

# Why the omicron variant causes less severe disease

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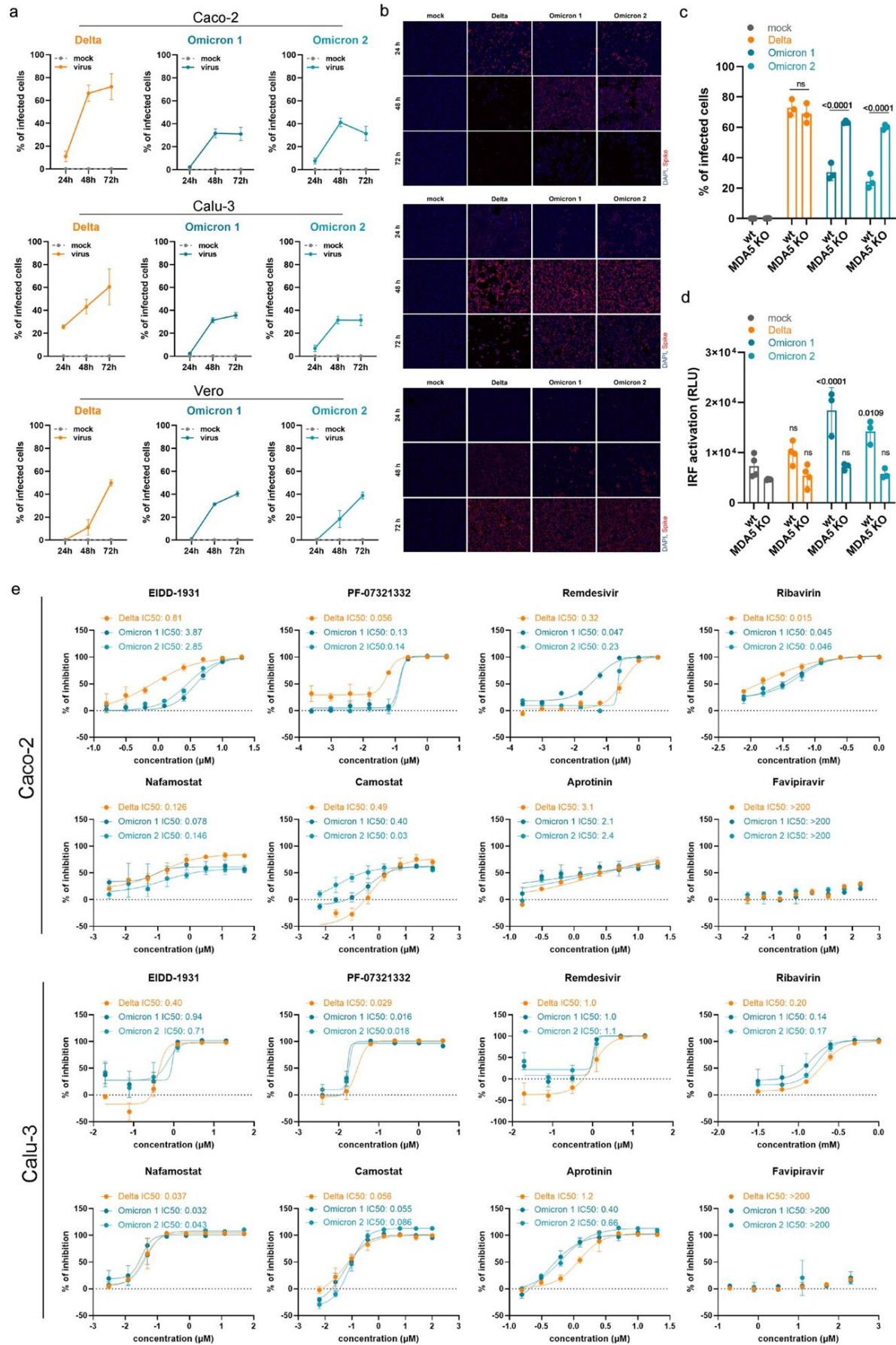


Fig. 1: Interferon antagonism and antiviral therapy against novel SARS-CoV-2 variant Omicron. a Caco-2 and Calu-3 cells were infected with SARS-CoV-2 variant Delta (GenBank ID: MZ315141), Omicron 1 (GenBank ID: OL800702) and Omicron 2 (GenBank ID: OL800703) at an MOI of 0.01. The number of infected cells at different time points post infection was determined by immunofluorescence staining of the SARS-CoV-2 S protein. Graphs represent means  $\pm$  SD of 12 biological replicates. b Representative immunofluorescence images of a are shown (4 $\times$  magnification). c Virus infection rates in A549-ACE2/TMPRSS2 MDA5-WT (wt) and A549-ACE2/TMPRSS2 MDA5 KO (MDA5 KO) cells 72 h post infection as determined by immunofluorescence staining of the S protein. Graph represents data of four biological replicates. d Induction of IRF transcriptional activity 24 h post infection in a promotor reporter assay. Graph displays means  $\pm$  SD of four biological replicates. e Dose-dependent effects of selected antiviral compounds on SARS-CoV-2 Omicron and Delta variant isolates. Compounds were added to confluent monolayers and cells were subsequently infected with viral variants at MOI of 0.01. The inhibition rate was evaluated 24 h (Caco-2) and 48 h (Calu-3) post infection by staining of the S protein. Graphs depict means  $\pm$  SD of three biological replicates. P-values were calculated using two-way ANOVA (c, d). ns, not significant. Credit: DOI: 10.1038/s41422-022-00619-9

The SARS-CoV-2 omicron variant causes less severe disease than Delta although it is better at escaping immune protection by vaccinations and previous infections. The reasons for this have so far remained elusive.

A new study by a research team with scientists from the University of Kent and the Goethe-University Frankfurt has now shown that omicron variant viruses are particularly sensitive to inhibition by the so-called interferon response, an unspecific immune response that is present in all body [cells](#). This provides the first explanation of why COVID-19 patients infected with the omicron variant are less likely to experience

severe disease.

The cell culture study also showed that omicron viruses remain sensitive to eight of the most important antiviral drugs and drug candidates for the treatment of COVID-19. This included

EIDD-1931 (active metabolite of molnupiravir), ribavirin, remdesivir, favipravir, PF-07321332 (nirmatrelvir, active ingredient of paxlovid), nafamostat, camostat, and aprotinin.

Prof Martin Michaelis, School of Bioscience, University of Kent, said: "Our study provides for the first time an explanation, why omicron infections are less likely to cause [severe disease](#). This is due to omicron, in contrast to Delta, does not effectively inhibit the host cell interferon immune response."

Prof. Jindrich Cinatl, Institute of Medical Virology at the Goethe-University, added: "Although cell culture experiments do not exactly reflect the more complex situation in a patient, our data provide encouraging evidence that the available antiviral COVID-19 drugs are also effective against [omicron](#)."

**More information:** Denisa Bojkova et al, Reduced interferon antagonism but similar drug sensitivity in Omicron variant compared to Delta variant of SARS-CoV-2 isolates, *Cell Research* (2022). [DOI: 10.1038/s41422-022-00619-9](https://doi.org/10.1038/s41422-022-00619-9)

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