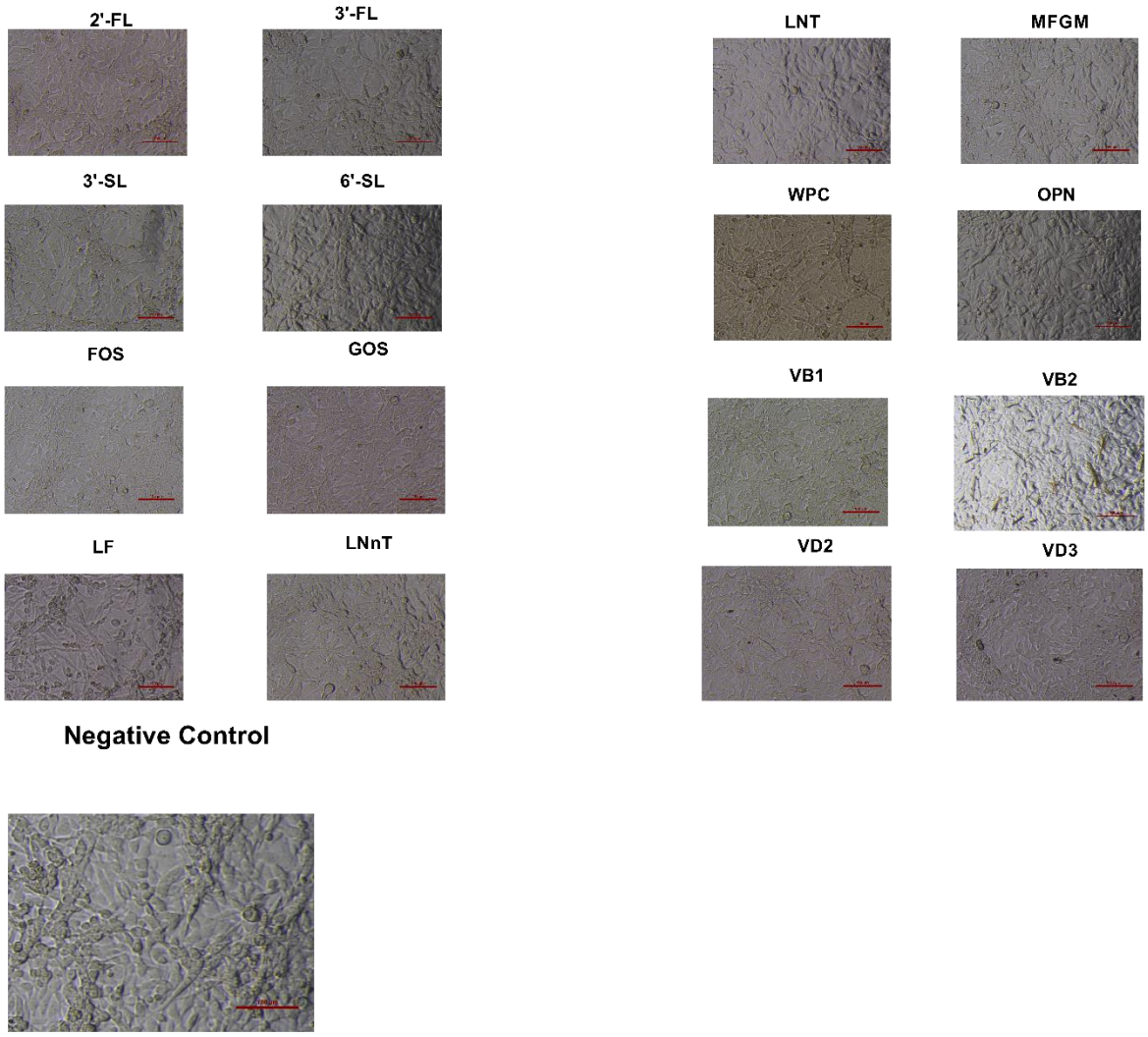
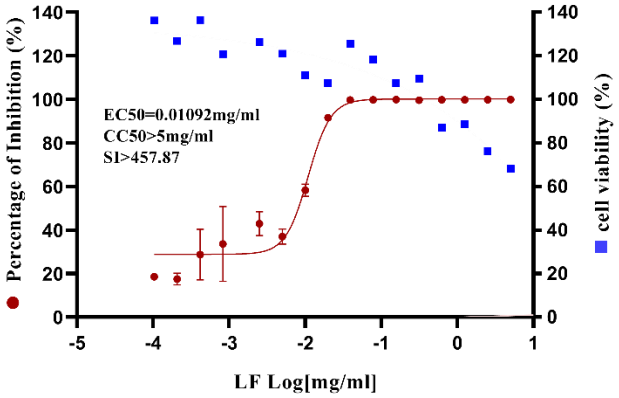


