

Description of Additional Supplementary Files

File name: Supplementary Data 1

Description: This Excel workbook contains the underlying raw source data for all main and supplementary figures, including individual data points for numerical plots, gating strategies and raw cell counts for flow cytometry assays.

File name: Supplementary Data 2

Description: Deep Mutational Scanning Libraries, NGS Counts, Functional Fitness Scores, and Human Genetic Variant Analyses. This Excel workbook provides comprehensive processed computational and experimental datasets generated in this study. It includes: (1) design sequences of the IFITM3 mutational libraries; (2) quality-controlled next-generation sequencing (NGS) read counts across screening conditions; (3) calculated variant-level functional/fitness scores and enrichment metrics; and (4) integrated variant annotations and comparative analyses with human population variation (gnomAD), pathogenic mutations (ClinVar), and AI-base

File name: Supplementary Data 3

Description: This text file contains the complete computational scripts used for processing, analyzing, and visualizing the IFITM3 deep mutational scanning datasets generated in this study. It includes: (1) processing and normalization of NGS-derived variant abundance data from individual screening libraries; (2) calculation of enrichment ratios, fold-change metrics, and functional fitness scores across different influenza virus screening conditions; (3) generation of mutation-level visualization analyses, including fitness distributions, density plots, violin plots, and amino acid substitution heatmaps; and (4) integrative analyses comparing experimentally determined functional effects with human genetic variation (gnomAD), predicted pathogenicity scores (AlphaMissense), and evolutionary conservation metrics. These scripts provide the computational framework used to derive variant-level functional landscapes and interpret the evolutionary and genetic constraints of IFITM3.