ± 0.1	0.8 ± 0.1	1.0 ± 0.0	2.0 ± 0.1	2.3 ± 0.3
5	1.0 ± 0.1	1.2 ± 0.3	2.2 ± 0.2	49.9 ± 3.2	79.5 ± 1.7
6	1.0 ± 0.0	1.1 ± 0.0	1.1 ± 0.1	1.6 ± 0.1	3.6 ± 0.3
7	1.0 ± 0.1	2.1 ± 0.1	2.5 ± 0.1	4.8 ± 0.6	1.2 ± 0.4
8	1.0 ± 0.1	8.3 ± 0.2	9.3 ± 0.5	27.9 ± 0.8	3.6 ± 0.7
9	1.0 ± 0.1	0.9 ± 0.1	1.3 ± 0.3	1.2 ± 0.1	1.3 ± 0.1
10	1.0 ± 0.2	0.9 ± 0.1	1.4 ± 0.1	4.4 ± 0.6	7.5 ± 0.0
11	1.0 ± 0.0	1.1 ± 0.1	0.2 ± 0.0	1.6 ± 0.0	ND
12	1.0 ± 0.0	0.8 ± 0.0	0.9 ± 0.0	1.6 ± 0.3	1.9 ± 0.3
13	1.0 ± 0.0	1.3 ± 0.0	12.9 ± 0.6	3.2 ± 0.1	3.1 ± 0.0
14	1.0 ± 0.0	1.2 ± 0.1	1.1 ± 0.0	5.4 ± 0.1	12.4 ± 1.4
15	1.0 ± 0.1	1.3 ± 0.1	1.1 ± 0.1	1.6 ± 0.2	3.6 ± 0.2
16	1.0 ± 0.0	1.1 ± 0.0	1.2 ± 0.1	3.1 ± 0.4	13.6 ± 1.0
17	1.0 ± 0.1	0.9 ± 0.0	1.1 ± 0.0	2.0 ± 0.4	8.6 ± 0.4
18	1.0 ± 0.0	0.8 ± 0.0	0.2 ± 0.0	0.8 ± 0.0	ND
19	1.0 ± 0.1	1.4 ± 0.1	0.9 ± 0.0	37.6 ± 0.7	15.8 ± 0.6
20	1.0 ± 0.1	0.8 ± 0.1	3.4 ± 0.7	0.9 ± 0.0	1.4 ± 0.1
21	1.0 ± 0.1	0.9 ± 0.0	0.8 ± 0.1	0.3 ± 0.1	1.3 ± 0.1
22	1.0 ± 0.1	0.7 ± 0.0	0.7 ± 0.0	0.6 ± 0.0	0.6 ± 0.0
23	1.0 ± 0.0	1.4 ± 0.2	1.2 ± 0.2	1.1 ± 0.2	1.3 ± 0.1
24	1.1 ± 0.4	0.6 ± 0.0	0.8 ± 0.1	0.6 ± 0.0	0.1 ± 0.0
25	1.0 ± 0.1	1.4 ± 0.1	1.3 ± 0.2	1.6 ± 0.4	2.9 ± 0.2
26	1.0 ± 0.1	1.6 ± 0.0	1.7 ± 0.1	4.4 ± 0.1	16.1 ± 1.2
27	1.0 ± 0.1	2.4 ± 0.1	2.4 ± 0.0	2.6 ± 0.2	0.6 ± 0.1
28	1.0 ± 0.1	1.1 ± 0.0	1.0 ± 0.1	1.5 ± 0.1	17.4 ± 0.8
29	1.0 ± 0.1	0.8 ± 0.0	0.7 ± 0.0	0.7 ± 0.0	0.8 ± 0.0
30	1.0 ± 0.0	1.8 ± 0.1	1.3 ± 0.1	1.2 ± 0.1	1.1 ± 0.0
31	1.0 ± 0.1	1.2 ± 0.1	1.1 ± 0.1	1.2 ± 0.1	1.6 ± 0.3
32	1.0 ± 0.1	1.3 ± 0.1	1.2 ± 0.1	1.0 ± 0.0	1.2 ± 0.1
33	1.0 ± 0.2	1.3 ± 0.1	1.1 ± 0.1	0.9 ± 0.1	0.4 ± 0.1
34	1.0 ± 0.0	1.2 ± 0.1	0.8 ± 0.0	0.5 ± 0.1	0.7 ± 0.1
35	1.0 ± 0.1	2.7 ± 0.8	1.6 ± 0.1	1.5 ± 0.2	0.2 ± 0.0
36	1.0 ± 0.0	2.7 ± 0.1	2.4 ± 0.1	1.8 ± 0.5	0.3 ± 0.0
37	1.0 ± 0.0	1.1 ± 0.3	0.8 ± 0.0	0.7 ± 0.0	0.3 ± 0.1
38	1.0 ± 0.1	1.0 ± 0.0	0.8 ± 0.1	1.2 ± 0.2	0.9 ± 0.1

39	1.0 ± 0.0	1.7 ± 0.5	1.2 ± 0.1	1.8 ± 0.3	3.1 ± 0.3
40	1.0 ± 0.0	1.1 ± 0.0	1.2 ± 0.0	1.1 ± 0.1	1.1 ± 0.0
41	1.0 ± 0.0	1.0 ± 0.0	0.7 ± 0.1	0.3 ± 0.1	ND