Figure S1. Cytogram after treatment with 16 primary screening drugs. RD cells were seeded in 96-well plates. At 80%–90% cell density, various drugs (2′-FL [10 mg/mL], 3′-Fucosyllactose [10 mg/mL], lacto-N-Tetraose [10 mg/mL], lacto-N-Neotetraose [10 mg/mL], 3′-Sialyllactose [10 mg/mL], 6′-Sialyllactose [10 mg/mL], whey protein concentrate [5 mg/mL], milk fat globule membrane [5 mg/mL], LF [5 mg/mL], OPN [5 mg/mL], Vitamin B2 [100 ug/mL], Vitamin B1 [1 mg/mL], Vitamin D2 [1 mg/mL], and Vitamin D3 [1 mg/mL]) were added. At 48 h.p.i., Perform cytography to observe cytopathic lesions.

A



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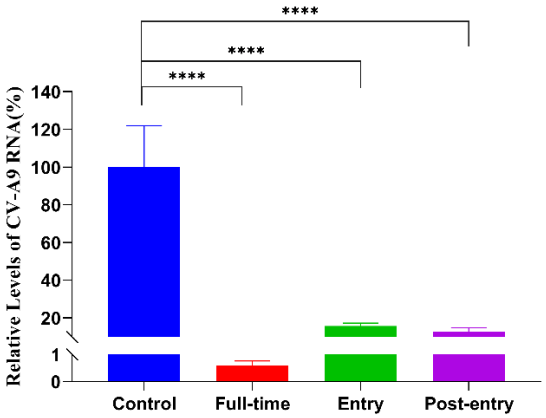

Figure S2. The anti-CV-A9 activity of lactoferrin (LF). (**A**) The anti-CV-A9 EC_{50} and CC_{50} of LF on RD. Cells were infected with CV-A9 at MOI = 0.001 and treated with LF at various concentrations (from 5mg/ml to 0.0001 mg/mL) to determine viral inhibition and cell viability. Concentration of ≥0.02 mg/mL was able to inhibit CV-A9 infection. The left and right Y-axis represent mean percentage of inhibition of virus yield and cytotoxicity, respectively. (**B**) Time-of-addition experiment of LF (0.04 mg/mL). The detailed steps for time-of-addition experiment were described in the method section, and virus and GAPDH mRNA levels in the infected cell were quantified by qRT-PCR at 48h p.i. ****$p < 0.0001$, Student's t-test compared to control.

