Supporting Information

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S A N O

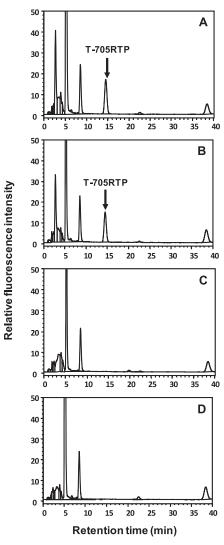


Fig. S1. Chromatogram of cellular extracts from T-705-treated A549 cells. The intracellular phosphorylation profile of T-705 in A549 cells treated with 5 μ M T-705 alone (*A*), or in combination with 50 μ M thymidine (*B*), adenosine (*C*), or guanosine (*D*) for 24 h was evaluated by fluorescence chromatogram analysis. The retention time of the pure standard of T-705RTP was 14.6 min.

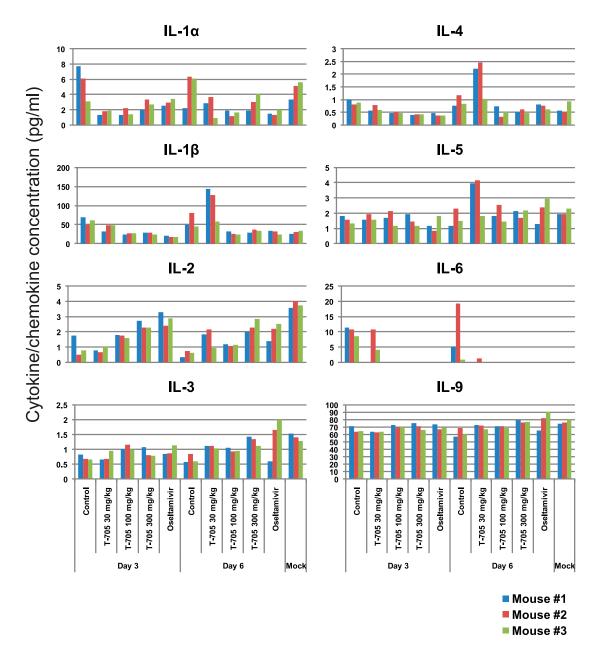
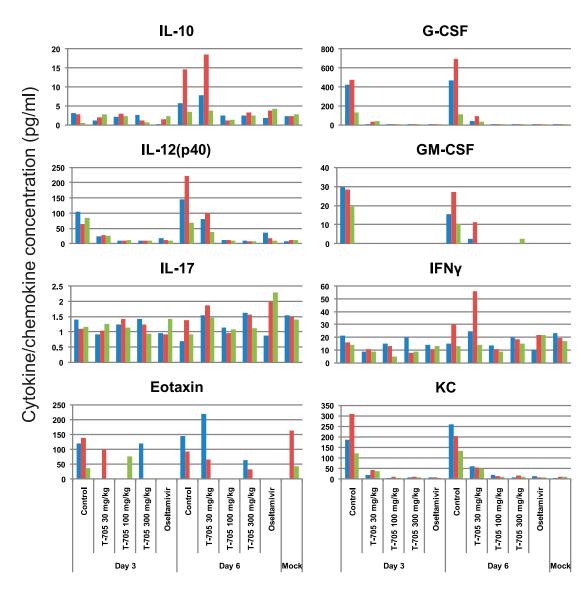