Table S4

Compound	HPTC 2, IL-8 Expression				
	0	1	10	100	1000
1	1.0 ± 0.0	1.1 ± 0.0	1.3 ± 0.0	1.4 ± 0.1	2.0 ± 0.1
2	1.0 ± 0.0	1.3 ± 0.1	1.2 ± 0.1	1.3 ± 0.1	1.5 ± 0.1
3	1.0 ± 0.1	1.9 ± 0.2	1.9 ± 0.0	1.8 ± 0.0	13.1 ± 3.0
4	1.0 ± 0.1	0.7 ± 0.1	0.9 ± 0.0	2.2 ± 0.1	3.6 ± 0.8
5	1.0 ± 0.0	1.4 ± 0.4	21.3 ± 4.7	89.1 ± 4.5	146.1 ± 3.1
6	1.0 ± 0.2	1.6 ± 0.1	1.6 ± 0.2	9.2 ± 0.2	3.3 ± 0.2
7	1.1 ± 0.3	1.9 ± 0.2	1.8 ± 0.2	3.8 ± 0.9	1.7 ± 0.2
8	1.0 ± 0.1	4.6 ± 0.2	5.0 ± 0.2	32.7 ± 0.9	3.9 ± 0.7
9	1.0 ± 0.1	1.2 ± 0.0	1.8 ± 0.4	1.4 ± 0.1	1.8 ± 0.2
10	1.1 ± 0.3	1.0 ± 0.2	1.3 ± 0.2	5.7 ± 0.8	13.2 ± 0.3
11	1.0 ± 0.1	1.2 ± 0.1	25.7 ± 3.8	2.3 ± 0.5	ND
12	1.0 ± 0.1	1.2 ± 0.1	1.3 ± 0.0	3.3 ± 0.7	22.5 ± 2.0
13	1.0 ± 0.1	1.9 ± 0.0	165.2 ± 14.7	3.1 ± 0.5	3.9 ± 0.1
14	1.0 ± 0.1	1.4 ± 0.1	1.4 ± 0.2	119.0 ± 5.4	11.3 ± 0.7
15	1.0 ± 0.1	1.5 ± 0.1	1.3 ± 0.1	1.7 ± 0.3	5.7 ± 0.2
16	1.0 ± 0.0	1.4 ± 0.1	1.3 ± 0.2	8.3 ± 0.5	2.2 ± 0.2
17	1.0 ± 0.1	1.2 ± 0.1	1.6 ± 0.2	4.1 ± 1.2	23.8 ± 2.9
18	1.0 ± 0.1	1.8 ± 0.0	2.7 ± 0.3	2.0 ± 0.1	ND
19	1.0 ± 0.1	0.9 ± 0.1	0.7 ± 0.0	29.3 ± 4.3	15.1 ± 0.3
20	1.0 ± 0.1	1.7 ± 0.2	6.5 ± 1.6	5.5 ± 0.7	67.4 ± 3.1
21	1.0 ± 0.1	1.6 ± 0.1	1.3 ± 0.1	4.9 ± 0.1	1.8 ± 0.2
22	1.0 ± 0.2	1.0 ± 0.0	0.9 ± 0.0	0.7 ± 0.0	0.5 ± 0.0
23	1.0 ± 0.1	1.8 ± 0.4	1.5 ± 0.4	1.5 ± 0.3	1.5 ± 0.2
24	1.1 ± 0.3	0.6 ± 0.0	0.9 ± 0.2	0.4 ± 0.0	0.4 ± 0.1
25	1.0 ± 0.1	1.4 ± 0.1	1.5 ± 0.1	1.5 ± 0.3	2.6 ± 0.1
26	1.0 ± 0.1	0.6 ± 0.0	0.4 ± 0.0	1.1 ± 0.2	4.3 ± 0.3
27	1.0 ± 0.0	2.6 ± 0.2	2.4 ± 0.0	2.3 ± 0.1	2.3 ± 0.1
28	1.0 ± 0.1	1.1 ± 0.1	1.0 ± 0.1	0.6 ± 0.1	20.5 ± 0.8
29	1.0 ± 0.1	0.9 ± 0.1	0.8 ± 0.0	0.8 ± 0.1	1.5 ± 0.1
30	1.0 ± 0.1	2.0 ± 0.1	1.4 ± 0.1	1.3 ± 0.0	1.2 ± 0.0
31	1.0 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	1.2 ± 0.2
32	1.0 ± 0.1	1.3 ± 0.1	1.3 ± 0.1	1.2 ± 0.0	1.4 ± 0.1
33	1.0 ± 0.1	1.6 ± 0.2	1.1 ± 0.1	1.0 ± 0.0	0.7 ± 0.1
34	1.0 ± 0.0	1.2 ± 0.1	0.9 ± 0.0	0.8 ± 0.0	1.4 ± 0.1
35	1.0 ± 0.1	1.1 ± 0.1	1.1 ± 0.1	1.3 ± 0.0	0.3 ± 0.0
36	1.0 ± 0.0	2.8 ± 0.0	2.9 ± 0.0	2.4 ± 0.7	0.5 ± 0.0
37	1.0 ± 0.1	1.2 ± 0.1	1.0 ± 0.0	0.7 ± 0.0	1.4 ± 0.2
38	1.0 ± 0.1	1.2 ± 0.0	1.1 ± 0.2	3.1 ± 0.2	2.1 ± 0.1

39	1.0 ± 0.1	1.6 ± 0.2	1.3 ± 0.0	2.0 ± 0.3	24.0 ± 3.4
40	1.0 ± 0.0	1.1 ± 0.0	1.3 ± 0.0	1.2 ± 0.0	1.2 ± 0.0
41	1.0 ± 0.0	1.6 ± 0.1	1.1 ± 0.2	0.9 ± 0.4	ND

