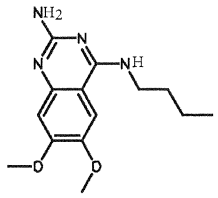
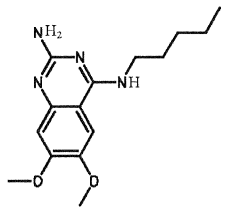
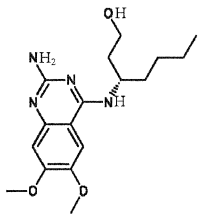
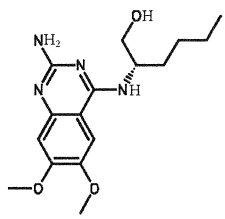
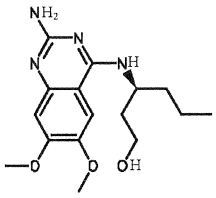
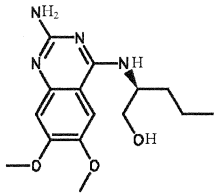
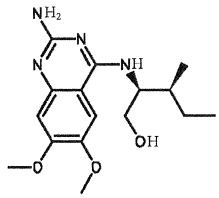
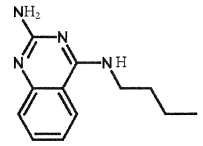
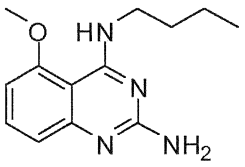
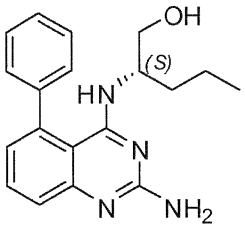
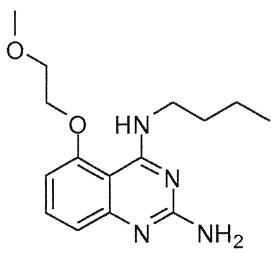
Table 1. Compounds of formula (I).

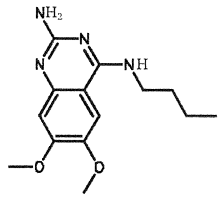
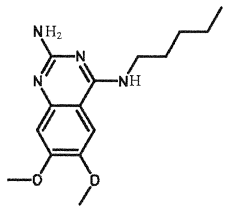
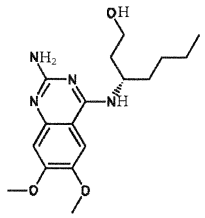
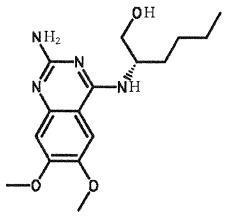
#	STRUCTURE	H NMR	Method, Rt	Synthetic Method
1		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.93 (t, J=7.3 Hz, 3 H), 1.31 - 1.43 (m, 2 H), 1.60 (t, J=7.1 Hz, 2 H), 3.40 - 3.48 (m, 2 H), 3.79 (s, 3 H), 3.79 (s, 3 H), 5.67 (s, 2 H), 6.63 (s, 1 H), 7.40 (s, 1 H), 7.44 - 7.50 (m, 1 H)	A, 0.67	
2		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.85 - 0.93 (m, 3 H), 1.27 - 1.37 (m, 4 H), 1.57 - 1.68 (m, 2 H), 3.39 - 3.49 (m, 2 H), 3.78 (s, 3 H), 3.79 (s, 3 H), 5.67 (s, 2 H), 6.63 (s, 1 H), 7.40 (s, 1 H), 7.47 (t, J=5.7 Hz, 1 H)	A, 0.86	Same method as to prepare 1.
3		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.79 - 0.91 (m, 3 H), 1.29 (m, J=3.3 Hz, 4 H), 1.59 (m, J=6.6 Hz, 2 H), 1.64 - 1.70 (m, 1 H), 1.72 - 1.79 (m, 1 H), 3.40 - 3.50 (m, 2 H), 3.80 (s, 3 H), 3.80 (s, 3 H), 4.33 - 4.43 (m, 1 H), 4.48 (t, J=5.1 Hz, 1 H), 5.68 (s, 2 H), 6.63 (s, 1 H), 7.09 (d, J=8.4 Hz, 1 H), 7.44 (s, 1 H)	A, 0.74	Same method as to prepare 1.
4		^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 0.91 (t, J=7.0 Hz, 3 H), 1.28 - 1.48 (m, 5 H), 1.58 - 1.77 (m, 2 H), 3.48 (s, 1 H), 3.72 (dd, J=11.0, 6.3 Hz, 1 H), 3.88 (s, 3 H), 3.91 (s, 3 H), 4.34 (td, J=6.8, 2.8 Hz, 1 H), 4.78 (br. s., 2 H), 5.64 (d, J=7.0 Hz, 1 H),	A, 0.68	Same method as to prepare 1.

