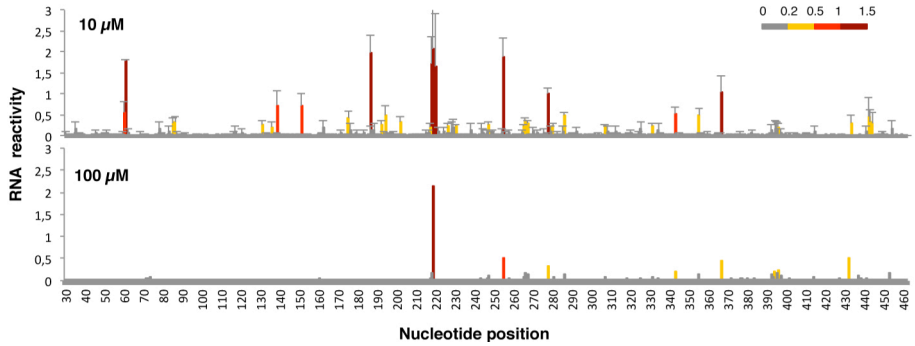
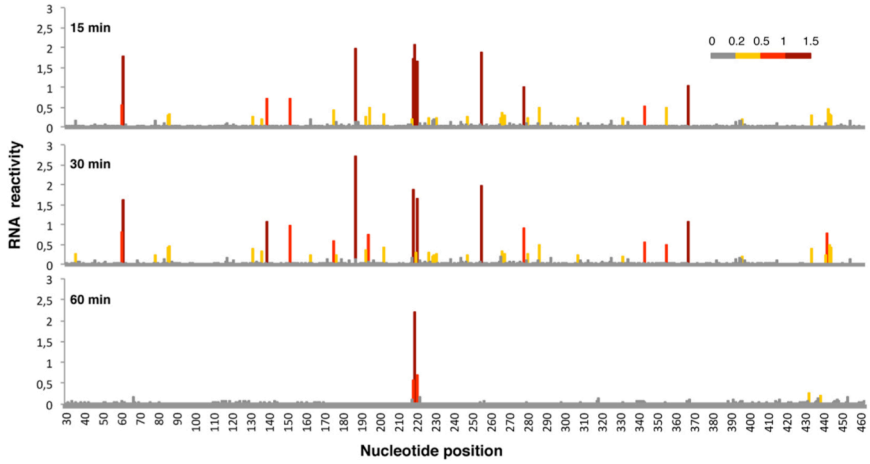
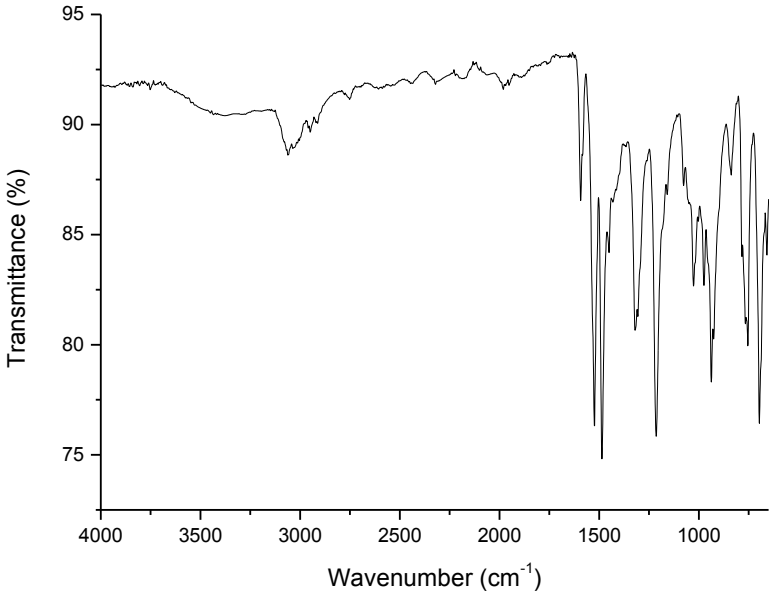
SUPPLEMENTAL MATERIAL



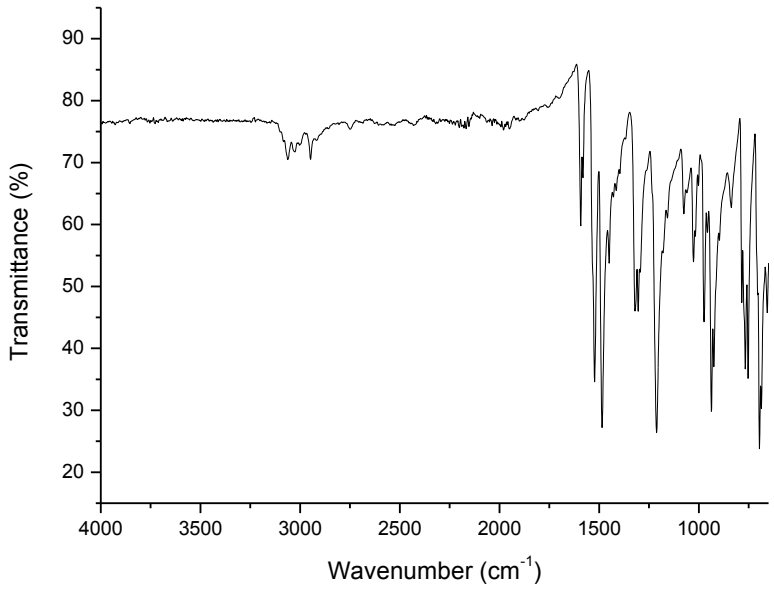
Supplemental Figure 1. RNA reactivity towards OPW-Ru is concentration dependent. RNA was incubated with OPW-Ru for 15 min at 37ºC. Normalized FMDV IRES reactivity as a function of nucleotide position, colored according to the scale shown at the top.