Table S5

Compound	HPTC 3, IL-6 Expression				
	0	1	10	100	1000
1	1.0 ± 0.2	1.6 ± 0.1	0.9 ± 0.1	0.8 ± 0.1	0.9 ± 0.1
2	1.0 ± 0.1	1.4 ± 0.1	1.1 ± 0.2	1.1 ± 0.0	1.2 ± 0.0
3	1.0 ± 0.1	5.3 ± 0.4	2.9 ± 0.8	1.4 ± 0.3	ND
4	1.0 ± 0.1	1.5 ± 0.2	1.4 ± 0.1	23.6 ± 2.8	3.5 ± 0.1
5	1.0 ± 0.0	0.7 ± 0.1	9.3 ± 0.7	59.2 ± 2.6	80.4 ± 2.7
6	1.0 ± 0.1	1.1 ± 0.0	1.2 ± 0.0	1.4 ± 0.1	0.2 ± 0.0
7	1.1 ± 0.4	7.5 ± 1.0	5.9 ± 0.2	12.0 ± 1.8	0.5 ± 0.1
8	1.0 ± 0.2	11.3 ± 0.7	12.1 ± 0.4	11.9 ± 0.9	5.2 ± 0.5
9	1.0 ± 0.0	1.3 ± 0.1	1.1 ± 0.1	1.1 ± 0.0	2.9 ± 0.3
10	1.0 ± 0.1	1.1 ± 0.1	1.4 ± 0.0	4.4 ± 0.1	11.8 ± 0.5
11	1.0 ± 0.0	0.9 ± 0.0	0.2 ± 0.1	31.4 ± 12.8	ND
12	1.0 ± 0.1	1.5 ± 0.1	1.3 ± 0.0	1.3 ± 0.1	4.0 ± 0.1
13	1.1 ± 0.4	2.7 ± 0.2	10.8 ± 1.2	3.5 ± 0.1	6.0 ± 0.4
14	1.0 ± 0.2	0.4 ± 0.1	0.5 ± 0.0	0.3 ± 0.0	0.9 ± 0.2
15	1.0 ± 0.0	1.3 ± 0.1	1.1 ± 0.1	1.5 ± 0.0	2.2 ± 0.2
16	1.0 ± 0.0	1.2 ± 0.1	1.1 ± 0.0	0.9 ± 0.1	5.8 ± 2.5
17	1.0 ± 0.0	1.2 ± 0.1	1.3 ± 0.2	1.1 ± 0.2	2.3 ± 0.2
18	1.0 ± 0.1	0.6 ± 0.2	0.3 ± 0.1	0.5 ± 0.0	0.4 ± 0.0
19	1.0 ± 0.0	0.9 ± 0.0	1.0 ± 0.0	38.1 ± 1.2	8.3 ± 0.3
20	1.0 ± 0.0	0.9 ± 0.1	0.9 ± 0.1	1.3 ± 0.1	ND
21	1.0 ± 0.0	0.8 ± 0.0	0.8 ± 0.0	1.2 ± 0.3	2.3 ± 0.3
22	1.0 ± 0.2	0.9 ± 0.0	1.1 ± 0.1	1.0 ± 0.1	0.8 ± 0.0
23	1.2 ± 0.6	1.0 ± 0.4	0.9 ± 0.0	0.7 ± 0.1	0.6 ± 0.1
24	1.6 ± 1.1	3.9 ± 0.5	3.1 ± 0.1	6.2 ± 1.0	0.6 ± 0.4
25	1.0 ± 0.1	0.6 ± 0.1	0.8 ± 0.1	0.6 ± 0.1	0.2 ± 0.0
26	1.1 ± 0.3	1.4 ± 0.6	0.5 ± 0.2	0.9 ± 0.2	2.9 ± 0.1
27	1.1 ± 0.3	9.0 ± 0.6	8.4 ± 0.3	8.1 ± 0.2	0.6 ± 0.2
28	1.0 ± 0.1	1.1 ± 0.2	0.9 ± 0.1	0.6 ± 0.1	0.2 ± 0.0
29	1.0 ± 0.1	0.9 ± 0.2	0.9 ± 0.1	0.7 ± 0.1	0.9 ± 0.2
30	1.0 ± 0.2	0.9 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	1.0 ± 0.2
31	1.0 ± 0.0	1.2 ± 0.2	1.1 ± 0.0	1.4 ± 0.2	1.4 ± 0.2
32	1.1 ± 0.3	1.0 ± 0.2	0.4 ± 0.0	0.4 ± 0.1	0.5 ± 0.1
33	1.1 ± 0.4	1.1 ± 0.2	0.4 ± 0.0	ND	2.9 ± 0.1
34	1.0 ± 0.2	1.2 ± 0.3	0.4 ± 0.0	0.5 ± 0.2	0.7 ± 0.3
35	1.0 ± 0.0	1.0 ± 0.1	0.9 ± 0.1	0.8 ± 0.0	0.9 ± 0.1
36	1.0 ± 0.2	1.4 ± 0.2	1.0 ± 0.1	1.1 ± 0.1	0.9 ± 0.2
37	1.0 ± 0.0	0.9 ± 0.1	0.8 ± 0.0	0.8 ± 0.0	0.1 ± 0.0
38	1.1 ± 0.3	0.6 ± 0.1	0.3 ± 0.0	0.3 ± 0.0	0.2 ± 0.0

39	1.0 ± 0.1	1.2 ± 0.1	1.2 ± 0.1	2.8 ± 0.4	3.4 ± 0.3
40	1.0 ± 0.0	1.3 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.1
41	1.0 ± 0.1	0.7 ± 0.0	0.5 ± 0.1	20.6 ± 1.9	128.5 ± 21.1