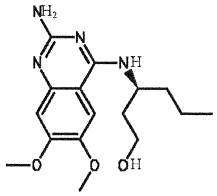
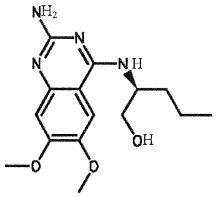
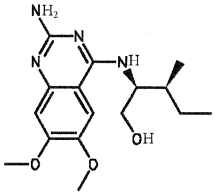
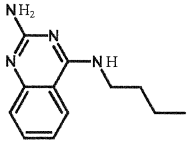
#	STRUCTURE	H NMR	Method, Rt	Synthetic Method
		6.81 (s, 1 H), 6.81 (s, 1 H)		
5		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.88 (t, J=7.3 Hz, 3 H), 1.23 - 1.42 (m, 2 H), 1.48 - 1.81 (m, 4 H), 3.39 - 3.48 (m, 2 H), 3.79 (s, 3 H), 3.80 (s, 3 H), 4.38 - 4.46 (m, 1 H), 4.49 (t, J=5.3 Hz, 1 H), 5.68 (s, 2 H), 6.63 (s, 1 H), 7.08 (d, J=8.4 Hz, 1 H), 7.44 (s, 1 H)	A, 0.69	Same method as to prepare 1.
6		^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 0.95 (t, J=7.3 Hz, 3 H), 1.35 - 1.52 (m, 2 H), 1.60 - 1.71 (m, 2 H), 3.48 (s, 1 H), 3.71 (dd, J=11.0, 6.3 Hz, 1 H), 3.85 (s, 3 H), 3.85 - 3.88 (m, 1 H), 3.90 (s, 3 H), 4.37 (td, J=6.7, 3.3 Hz, 1 H), 4.85 (br. s., 2 H), 5.82 (d, J=7.3 Hz, 1 H), 6.78 (s, 1 H), 6.85 (s, 1 H)	A, 0.69	Same method as to prepare 1.
7		^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 0.89 - 0.96 (m, 4 H), 1.01 (d, J=1.0 Hz, 4 H), 1.25 (ddd, J=13.7, 8.5, 7.4 Hz, 1 H), 1.47 - 1.65 (m, 1 H), 1.77 - 1.92 (m, 1 H), 3.48 (s, 0 H), 3.81 - 3.84 (m, 1 H), 3.87 (s, 3 H), 3.87 (s, 3 H), 4.21 - 4.31 (m, 1 H), 5.15 (br. s., 2 H), 6.04 - 6.11 (m, 1 H), 6.74 (s, 1 H), 6.86 (s, 1 H)		Same method as to prepare 1.

#	STRUCTURE	H NMR	Method, Rt	Synthetic Method
8		^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.89 - 0.96 (m, 3 H), 1.31 - 1.43 (m, 2 H), 1.57 - 1.67 (m, 2 H), 3.44 - 3.52 (m, 2 H), 6.04 (s, 2 H), 7.01 (ddd, J=8.1, 7.0, 1.0 Hz, 1 H), 7.20 (dd, J=8.4, 0.9 Hz, 1 H), 7.46 (ddd, J=8.3, 6.9, 1.4 Hz, 1 H), 7.75 (t, J=5.4 Hz, 1 H), 7.98 (dd, J=8.2, 0.9 Hz, 1 H)	A, 0.64	Same method as to prepare 1.
9		^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.94 (t, J=7.4 Hz, 3 H), 1.29 - 1.44 (m, 2 H), 1.63 (t, J=7.3 Hz, 2 H), 3.55 - 3.64 (m, 2 H), 4.02 (s, 3 H), 6.99 (dd, J=8.3, 1.8 Hz, 2 H), 7.69 (t, J=8.3 Hz, 1 H), 7.81 - 8.29 (m, 2 H), 9.10 (s, 1 H), 12.49 (s, 1 H)	C,0.83	
10		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.80 (t, J=1.00 Hz, 3 H) 0.83 - 0.93 (m, 1 H) 0.96 - 1.17 (m, 2 H) 1.20 - 1.35 (m, 1 H) 3.10 - 3.26 (m, 2 H) 3.36 (br. s., 2 H) 4.12 (td, J=8.23, 4.39 Hz, 1 H) 4.56 - 4.74 (m, 1 H) 5.96 (d, J=8.42 Hz, 1 H) 7.18 (d, J=1.00 Hz, 1 H) 7.37 - 7.64 (m, 6 H) 7.81 (t, J=1.00 Hz, 1 H)	C,0.88	
11		^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.94 (t, J=7.28 Hz, 3 H) 1.36 - 1.46 (m, 2 H) 1.55 - 1.63 (m, 2 H) 3.37 (s, 3 H) 3.44 (td, J=6.96, 5.14 Hz, 2 H) 3.74 - 3.80 (m, 2 H) 4.24 (dd, J=5.27, 3.76 Hz, 2 H) 6.04 (br. s, 2 H) 6.57 (d, J=7.53	C,0.85	See experimental section

