

Expanded View Figures

Figure EV1. Mutational frequency of the DENV1-4 E proteins.

A–C There were 7, 23, and 11 sites of effective variants in DENV1-I (A), DENV1-IV (B), and DENV1-V (C), respectively.

D–F There were 3, 12, and 12 sites of effective variants in DENV2-Asian I (D), DENV2-Asian American (E), and DENV2-Cosmopolitan (F), respectively.

G–I There were 12, 12, and 8 sites of effective variants in DENV3-I (G), DENV3-II (H), and DENV3-III (I), respectively.

J, K There were 23 and 11 sites of effective variants in DENV4-I (J) and DENV4-II (K).

Source data are available online for this figure.

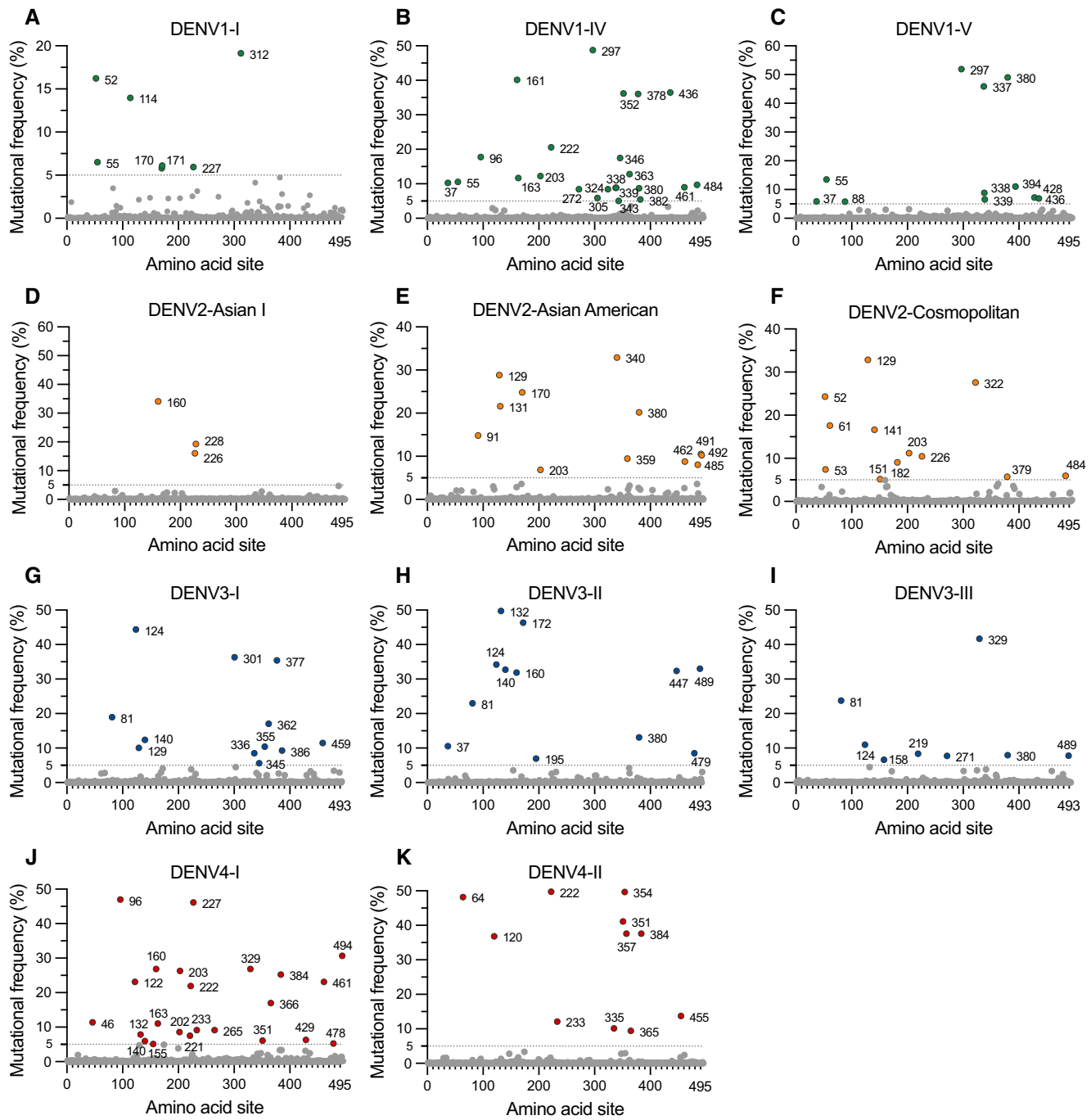


Figure EV1.