Table S6

Compound	HPTC 3, IL-8 Expression				
	0	1	10	100	1000
1	1.0 ± 0.2	1.9 ± 0.3	0.8 ± 0.1	0.8 ± 0.0	1.2 ± 0.1
2	1.0 ± 0.0	2.0 ± 0.1	1.3 ± 0.2	1.3 ± 0.0	1.8 ± 0.2
3	1.2 ± 0.5	3.2 ± 0.6	3.0 ± 0.4	7.3 ± 2.7	ND
4	1.0 ± 0.1	1.6 ± 0.4	1.3 ± 0.1	35.5 ± 4.4	8.2 ± 0.9
5	1.0 ± 0.1	0.9 ± 0.0	18.9 ± 0.4	29.1 ± 3.6	46.4 ± 1.2
6	1.0 ± 0.2	1.1 ± 0.0	1.1 ± 0.1	2.4 ± 0.6	0.1 ± 0.0
7	1.0 ± 0.2	2.2 ± 0.2	2.6 ± 0.1	5.4 ± 0.4	4.4 ± 0.5
8	1.1 ± 0.3	17.2 ± 2.6	21.9 ± 0.8	18.8 ± 0.5	3.2 ± 0.5
9	1.0 ± 0.0	1.5 ± 0.1	1.3 ± 0.1	1.1 ± 0.0	2.6 ± 0.2
10	1.0 ± 0.1	0.8 ± 0.1	1.0 ± 0.0	3.3 ± 0.1	9.7 ± 0.2
11	1.0 ± 0.0	0.7 ± 0.0	5.3 ± 0.3	22.8 ± 4.0	ND
12	1.0 ± 0.1	1.4 ± 0.2	1.2 ± 0.1	1.5 ± 0.3	9.6 ± 1.8
13	1.1 ± 0.4	2.2 ± 0.3	13.3 ± 1.4	2.4 ± 0.1	1.5 ± 0.1
14	1.1 ± 0.3	0.6 ± 0.1	1.5 ± 0.2	9.9 ± 1.1	2.6 ± 0.2
15	1.0 ± 0.0	1.3 ± 0.1	1.1 ± 0.0	1.5 ± 0.2	3.4 ± 0.5
16	1.0 ± 0.0	1.1 ± 0.1	1.3 ± 0.0	3.5 ± 1.0	1.0 ± 0.2
17	1.0 ± 0.1	1.3 ± 0.2	1.3 ± 0.2	1.1 ± 0.2	2.8 ± 0.4
18	1.0 ± 0.0	1.6 ± 0.3	2.2 ± 0.3	2.2 ± 0.4	10.1 ± 0.9
19	1.0 ± 0.0	1.1 ± 0.0	1.2 ± 0.0	25.0 ± 0.8	9.5 ± 0.3
20	1.0 ± 0.1	1.2 ± 0.1	1.2 ± 0.1	17.8 ± 1.6	ND
21	1.0 ± 0.0	1.2 ± 0.0	1.1 ± 0.1	1.5 ± 0.1	1.3 ± 0.0
22	1.1 ± 0.3	1.4 ± 0.1	1.7 ± 0.1	2.0 ± 0.2	1.0 ± 0.2
23	1.3 ± 0.6	0.8 ± 0.2	0.7 ± 0.0	0.6 ± 0.1	0.5 ± 0.0
24	1.2 ± 0.5	1.4 ± 0.1	1.8 ± 0.1	3.6 ± 0.3	2.3 ± 0.7
25	1.0 ± 0.1	0.9 ± 0.0	0.9 ± 0.0	0.6 ± 0.0	0.2 ± 0.0
26	1.0 ± 0.1	0.7 ± 0.3	0.8 ± 0.1	1.5 ± 0.3	0.3 ± 0.1
27	1.0 ± 0.2	8.2 ± 0.7	7.5 ± 0.3	5.8 ± 0.1	3.8 ± 0.6
28	1.0 ± 0.1	1.3 ± 0.3	0.9 ± 0.1	0.8 ± 0.0	0.5 ± 0.0
29	1.0 ± 0.1	1.1 ± 0.2	1.0 ± 0.0	0.8 ± 0.0	1.2 ± 0.0
30	1.0 ± 0.1	1.2 ± 0.3	0.8 ± 0.2	0.9 ± 0.2	1.1 ± 0.1
31	1.0 ± 0.1	1.2 ± 0.2	1.1 ± 0.1	1.3 ± 0.2	1.0 ± 0.1
32	1.0 ± 0.1	1.1 ± 0.2	0.8 ± 0.1	0.8 ± 0.0	0.8 ± 0.1
33	1.0 ± 0.1	0.8 ± 0.1	0.5 ± 0.1	ND	3.2 ± 0.3
34	1.0 ± 0.1	1.0 ± 0.1	0.6 ± 0.1	0.8 ± 0.2	1.7 ± 0.4
35	1.0 ± 0.0	1.0 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	1.2 ± 0.1
36	1.0 ± 0.1	1.7 ± 0.3	1.0 ± 0.2	1.0 ± 0.0	1.1 ± 0.1
37	1.0 ± 0.0	1.3 ± 0.1	1.2 ± 0.1	0.9 ± 0.0	1.3 ± 0.0
38	1.0 ± 0.2	1.0 ± 0.3	0.9 ± 0.0	1.2 ± 0.0	1.3 ± 0.2

39	1.0 ± 0.1	0.4 ± 0.0	0.4 ± 0.0	1.2 ± 0.3	5.1 ± 0.3
40	1.0 ± 0.1	1.2 ± 0.1	1.1 ± 0.1	1.3 ± 0.1	1.3 ± 0.1
41	1.0 ± 0.2	0.4 ± 0.0	0.4 ± 0.1	27.7 ± 0.8	38.2 ± 7.1