two fold above the standard deviation of the assay. The LEC in turn indicates the degree of ISRE activation on transfer of a defined amount of PBMC culture medium. Recombinant interferon α-2a (Roferon-A) was used as a standard control compound.

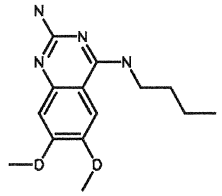
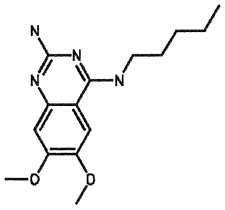
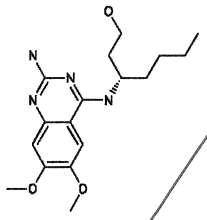
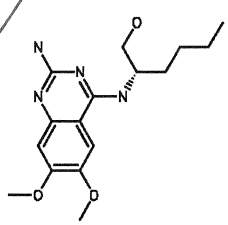
For a given compound, the LEC value obtained from this assay were in the same range as the EC_{50} values obtained from the "suppression of HCV replication assay." Thus, it is possible to compare the potential of compounds to induce IFN-I by PBMC, measured by either of the 2 assays.

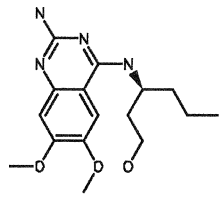
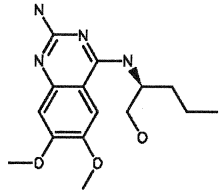
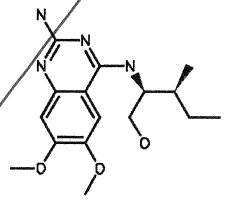
#	STRUCTURE	TLR7-wt_LEC	TLR7-dIRR2_LEC	TLR8-wt_LEC	TLR8-dIRR2_LEC	PBMC-HUH7_EC50
1		5.0	0.4	1.1	0.6	1.9
2		NA	1.2	1.5	0.6	4.4
3		**4.0** *	0.9	5.5	2.4	0.6
4		NA	2.4	2.6	1.7	3.0

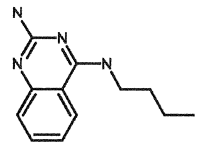
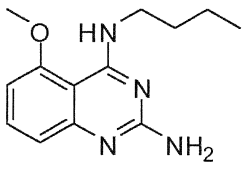
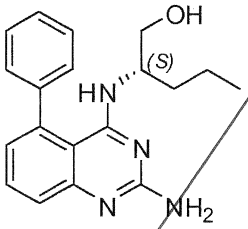
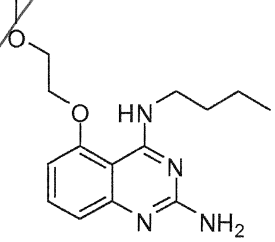
#	STRUCTURE	TLR7-wt_LEC	TLR7-dIRR2_LEC	TLR8-wt_LEC	TLR8-dIRR2_LEC	PBMC-HUH7_EC50
5		NA	2.6	6.7	2.6	3.3
6		NA	3.4	4.4	2.3	3.0
7		NA	3.8	13.8	9.0	12.4
8		0.1	0.02	0.1	0.02	NA

* Assay run at 48 hours

Table 1. Compounds of formula (I).