Figure EV2. Annual occurrence frequency of 10 stable substitutions in DENV1-4 E proteins.

A–J The annual occurrence frequency (AOF) of 10 stable substitutions was assessed, including 171T in DENV1-I (A), 226K and 228E in DENV2-Asian I (B and C), 131Q, 170T, 340T, and 380V in DENV2-Asian American (D–G), 301S and 377I in DENV3-I (H and I), and 265A in DENV4-I (J).

Source data are available online for this figure.

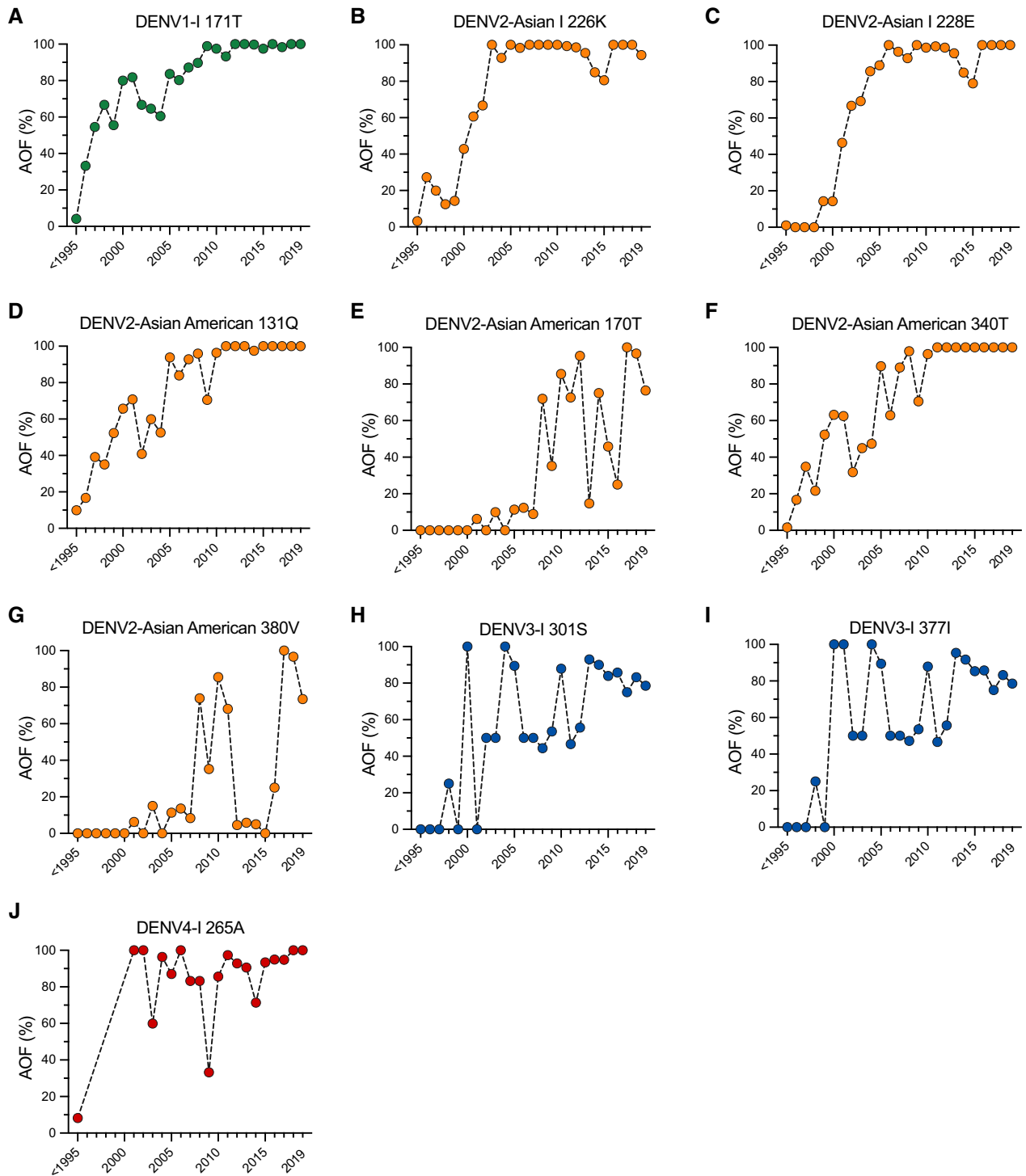


Figure EV2.