Table S7

Compound	HK-2, IL-6 Expression				
	0	1	10	100	1000
1	1.0 ± 0.0	1.2 ± 0.1	1.1 ± 0.2	1.0 ± 0.1	0.9 ± 0.1
2	1.0 ± 0.0	1.4 ± 0.2	0.9 ± 0.0	0.9 ± 0.2	1.0 ± 0.0
3	1.0 ± 0.1	8.3 ± 0.2	7.6 ± 0.3	6.1 ± 0.1	12.8 ± 1.7
4	1.0 ± 0.1	1.4 ± 0.3	0.9 ± 0.0	8.6 ± 1.3	4.0 ± 0.7
5	1.0 ± 0.2	0.7 ± 0.2	3.6 ± 0.2	25.2 ± 2.7	120.5 ± 26.1
6	1.0 ± 0.1	1.3 ± 0.1	1.0 ± 0.1	1.0 ± 0.0	2.6 ± 0.3
7	1.0 ± 0.2	3.6 ± 0.8	2.2 ± 0.2	2.8 ± 0.0	1.5 ± 0.0
8	1.0 ± 0.2	1.7 ± 0.1	1.1 ± 0.1	0.2 ± 0.1	ND
9	1.0 ± 0.2	1.2 ± 0.1	0.7 ± 0.2	0.5 ± 0.2	0.8 ± 0.0
10	1.0 ± 0.0	1.1 ± 0.1	1.0 ± 0.0	1.2 ± 0.1	0.8 ± 0.1
11	1.0 ± 0.1	0.3 ± 0.0	1.6 ± 1.0	4.0 ± 1.4	5.9 ± 0.5
12	1.1 ± 0.3	0.7 ± 0.1	0.5 ± 0.0	0.8 ± 0.4	1.3 ± 0.0
13	1.0 ± 0.1	1.5 ± 0.0	2.3 ± 0.0	2.8 ± 0.8	2.6 ± 0.0
14	1.0 ± 0.1	1.0 ± 0.1	0.9 ± 0.0	0.5 ± 0.0	16.1 ± 1.1
15	1.0 ± 0.2	0.7 ± 0.1	0.7 ± 0.1	0.6 ± 0.0	0.3 ± 0.0
16	1.0 ± 0.1	1.6 ± 0.3	1.1 ± 0.2	1.1 ± 0.1	3.5 ± 0.5
17	1.0 ± 0.2	1.4 ± 0.2	0.9 ± 0.1	1.5 ± 0.2	2.0 ± 0.4
18	1.0 ± 0.1	0.1 ± 0.0	0.1 ± 0.0	0.6 ± 0.0	ND
19	1.0 ± 0.1	4.0 ± 0.3	5.1 ± 0.2	7.8 ± 0.4	5.8 ± 1.6
20	1.0 ± 0.1	0.8 ± 0.1	0.6 ± 0.1	1.1 ± 0.1	1.2 ± 0.1
21	1.0 ± 0.1	1.5 ± 0.0	1.4 ± 0.0	1.3 ± 0.0	14.7 ± 1.5
22	1.0 ± 0.1	2.0 ± 0.3	1.8 ± 0.1	2.0 ± 0.1	1.1 ± 0.0
23	1.0 ± 0.1	0.8 ± 0.0	0.6 ± 0.0	0.4 ± 0.0	0.7 ± 0.1
24	1.4 ± 0.8	0.7 ± 0.1	0.5 ± 0.0	0.2 ± 0.0	0.4 ± 0.1
25	1.1 ± 0.3	1.2 ± 0.2	0.6 ± 0.1	0.7 ± 0.1	0.6 ± 0.1
26	1.0 ± 0.1	0.9 ± 0.5	0.3 ± 0.1	0.3 ± 0.0	ND
27	1.1 ± 0.5	1.0 ± 0.1	0.7 ± 0.1	0.5 ± 0.0	0.2 ± 0.0
28	1.0 ± 0.1	1.6 ± 0.0	1.1 ± 0.0	0.9 ± 0.1	0.4 ± 0.0
29	1.0 ± 0.1	0.3 ± 0.0	1.5 ± 0.6	0.1 ± 0.0	0.1 ± 0.0
30	1.0 ± 0.2	1.3 ± 0.1	1.0 ± 0.2	1.0 ± 0.1	0.9 ± 0.0
31	1.1 ± 0.3	1.4 ± 0.0	0.7 ± 0.0	0.6 ± 0.0	0.8 ± 0.0
32	1.0 ± 0.1	0.8 ± 0.1	0.7 ± 0.0	0.9 ± 0.2	0.8 ± 0.0
33	1.1 ± 0.3	1.1 ± 0.1	0.8 ± 0.0	0.9 ± 0.1	ND
34	1.0 ± 0.1	1.3 ± 0.1	0.8 ± 0.1	0.6 ± 0.1	0.7 ± 0.0
35	1.0 ± 0.1	1.3 ± 0.1	1.1 ± 0.0	0.8 ± 0.3	1.3 ± 0.0
36	1.0 ± 0.2	1.0 ± 0.1	0.7 ± 0.1	0.6 ± 0.1	0.5 ± 0.0
37	1.1 ± 0.4	0.5 ± 0.1	0.3 ± 0.0	0.2 ± 0.0	0.8 ± 0.0
38	1.0 ± 0.1	1.5 ± 0.3	0.7 ± 0.2	0.6 ± 0.0	0.2 ± 0.0

39	1.0 ± 0.1	0.9 ± 0.1	0.5 ± 0.0	0.4 ± 0.1	2.4 ± 0.6
40	1.0 ± 0.1	1.2 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	0.8 ± 0.1
41	1.0 ± 0.1	2.2 ± 0.1	0.9 ± 0.0	0.7 ± 0.0	35.0 ± 4.3