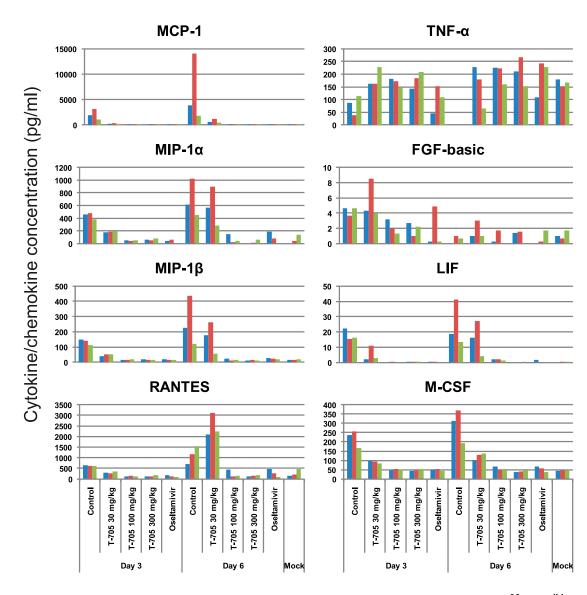
Fig. S2. Proinflammatory cytokines/chemokines in the lungs of infected mice. The concentrations of various cytokines/chemokines in the lungs of infected mice on days 3 and 6 postinfection were measured by protein array analysis with the Bio-Plex Mouse Cytokine 23-Plex and 9-Plex panel (Bio-Rad laboratories), with the exception of IFN- α and - β measurements, which were done by ELISA with the Mouse IFN Alpha or Beta ELISA Kit (Invitrogen). We were unable to detect IL-12 (p70), IL-13, or IL-15. IL-18 data are not available because of a technical problem with the manufacturer.



Mouse #1Mouse #2

Mouse #3

Fig. S2. continued.



Mouse #1Mouse #2

Mouse #3

Fig. S2. continued.

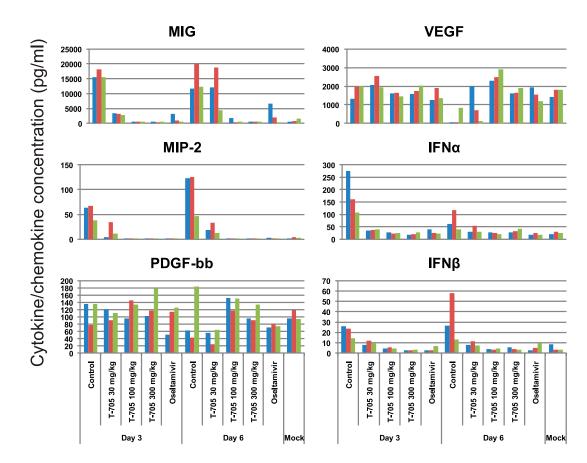




Fig. S2. continued.

Table S1. Effect of T-705RTP and Ribavirin TP on human DNApolymerase activity*

	Polymerase [†]	Inhibition rate [‡] (%) with	
Compound (mM)		dTTP	dGTP
T-705RTP 0.1	α	-1.82	1.61
	β	-2.36	1.12
	γ	1.93	-4.10
1	α	-9.12	-1.81
	β	9.08	13.5
	γ	41.2	11.7
Ribavirin TP 0.1	α	8.78	-1.47
	β	23.1	22.7
	γ	1.83	1.54
1	α	65.0	63.0
	β	50.8	63.8
	γ	27.1	24.8
	1 0.1	0.1 α β γ 1 α β γ 0.1 α γ γ 1 α β γ 1 α β γ 1 α β γ	$\begin{tabular}{ c c c c c } \hline Polymerase' & dTTP \\ \hline 0.1 & \alpha & -1.82 \\ \hline & & & & -1.82 \\ \hline & & & & & & & \\ \hline & & & & & & & \\ \hline & & & &$

*The effect of compounds on DNA synthesis in human cells is shown as the rate of inhibition of human DNA polymerase activity.

 † Polymerase: $\alpha,$ human DNA polymerase $\alpha;$ $\beta,$ human DNA polymerase $\beta;$ $\gamma,$ human DNA polymerase $\gamma.$

^{*}The inhibition rate of DNA polymerase activity was calculated from the incorporation efficiency of [methyl-³H]dTTP or [methyl-³H]dGTP into the macro DNA molecule.

Table S2. Number of mice with lung lesions*

_	Number of mice with lung lesions on		
Compound and dosage (mg/kg/day)	Day 3	Day 6	
Control	3/3	3/3	
T-705 30	3/3	3/3	
T-705 100	1/3	1/3	
T-705 300	0/3	0/3	
GS4104 50	1/3	2/3	

*Mice with lung lesions in at least in one lung lobe were counted.

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