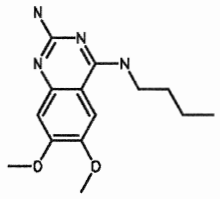
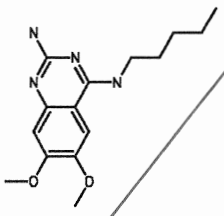
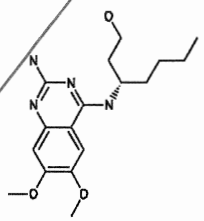
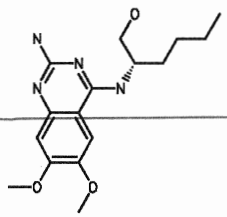
#	STRUCTURE	H NMR	Method, Rt	Synthetic Method
1		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.93 (t, J=7.3 Hz, 3 H), 1.31 - 1.43 (m, 2 H), 1.60 (t, J=7.1 Hz, 2 H), 3.40 - 3.48 (m, 2 H), 3.79 (s, 3 H), 3.79 (s, 3 H), 5.67 (s, 2 H), 6.63 (s, 1 H), 7.40 (s, 1 H), 7.44 - 7.50 (m, 1 H)	A, 0.67	
2		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.85 - 0.93 (m, 3 H), 1.27 - 1.37 (m, 4 H), 1.57 - 1.68 (m, 2 H), 3.39 - 3.49 (m, 2 H), 3.78 (s, 3 H), 3.79 (s, 3 H), 5.67 (s, 2 H), 6.63 (s, 1 H), 7.40 (s, 1 H), 7.47 (t, J=5.7 Hz, 1 H)	A, 0.86	Same method as to prepare 1.
3		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.79 - 0.91 (m, 3 H), 1.29 (m, J=3.3 Hz, 4 H), 1.59 (m, J=6.6 Hz, 2 H), 1.64 - 1.70 (m, 1 H), 1.72 - 1.79 (m, 1 H), 3.40 - 3.50 (m, 2 H), 3.80 (s, 3 H), 3.80 (s, 3 H), 4.33 - 4.43 (m, 1 H), 4.48 (t, J=5.1 Hz, 1 H), 5.68 (s, 2 H), 6.63 (s, 1 H), 7.09 (d, J=8.4 Hz, 1 H), 7.44 (s, 1 H)	A, 0.74	Same method as to prepare 1.
4		^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 0.91 (t, J=7.0 Hz, 3 H), 1.28 - 1.48 (m, 5 H), 1.58 - 1.77 (m, 2 H), 3.48 (s, 1 H), 3.72 (dd, J=11.0, 6.3 Hz, 1 H), 3.88 (s, 3 H), 3.91 (s, 3 H), 4.34 (td, J=6.8, 2.8 Hz, 1 H), 4.78 (br. s., 2 H), 5.64 (d, J=7.0 Hz, 1 H),	A, 0.68	Same method as to prepare 1.

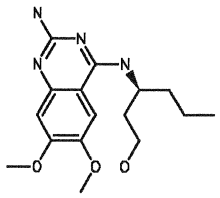
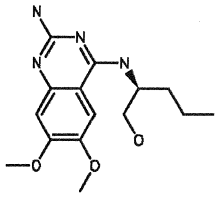
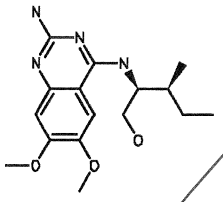
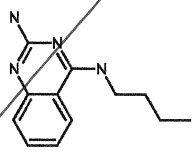
#	STRUCTURE	H NMR	Method, Rt	Synthetic Method
		6.81 (s, 1 H), 6.81 (s, 1 H)		
5		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.88 (t, J=7.3 Hz, 3 H), 1.23 - 1.42 (m, 2 H), 1.48 - 1.81 (m, 4 H), 3.39 - 3.48 (m, 2 H), 3.79 (s, 3 H), 3.80 (s, 3 H), 4.38 - 4.46 (m, 1 H), 4.49 (t, J=5.3 Hz, 1 H), 5.68 (s, 2 H), 6.63 (s, 1 H), 7.08 (d, J=8.4 Hz, 1 H), 7.44 (s, 1 H)	A, 0.69	Same method as to prepare 1.
6		^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 0.95 (t, J=7.3 Hz, 3 H), 1.35 - 1.52 (m, 2 H), 1.60 - 1.71 (m, 2 H), 3.48 (s, 1 H), 3.71 (dd, J=11.0, 6.3 Hz, 1 H), 3.85 (s, 3 H), 3.85 - 3.88 (m, 1 H), 3.90 (s, 3 H), 4.37 (td, J=6.7, 3.3 Hz, 1 H), 4.85 (br. s., 2 H), 5.82 (d, J=7.3 Hz, 1 H), 6.78 (s, 1 H), 6.85 (s, 1 H)	A, 0.69	Same method as to prepare 1.
7		^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 0.89 - 0.96 (m, 4 H), 1.01 (d, J=1.0 Hz, 4 H), 1.25 (ddd, J=13.7, 8.5, 7.4 Hz, 1 H), 1.47 - 1.65 (m, 1 H), 1.77 - 1.92 (m, 1 H), 3.48 (s, 0 H), 3.81 - 3.84 (m, 1 H), 3.87 (s, 3 H), 3.87 (s, 3 H), 4.21 - 4.31 (m, 1 H), 5.15 (br. s., 2 H), 6.04 - 6.11 (m, 1 H), 6.74 (s, 1 H), 6.86 (s, 1 H)		Same method as to prepare 1.