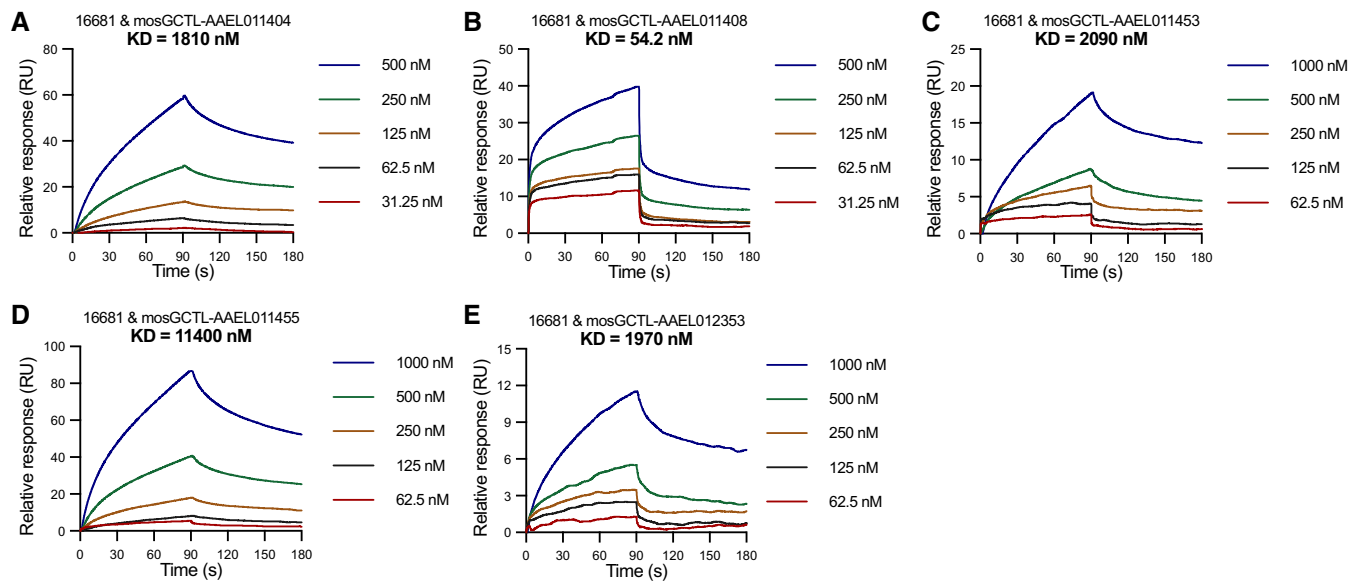


Figure EV3. The binding affinity between 16681 virions and mosquito C-type lectins.

A–E The binding affinity between purified 16681 virions and mosquito C-type lectins measured by an SPR assay.

Source data are available online for this figure.

