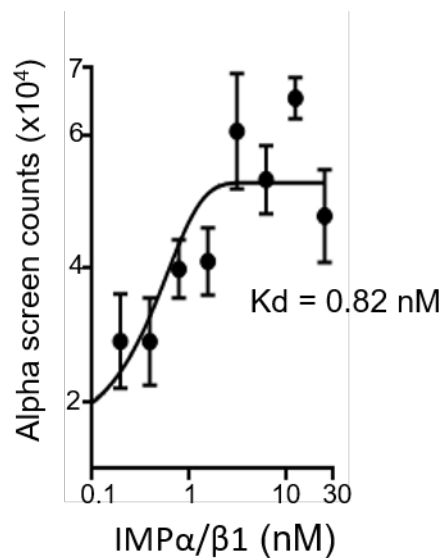
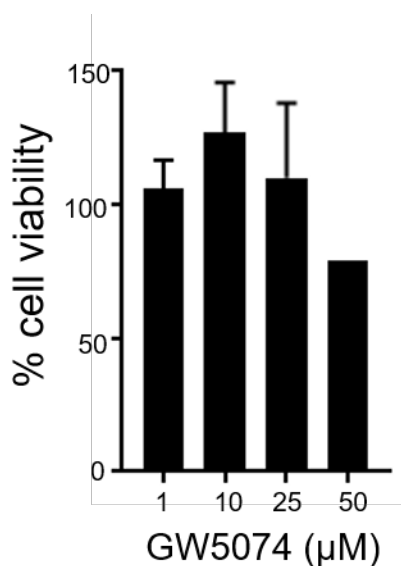


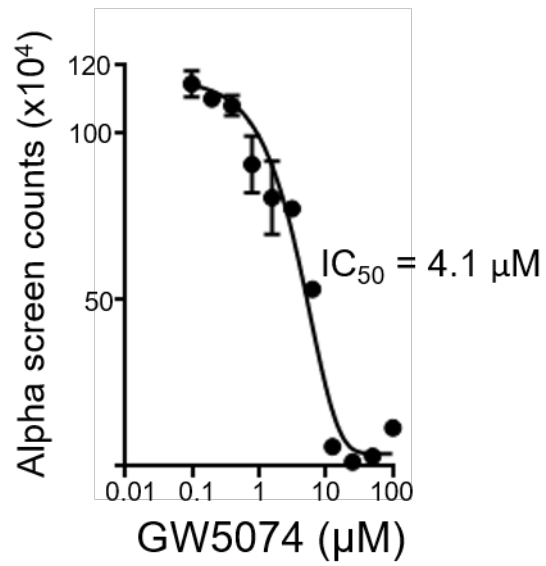
## Supplementary Figures



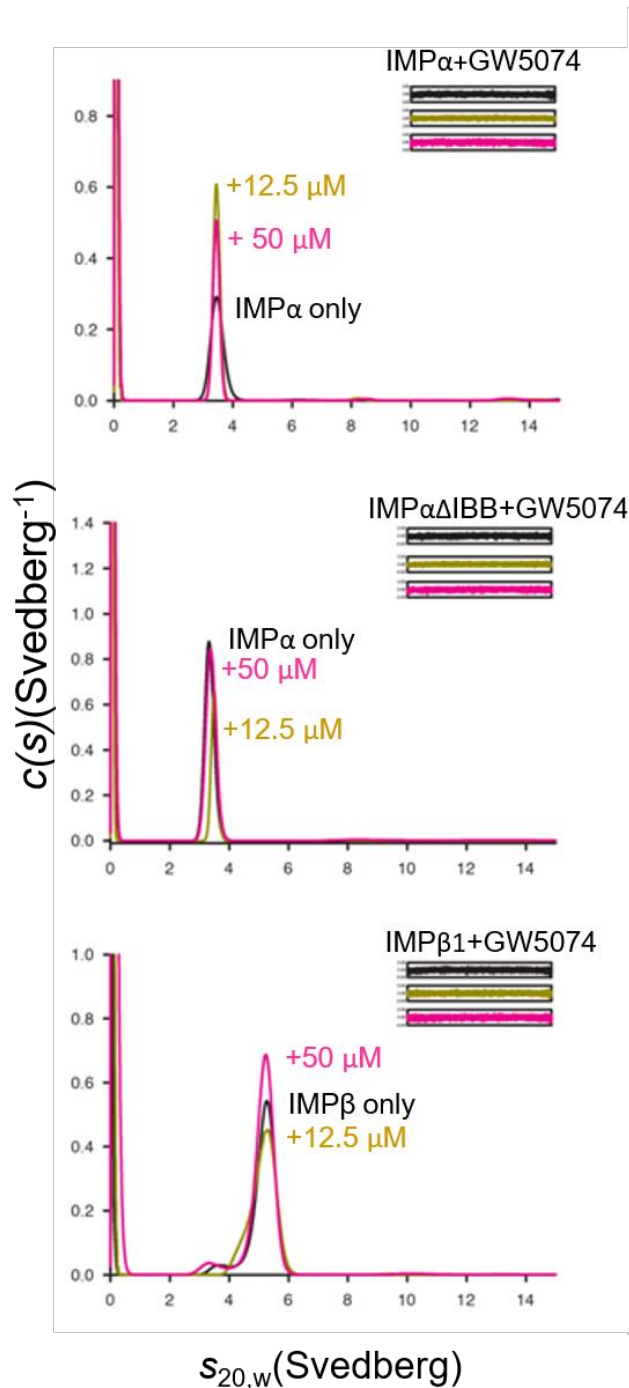
**Fig. S1. High affinity recognition of DENV NS5 by the IMP $\alpha$ / $\beta$ 1 heterodimer.** AlphaScreen technology was used to determine the dissociation constant ( $K_d$ ) of binding of IMP $\alpha$ / $\beta$ 1 (prebound IMP $\alpha$ / $\beta$ 1 heterodimer with biotinylated IMP $\beta$ 1) to His<sub>6</sub>-DENV NS5 (30 nM). Data represent the mean  $\pm$  SD for triplicate wells from a single typical experiment, from a series of 2 independent experiments (see Table 1 column 1 for pooled data).