Table S8

Compound	HK-2, IL-8 Expression				
	0	1	10	100	1000
1	1.0 ± 0.0	1.1 ± 0.1	1.0 ± 0.1	1.0 ± 0.1	1.3 ± 0.5
2	1.0 ± 0.0	1.1 ± 0.1	0.8 ± 0.1	0.8 ± 0.1	0.7 ± 0.0
3	1.0 ± 0.1	5.1 ± 0.2	4.3 ± 0.1	3.5 ± 0.1	4.1 ± 0.2
4	1.0 ± 0.0	1.6 ± 0.6	1.0 ± 0.1	13.9 ± 2.6	18.8 ± 5.3
5	1.0 ± 0.0	1.3 ± 0.4	5.0 ± 1.1	13.5 ± 1.8	30.5 ± 2.7
6	1.0 ± 0.1	1.2 ± 0.2	1.0 ± 0.1	1.0 ± 0.1	1.9 ± 0.3
7	1.0 ± 0.1	9.0 ± 0.7	8.6 ± 0.5	14.3 ± 1.2	0.9 ± 0.0
8	1.0 ± 0.2	2.5 ± 0.1	2.2 ± 0.1	1.6 ± 0.1	ND
9	1.0 ± 0.2	1.7 ± 0.1	0.8 ± 0.0	0.6 ± 0.1	0.7 ± 0.0
10	1.0 ± 0.1	1.2 ± 0.1	0.9 ± 0.0	0.9 ± 0.1	1.4 ± 0.5
11	1.0 ± 0.1	0.2 ± 0.0	2.0 ± 1.0	1.3 ± 0.5	1.0 ± 0.1
12	1.0 ± 0.2	1.3 ± 0.1	1.2 ± 0.1	1.2 ± 0.1	3.0 ± 0.0
13	1.0 ± 0.1	0.9 ± 0.1	3.7 ± 0.7	2.3 ± 0.4	2.5 ± 0.0
14	1.0 ± 0.1	1.0 ± 0.0	0.8 ± 0.1	0.2 ± 0.0	1.2 ± 0.1
15	1.0 ± 0.1	1.5 ± 0.2	1.5 ± 0.2	1.5 ± 0.1	1.1 ± 0.2
16	1.0 ± 0.0	1.9 ± 0.4	1.5 ± 0.3	1.1 ± 0.2	0.4 ± 0.0
17	1.0 ± 0.1	1.4 ± 0.1	1.2 ± 0.2	2.1 ± 0.1	2.1 ± 0.4
18	1.0 ± 0.0	0.5 ± 0.1	0.6 ± 0.1	0.4 ± 0.0	ND
19	1.0 ± 0.0	2.8 ± 0.1	2.1 ± 0.2	2.6 ± 0.3	2.5 ± 0.5
20	1.0 ± 0.2	0.6 ± 0.1	0.5 ± 0.0	1.3 ± 0.2	1.6 ± 0.3
21	1.0 ± 0.0	1.1 ± 0.0	1.1 ± 0.0	0.8 ± 0.1	1.7 ± 0.0
22	1.0 ± 0.0	3.9 ± 0.5	3.8 ± 0.4	3.1 ± 0.5	1.2 ± 0.2
23	1.0 ± 0.1	1.2 ± 0.2	0.8 ± 0.1	0.7 ± 0.1	0.7 ± 0.1
24	1.1 ± 0.3	4.7 ± 0.6	3.6 ± 0.8	2.2 ± 0.0	0.5 ± 0.3
25	1.0 ± 0.1	1.2 ± 0.1	1.2 ± 0.1	1.1 ± 0.1	1.1 ± 0.1
26	1.0 ± 0.0	0.5 ± 0.2	0.3 ± 0.0	0.4 ± 0.1	ND
27	1.0 ± 0.2	8.3 ± 0.7	5.4 ± 0.2	3.2 ± 0.2	2.4 ± 1.0
28	1.0 ± 0.0	1.4 ± 0.1	1.3 ± 0.1	1.4 ± 0.1	0.8 ± 0.1
29	1.0 ± 0.0	0.3 ± 0.1	0.1 ± 0.0	0.4 ± 0.1	0.5 ± 0.0
30	1.0 ± 0.2	1.6 ± 0.1	1.2 ± 0.2	1.1 ± 0.1	1.3 ± 0.0
31	1.0 ± 0.1	1.7 ± 0.3	1.1 ± 0.1	1.0 ± 0.1	1.0 ± 0.0
32	1.0 ± 0.1	1.1 ± 0.1	1.0 ± 0.1	1.1 ± 0.2	1.1 ± 0.0
33	1.0 ± 0.2	0.9 ± 0.1	1.0 ± 0.1	1.2 ± 0.1	ND
34	1.0 ± 0.0	1.2 ± 0.1	1.3 ± 0.1	0.8 ± 0.0	0.5 ± 0.0
35	1.0 ± 0.1	1.4 ± 0.1	0.9 ± 0.1	0.9 ± 0.0	1.5 ± 0.0
36	1.0 ± 0.0	0.8 ± 0.1	0.6 ± 0.1	0.5 ± 0.0	0.4 ± 0.0
37	1.0 ± 0.1	0.3 ± 0.0	0.3 ± 0.0	0.2 ± 0.0	0.3 ± 0.0
38	1.0 ± 0.1	1.1 ± 0.0	0.8 ± 0.1	0.7 ± 0.0	1.2 ± 0.1

39	1.0 ± 0.0	0.4 ± 0.0	0.4 ± 0.0	0.4 ± 0.0	10.2 ± 3.5
40	1.0 ± 0.0	1.0 ± 0.0	0.9 ± 0.0	0.9 ± 0.1	0.9 ± 0.1
41	1.0 ± 0.0	4.3 ± 0.4	1.7 ± 0.1	2.1 ± 0.1	82.4 ± 8.2