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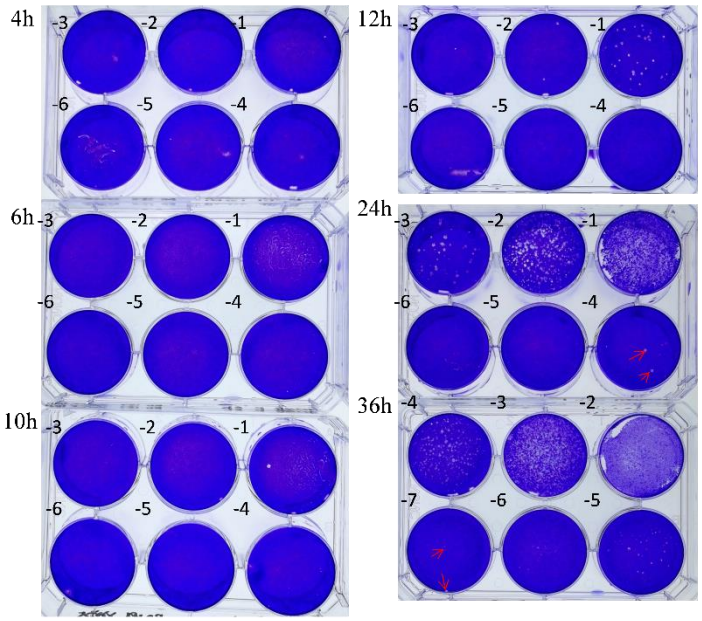
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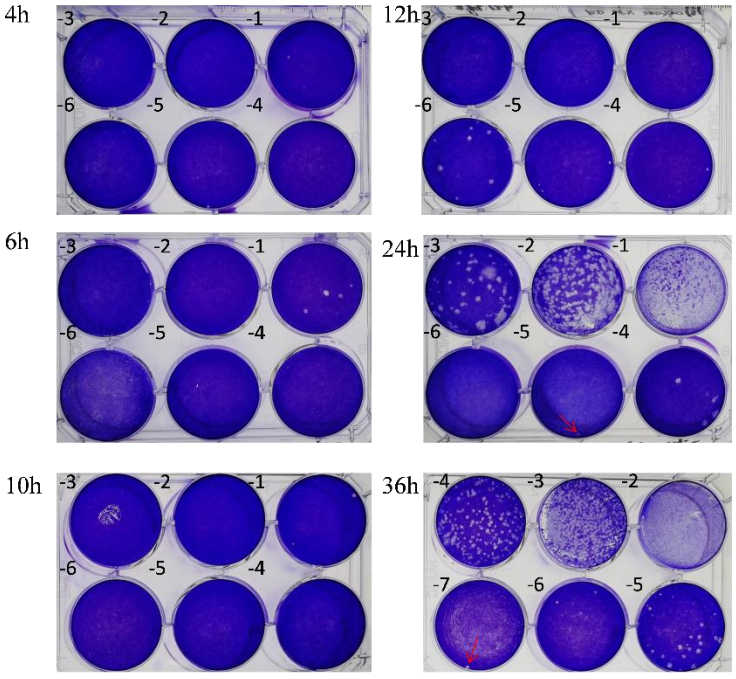
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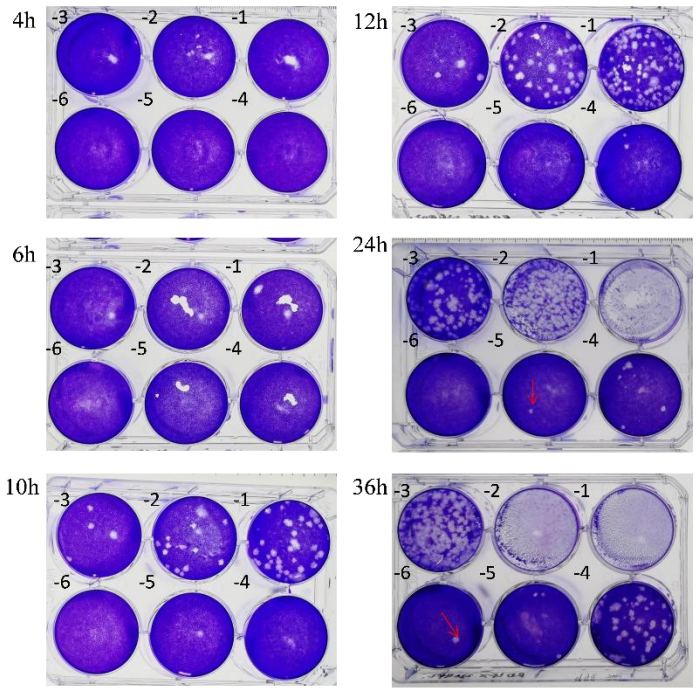

Figure S3. Plaque assay corresponding to the CV-A9 single-step growth curve in RD cells (**A**) without any drug treatment, (**B**) with a single dose of 2′FL (10 mg/ml) and (**C**) with a single dose of LF (0.04 mg/mL) treatment.