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Supplemental information

Disrupting autorepression circuitry generates

"open-loop lethality" to yield

escape-resistant antiviral agents

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FD^{Scram} vs Mock



FD⁸⁶ vs Mock Cytokine-mediated signaling pathway



Inflammatory response











ORF1a RNA 12hpi * 8hpi 24hpi * 2.5 25-* 4 relative fold change 20 2.0 3-15 1.5 2-10-1.0 5 1. 0.5 0 0.0 0 -5 **FD**^{Scram}**FD**^{TRS} FD^{Scram} FD^{TRS} **FD**^{Scram} **FD**^{TRS} **FD**^{TRS} **FD**^{Scram} 250K 200K SSC 150K 100K 50K 0 10² 10³ 10⁴ 10⁵ $10^2 \ 10^3 \ 10^4$ 10⁵ TUNEL [R.F.U.] TUNEL [R.F.U.]

a

b