Table S9

Compound	LLC-PK1, IL-6 Expression				
	0	1	10	100	1000
1	1.0 ± 0.1	0.7 ± 0.2	2.3 ± 0.8	5.2 ± 1.0	1.8 ± 0.5
2	1.0 ± 0.1	0.9 ± 0.1	0.9 ± 0.0	1.0 ± 0.0	1.2 ± 0.0
3	1.0 ± 0.1	1.4 ± 0.2	0.7 ± 0.1	0.5 ± 0.0	0.3 ± 0.1
4	1.0 ± 0.1	1.1 ± 0.1	1.9 ± 0.7	1.0 ± 0.0	4.8 ± 0.3
5	1.0 ± 0.1	1.2 ± 0.2	15.1 ± 2.7	313.7 ± 31.4	180.5 ± 16.1
6	1.0 ± 0.2	0.6 ± 0.1	0.5 ± 0.0	0.9 ± 0.0	1.1 ± 0.0
7	1.0 ± 0.1	1.6 ± 0.0	1.8 ± 0.1	1.8 ± 0.1	1.4 ± 0.0
8	1.0 ± 0.0	1.4 ± 0.1	1.7 ± 0.1	1.1 ± 0.1	ND
9	1.1 ± 0.3	1.0 ± 0.1	0.8 ± 0.1	0.8 ± 0.0	0.9 ± 0.0
10	1.0 ± 0.0	1.1 ± 0.2	2.8 ± 0.3	6.3 ± 0.3	4.7 ± 0.5
11	1.0 ± 0.2	0.3 ± 0.0	0.5 ± 0.0	0.9 ± 0.1	ND
12	1.0 ± 0.1	0.9 ± 0.0	1.1 ± 0.1	1.3 ± 0.1	1.8 ± 0.1
13	1.0 ± 0.1	2.2 ± 0.1	12.9 ± 7.2	ND	ND
14	1.0 ± 0.1	1.1 ± 0.0	1.1 ± 0.1	3.3 ± 0.5	3.7 ± 0.2
15	1.0 ± 0.0	0.8 ± 0.0	0.9 ± 0.0	1.0 ± 0.0	2.4 ± 0.0
16	1.0 ± 0.1	1.3 ± 0.0	1.1 ± 0.1	1.2 ± 0.1	2.8 ± 0.0
17	1.0 ± 0.0	0.9 ± 0.0	1.3 ± 0.0	1.4 ± 0.0	2.5 ± 0.2
18	1.0 ± 0.1	0.9 ± 0.0	0.5 ± 0.0	0.9 ± 0.0	0.7 ± 0.1
19	1.0 ± 0.1	1.5 ± 0.1	1.5 ± 0.0	7.4 ± 1.0	1.4 ± 0.3
20	1.1 ± 0.3	0.7 ± 0.1	1.1 ± 0.3	2.2 ± 0.2	2.4 ± 0.6
21	1.0 ± 0.0	0.9 ± 0.1	1.0 ± 0.1	0.9 ± 0.0	1.7 ± 0.5
22	1.0 ± 0.0	1.5 ± 0.1	1.5 ± 0.1	1.4 ± 0.0	1.4 ± 0.0
23	1.0 ± 0.1	0.9 ± 0.1	0.7 ± 0.0	0.8 ± 0.1	0.9 ± 0.1
24	1.0 ± 0.2	1.3 ± 0.1	0.8 ± 0.0	0.7 ± 0.0	0.8 ± 0.1
25	1.0 ± 0.1	0.9 ± 0.1	1.3 ± 0.1	2.3 ± 0.4	1.7 ± 0.4
26	1.0 ± 0.2	0.3 ± 0.0	0.3 ± 0.0	0.4 ± 0.1	2.1 ± 0.5
27	1.0 ± 0.2	1.8 ± 0.1	1.9 ± 0.2	2.6 ± 0.1	1.6 ± 0.2
28	1.0 ± 0.1	0.8 ± 0.0	1.0 ± 0.0	0.9 ± 0.0	1.0 ± 0.0
29	1.0 ± 0.1	0.6 ± 0.1	0.5 ± 0.1	0.3 ± 0.1	0.9 ± 0.2
30	1.0 ± 0.2	1.1 ± 0.1	0.8 ± 0.1	0.8 ± 0.0	1.0 ± 0.1
31	1.0 ± 0.0	1.1 ± 0.1	1.2 ± 0.1	1.4 ± 0.2	1.6 ± 0.3
32	1.0 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	1.1 ± 0.2	0.9 ± 0.1
33	1.0 ± 0.2	0.9 ± 0.0	0.9 ± 0.1	1.1 ± 0.2	8.2 ± 2.6
34	1.0 ± 0.2	0.7 ± 0.0	0.5 ± 0.0	0.6 ± 0.1	1.8 ± 0.0
35	1.0 ± 0.0	0.7 ± 0.0	0.7 ± 0.0	0.7 ± 0.0	0.9 ± 0.1
36	1.0 ± 0.0	0.7 ± 0.0	0.7 ± 0.0	0.7 ± 0.1	0.8 ± 0.0
37	1.3 ± 0.7	0.5 ± 0.1	2.4 ± 0.3	1.1 ± 0.7	1.1 ± 0.5
38	1.0 ± 0.0	0.7 ± 0.0	0.7 ± 0.1	0.8 ± 0.0	0.7 ± 0.0

39	1.0 ± 0.0	0.6 ± 0.1	0.5 ± 0.0	0.7 ± 0.1	7.7 ± 0.6
40	1.0 ± 0.1	1.0 ± 0.0	1.1 ± 0.0	1.1 ± 0.0	1.1 ± 0.0
41	1.0 ± 0.2	0.9 ± 0.0	0.8 ± 0.0	0.4 ± 0.0	0.5 ± 0.1