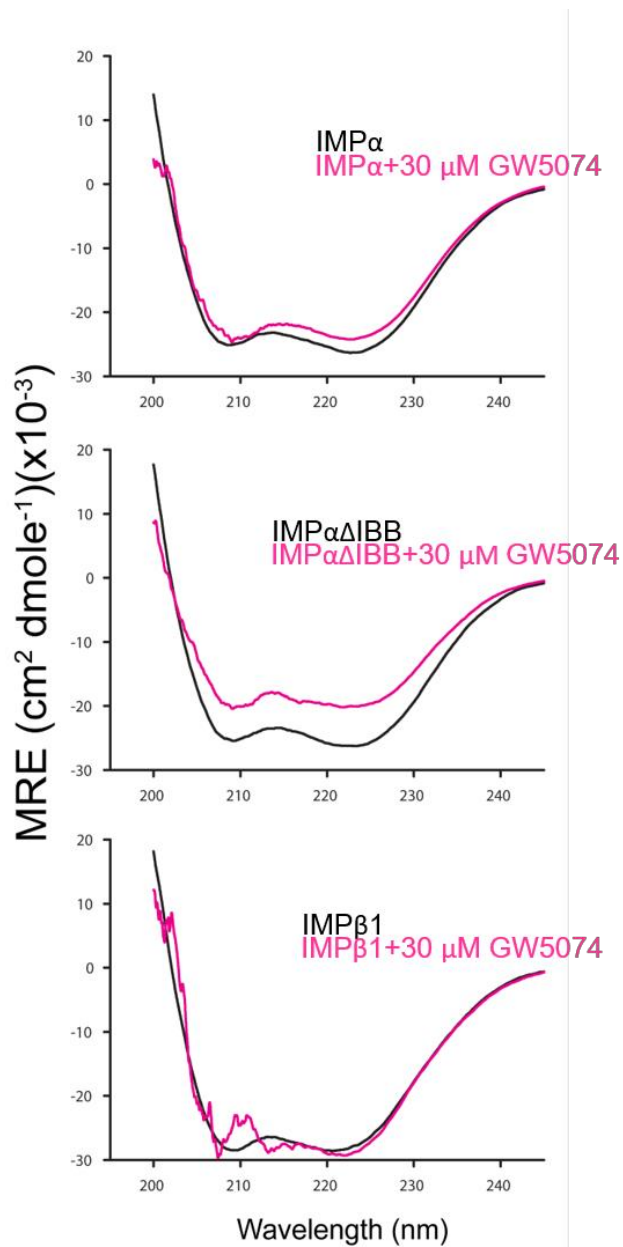
**Fig. S2. Lack of toxicity of GW5074 at concentrations effective in inhibiting flavivirus.** Cell viability was determined by addition of XTT reagent (Sigma-Aldrich) following compound treatments, as indicated. Cell survival is plotted relative to an untreated control. Data represent the mean  $\pm$  SD for duplicate wells from a single typical experiment, from a series of 2 independent experiments.



**Fig. S3. GW5074 inhibits recognition of SV40 T-antigen by the IMP $\alpha$ / $\beta$ 1 heterodimer.** AlphaScreen technology was used to determine the IC<sub>50</sub> for inhibition by GW5074 of T-ag binding to IMP $\alpha$ / $\beta$ 1. Data represent the mean  $\pm$  SD for triplicate wells from a single typical experiment, from a series of 2 independent experiments.



**Fig. S4. GW5074 does not alter the sedimentation coefficients of IMP $\alpha$ , IMP $\alpha$ ΔIBB or IMP $\beta$ 1.** Sedimentation velocity analytical ultracentrifugation experiments were performed on purified recombinant IMP $\alpha$ , IMP $\alpha$ ΔIBB and IMP $\beta$ 1, in the absence or presence of GW5074. The continuous sedimentation coefficient distribution  $[(c)s]$  was plotted as a function of  $s_{20,w}$  for IMPs alone, in the presence of the indicated concentrations of GW5074. The residual plots are shown in insets. Results are from a single typical experiment, from a series of 2 independent experiments.



**Fig. S5. CD spectra for IMPs in the absence and presence of GW5074.** CD spectra were collected for IMP $\alpha$ , IMP $\alpha\Delta$ IBB and IMP $\beta$ 1 in the absence or presence of 30  $\mu$ M GW5074. The plots are representative of 2 independent experiments.

## Supplementary Materials

**Table S1.** Hydrodynamic properties of recombinant IMP proteins.

Protein	Parameter			
	$M_r^a$	$M^b$	$s_{20,w}^c$	$f/f_0^d$
IMP $\alpha$	58072	50316	3.5	2.4
IMP $\beta$ 1	98557	106358	5.3	2.1
IMP $\alpha/\beta$ 1	156629	155055	6.7	2.7

<sup>a</sup> Relative molecular weight calculated from the amino acid sequence.

<sup>b</sup> Molar mass determined from the ordinate maximum of  $c(M)$  distribution best fits (data not shown).

<sup>c</sup> Standardized sedimentation coefficient taken from the ordinate maximum of the  $c(s)$  distribution best fits (Fig. 2C).

<sup>d</sup> Frictional coefficient calculated from  $s_{20,w}$  using the  $\bar{v}$  method employing SEDNTERP.