Supplemental Figure 2. RNA reactivity towards OPW-Ru as a function of incubation time. RNA incubated with OPW-Ru (10 μM) at 37 ºC. Normalized FMDV IRES reactivity is plotted as a function of nucleotide position, colored according to the scale shown at the top.



Supplemental Figure 3. IR spectrum of $[Ru_2Cl_2(\mu\text{-}DPhF)_3(DMSO)]\cdot H_2O$.



Supplemental Figure 4. IR spectrum of $[Ru_2Cl_2(\mu\text{-}DPhF)_3(DMSO)]$ (OPW-Ru).

Supplemental Table 1. Selected bond distances (Å) and angles (º) for compound OPW-Ru.

Bond distances		Bond angles	
Ru1-Ru2	2.3408(4)	**Ru2-Ru1-Cl1**	94.87(3)
Ru1-Cl1	2.3756(10)	**Ru1-Ru2-Cl2**	114.22(3)
Ru2-Cl2	2.3533(10)	**O1-Ru1-Ru2**	177.13(6)
Ru1-O1	2.221(2)	**O1-Ru1-Cl1**	85.21(6)
Ru1-N1	2.089(3)	**N5-Ru1-Cl1**	91.29(8)
Ru1-N3	2.080(3)	**N6-Ru2-Cl2**	92.59(8)
Ru1-N5	2.079(3)	**N5-Ru1-N1**	90.25(11)
Ru2-N2	2.035(3)	**N3-Ru1-N1**	87.37(11)
Ru2-N4	2.055(3)	**N2-Ru2-N6**	88.26(11)
Ru2-N6	2.055(3)	**N2-Ru2-N4**	89.80(12)

Supplemental Table 2. Solvent accessibility and OPW-Ru reactivity of the FMDV IRES.

nt position [a]	OPW-Ru normalized reactivity	Secondary structure	Solvent accessibility [b]	·OH radical reactivity [c]
60	0.555	paired	Prot	0.16
61	1.780	paired	Acc	0.26
139	0.735	paired	Prot	0.14
151	0.711	paired	Acc	0.19
187	1.975	paired	Acc	0.24
194	0.496	paired	Acc	0.53
218	1.725	paired	Prot	0
219	2.074	paired	Prot	0
220	1.648	paired	Prot	0.1
255	1.886	paired	Acc	0.39
278	1.012	paired	Acc	0.25
286	0.493	paired	Prot	0
343	0.531	unpaired	Acc	2.66
367	1.030	paired	Prot	0

[a] only the most reactive nucleotides (marked in red on Fig. 3A) are included in the table.

[b] Prot, protected; Acc, accessible. Hydroxyl radical cleavage intensities were normalized to a scale from 0 to 1.5, where 1.0 is defined as the average intensity of highly reactive residues (Chakraborty et al. 2012). Nucleotides with reactivity values lower than half the mean (0.176) reactivity are defined as solvent-inaccessible

[c] determined as in Lozano et al. 2014

Supplemental Table 3. Structural features and OPW-Ru reactivity of the HCV IRES

Nt Position [a]	OPW-RU normalized reactivity	Secondary structure	Solvent accesibility [b]	Interacting edges [c]	Sugar conformation [c]	Backbone turn [c]
47	0.213	paired	Acc	WC	C2' endo	No
55	0.243	unpaired	Acc	-	C3' endo	Turn
56	0.336	unpaired	Acc	-	C2' endo	Turn
131	0.198	paired	Acc	WC	C3' endo	No
132	0.415	paired	Prot	WC	C3' endo	No
133	0.261	paired	Prot	WC	C3' endo	No
163	0.252	unpaired	Acc	-	C3' endo	-
164	0.349	unpaired	Acc	-	C3' endo	-
166	0.790	unpaired	Acc	-	C3' endo	No
171	0.678	paired	Acc	WC	C3' endo	No
172	0.201	paired	Acc	WC	C3' endo	No
201	0.426	unpaired	Acc	-	C3' endo	No
317	0.060	paired	Prot	WC	C3' endo	No
318	0.390	paired	Prot	WC	C3' endo	No
319	2.046	paired	Acc	WC	C3' endo	Turn
320	0.000	paired	Acc	WC	C3' endo	No
321	0.328	paired	Acc	WC	C3' endo	No
322	0.021	paired	Acc	WC	C3' endo	No
325	0.346	paired	Acc	WC	C3' endo	No

[a] The positions surrounding the reactive nucleotides (marked in red and yellow on Fig. 4B) for which three-dimensional RNA structure is available are included in the table.

[b] Prot, protected; Acc, accessible. Hydroxyl radical cleavage intensities were determined by Kieft et al. 1999.

[c] Adapted from Kieft et al. 2002; Lukavsky et al. 2003; Berry et al. 2010; Perard et al. 2011.