Table S10

Compound	LLC-PK1, IL-8 Expression				
	0	1	10	100	1000
1	1.0 ± 0.1	1.3 ± 0.1	1.1 ± 0.3	2.7 ± 0.1	2.1 ± 0.5
2	1.0 ± 0.0	1.0 ± 0.0	1.3 ± 0.1	1.8 ± 0.2	2.3 ± 0.2
3	1.0 ± 0.1	7.8 ± 1.5	3.9 ± 0.4	2.1 ± 0.0	8.4 ± 0.1
4	1.0 ± 0.1	0.9 ± 0.1	1.2 ± 0.4	1.0 ± 0.0	8.9 ± 0.3
5	1.0 ± 0.0	0.9 ± 0.1	23.1 ± 3.9	413.7 ± 28.8	839.4 ± 305.9
6	1.0 ± 0.1	0.7 ± 0.1	0.6 ± 0.0	1.6 ± 0.2	0.8 ± 0.0
7	1.0 ± 0.1	10.1 ± 0.7	8.1 ± 0.7	9.1 ± 0.4	1.8 ± 0.0
8	1.0 ± 0.1	1.0 ± 0.4	0.7 ± 0.3	1.2 ± 0.4	ND
9	1.0 ± 0.2	1.7 ± 0.0	1.5 ± 0.2	1.5 ± 0.1	1.2 ± 0.1
10	1.0 ± 0.1	0.5 ± 0.1	1.5 ± 0.1	20.3 ± 2.0	15.8 ± 2.1
11	1.1 ± 0.3	0.8 ± 0.4	6.9 ± 0.3	0.4 ± 0.0	ND
12	1.0 ± 0.1	0.7 ± 0.0	0.9 ± 0.0	1.7 ± 0.1	4.3 ± 0.9
13	1.0 ± 0.1	2.1 ± 0.1	12.2 ± 4.3	ND	ND
14	1.0 ± 0.0	1.2 ± 0.1	1.8 ± 0.3	37.0 ± 4.4	1.6 ± 0.1
15	1.0 ± 0.1	0.7 ± 0.1	1.0 ± 0.1	1.3 ± 0.1	2.5 ± 0.1
16	1.0 ± 0.0	0.9 ± 0.1	1.2 ± 0.2	1.6 ± 0.3	0.7 ± 0.0
17	1.0 ± 0.1	1.0 ± 0.1	1.6 ± 0.0	2.0 ± 0.2	16.3 ± 4.3
18	1.0 ± 0.1	0.5 ± 0.0	0.4 ± 0.0	1.4 ± 0.2	0.4 ± 0.0
19	1.0 ± 0.2	5.9 ± 0.4	7.1 ± 0.5	301.3 ± 27.5	47.9 ± 6.0
20	1.0 ± 0.1	1.2 ± 0.3	0.7 ± 0.2	3.9 ± 0.1	4.9 ± 1.2
21	1.0 ± 0.1	2.2 ± 0.2	1.8 ± 0.1	1.2 ± 0.2	2.6 ± 0.3
22	1.0 ± 0.1	4.0 ± 0.3	2.2 ± 0.1	2.4 ± 0.2	1.5 ± 0.1
23	1.0 ± 0.1	1.2 ± 0.1	0.4 ± 0.0	0.6 ± 0.1	0.7 ± 0.1
24	1.1 ± 0.3	16.1 ± 0.4	8.4 ± 0.7	7.1 ± 1.3	1.4 ± 0.1
25	1.0 ± 0.0	0.9 ± 0.1	1.1 ± 0.0	1.8 ± 0.3	0.5 ± 0.1
26	1.0 ± 0.1	0.7 ± 0.1	0.5 ± 0.1	0.9 ± 0.0	2.9 ± 1.0
27	1.0 ± 0.2	7.6 ± 1.1	5.7 ± 0.7	13.7 ± 1.2	0.4 ± 0.0
28	1.0 ± 0.1	0.6 ± 0.1	0.9 ± 0.1	0.9 ± 0.1	1.0 ± 0.1
29	1.1 ± 0.2	0.9 ± 0.2	0.8 ± 0.1	0.6 ± 0.1	1.2 ± 0.1
30	1.0 ± 0.0	2.6 ± 0.1	1.8 ± 0.6	1.6 ± 0.3	1.5 ± 0.0
31	1.0 ± 0.1	0.8 ± 0.0	1.0 ± 0.0	1.3 ± 0.1	1.3 ± 0.0
32	1.0 ± 0.0	2.1 ± 0.1	1.3 ± 0.1	1.1 ± 0.2	0.7 ± 0.0
33	1.0 ± 0.2	0.9 ± 0.0	0.8 ± 0.1	0.8 ± 0.0	9.1 ± 0.6
34	1.0 ± 0.1	0.8 ± 0.0	0.7 ± 0.1	0.7 ± 0.0	0.5 ± 0.0
35	1.0 ± 0.1	0.7 ± 0.1	0.7 ± 0.1	0.7 ± 0.0	1.0 ± 0.0
36	1.0 ± 0.1	0.6 ± 0.0	0.6 ± 0.1	0.7 ± 0.1	0.6 ± 0.0
37	1.2 ± 0.5	0.7 ± 0.1	2.6 ± 0.2	1.3 ± 0.7	0.9 ± 0.3
38	1.0 ± 0.0	0.9 ± 0.1	1.0 ± 0.2	0.8 ± 0.1	1.1 ± 0.0

39	1.0 ± 0.0	0.8 ± 0.0	0.7 ± 0.0	0.7 ± 0.1	164.4 ± 4.0
40	1.0 ± 0.1	1.0 ± 0.1	1.0 ± 0.0	1.0 ± 0.0	1.1 ± 0.0
41	1.1 ± 0.2	2.4 ± 0.3	1.8 ± 0.1	2.0 ± 0.1	11.0 ± 1.0

Table S11

Details of primer pairs and amplicons. The sequences of the primer pairs (forward: F, reverse: R) for the different markers are shown. The sizes of the amplicons are provided in base pairs (bp).

Marker	Primer Pairs	Amplicon (bp)
VIM	F 5'-ACCTGAGGGAACTAATCTG-3' R 5'-CGTTGATAACCTGTCCATCT-3'	105
KIM-1	F 5'-CAGGCTGATCCCATAATGCA-3' R 5'-CTGCCTCTCCACCAACCTTTAC-3'	100
NGAL	F 5'-CAAGGAGCTGACTTCGGAATAA-3' R 5'-TGCACTCAGCCGTCGATACA-3'	120
IL-6	F 5'-TGGCTGCAGGACATGACAAC-3' R 5'-TGAGGTGCCCATGCTACATTT-3'	100
IL-8	F 5'-TTGGCAGCCTTCCTGATTTCT-3' R 5'-GGGTGGAAAGGTTTGGAGTATG-3'	110
IL-18	F 5'-GAACCAGTAGAAGACAATTGCATCA-3' R 5'-CCAGGTTTTTCATCATCTTCAGCTA-3'	91
GAPDH	F 5'-CCCCTTCATTGACCTCAACTACA-3' R 5'-GACGGTGCCATGGAATTTG-3'	76

Reference

1. A. Saito, K. Sawada and S. Fujimura, *Hemodial Int*, 2011, **15**, 183-192.