#	STRUCTURE	H NMR	Method, Rt	Synthetic Method
8		^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.89 - 0.96 (m, 3 H), 1.31 - 1.43 (m, 2 H), 1.57 - 1.67 (m, 2 H), 3.44 - 3.52 (m, 2 H), 6.04 (s, 2 H), 7.01 (ddd, J=8.1, 7.0, 1.0 Hz, 1 H), 7.20 (dd, J=8.4, 0.9 Hz, 1 H), 7.46 (ddd, J=8.3, 6.9, 1.4 Hz, 1 H), 7.75 (t, J=5.4 Hz, 1 H), 7.98 (dd, J=8.2, 0.9 Hz, 1 H)	A, 0.64	Same method as to prepare 1.
9		^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.94 (t, J=7.4 Hz, 3 H), 1.29 - 1.44 (m, 2 H), 1.63 (t, J=7.3 Hz, 2 H), 3.55 - 3.64 (m, 2 H), 4.02 (s, 3 H), 6.99 (dd, J=8.3, 1.8 Hz, 2 H), 7.69 (t, J=8.3 Hz, 1 H), 7.81 - 8.29 (m, 2 H), 9.10 (s, 1 H), 12.49 (s, 1 H)	C,0.83	
10		^{1}H NMR (360 MHz, DMSO-d_6) δ ppm 0.80 (t, J=1.00 Hz, 3 H) 0.83 - 0.93 (m, 1 H) 0.96 - 1.17 (m, 2 H) 1.20 - 1.35 (m, 1 H) 3.10 - 3.26 (m, 2 H) 3.36 (br. s., 2 H) 4.12 (td, J=8.23, 4.39 Hz, 1 H) 4.56 - 4.74 (m, 1 H) 5.96 (d, J=8.42 Hz, 1 H) 7.18 (d, J=1.00 Hz, 1 H) 7.37 - 7.64 (m, 6 H) 7.81 (t, J=1.00 Hz, 1 H)	C,0.88	
11		^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 0.94 (t, J=7.28 Hz, 3 H) 1.36 - 1.46 (m, 2 H) 1.55 - 1.63 (m, 2 H) 3.37 (s, 3 H) 3.44 (td, J=6.96, 5.14 Hz, 2 H) 3.74 - 3.80 (m, 2 H) 4.24 (dd, J=5.27, 3.76 Hz, 2 H) 6.04 (br. s, 2 H) 6.57 (d, J=7.53	C,0.85	See experimental section

two fold above the standard deviation of the assay. The LEC in turn indicates the degree of ISRE activation on transfer of a defined amount of PBMC culture medium. Recombinant interferon α-2a (Roferon-A) was used as a standard control compound.

For a given compound, the LEC value obtained from this assay were in the same range as the EC_{50} values obtained from the "suppression of HCV replication assay." Thus, it is possible to compare the potential of compounds to induce IFN-I by PBMC, measured by either of the 2 assays.

#	STRUCTURE	TLR7-wt_LEC	TLR7-dIRR2_LEC	TLR8-wt_LEC	TLR8-dIRR2_LEC	PBMC-HUH7_EC50
1		5.0	0.4	1.1	0.6	1.9
2		NA	1.2	1.5	0.6	4.4
3		**4.0** *	0.9	5.5	2.4	0.6
4		NA	2.4	2.6	1.7	3.0

#	STRUCTURE	TLR7-wt_LEC	TLR7-dIRR2_LEC	TLR8-wt_LEC	TLR8-dIRR2_LEC	PBMC-HUH7_EC50
5		NA	2.6	6.7	2.6	3.3
6		NA	3.4	4.4	2.3	3.0
7		NA	3.8	13.8	9.0	12.4
8		0.1	0.02	0.1	0.02	NA

* Assay run at 48 hours