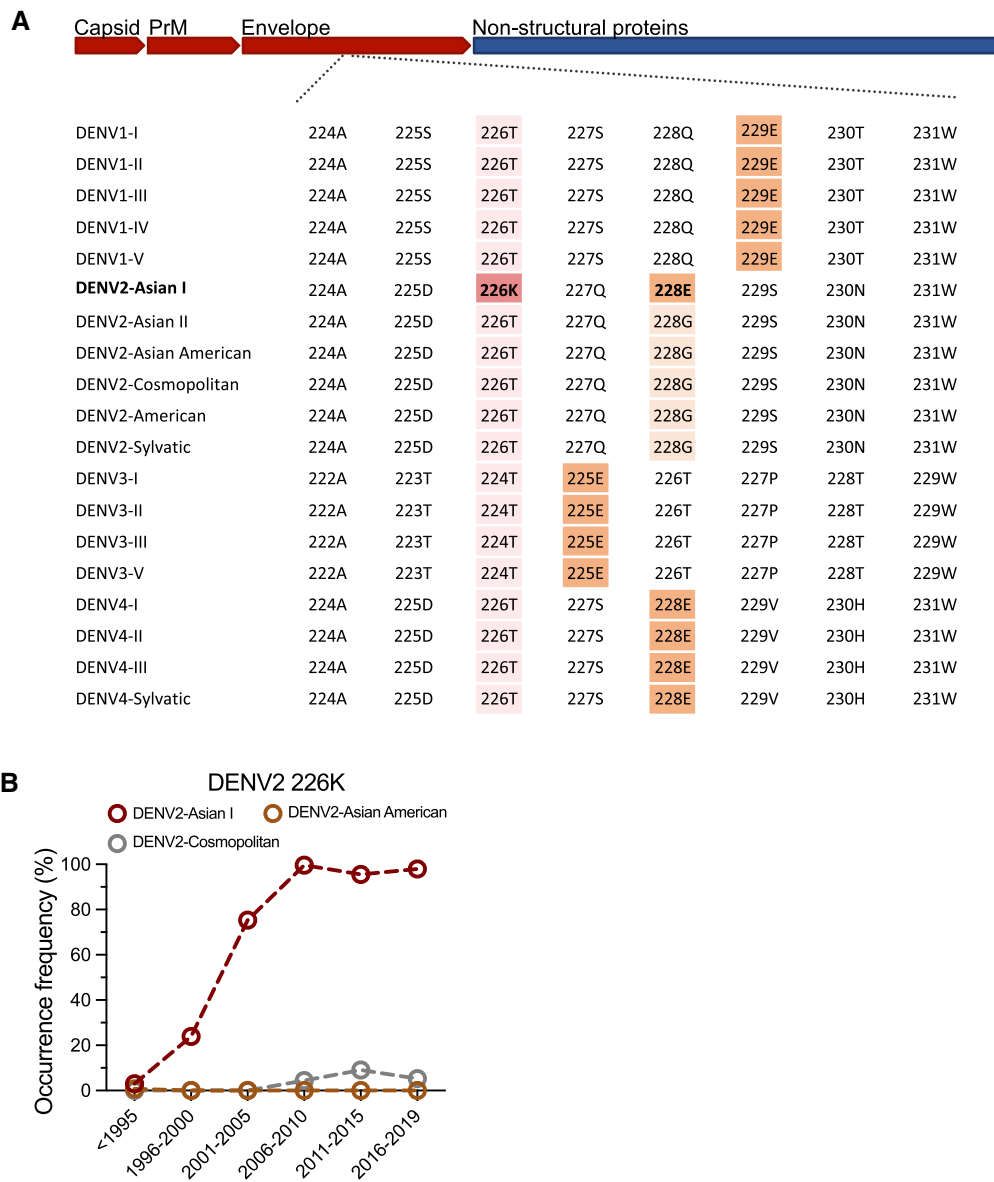


Figure EV4. T226K and G228E substitutions in DENV1-4 E proteins.

A Sequence alignment of DENV E proteins. The consensus sequences of DENV1-4 genotypes were obtained from Jalview and were aligned by MUSCLE.
 B The 5-year occurrence frequency of 226K in DENV2 Asian I, Asian American, and Cosmopolitan genotypes.

Source data are available online for this figure.

Figure EV5. Modeling of the annual occurrence frequency of the T226K/G228E substitutions in DENV2 genotypes and modeling results of the Gaussian process regression (GPR-2).

- A The numerical kinetics modeling process of the annual occurrence frequency of the T226K/G228E substitutions in DENV2 genotypes. The dark gray and orange circles denote the AOF of the T226K and G228E substitutions, respectively. The gray and orange circles denote the AOF of T226 and G228 ($100\% - (\text{AOF of T226K})$ and $100\% - (\text{AOF of G228E})$), respectively. The upper and lower dashed boxes denote the AOF of T226K and G228E substitutions and the AOF of 226T and 228G in Year (t) and Year (t + 1), starting from 1995.
- B The support vector machine regression (SVR) modeling process of the annual occurrence frequency of T226K/G228E substitutions in DENV2 genotypes. The gray and orange rectangle boxes denote the input data and output data of the SVR models.
- C The AOF prediction of the T226K substitution (left panel) and G228E substitution (right panel) in the DENV2 Asian I genotype.
- D The AOF prediction of the T226K substitution (left panel) and G228E substitution (right panel) in the DENV2 Cosmopolitan genotype.
- E The regression results for GPR-2.
- F The case number of the DENV2 Asian I genotype from 1995 to 2019.

Source data are available online for this figure.

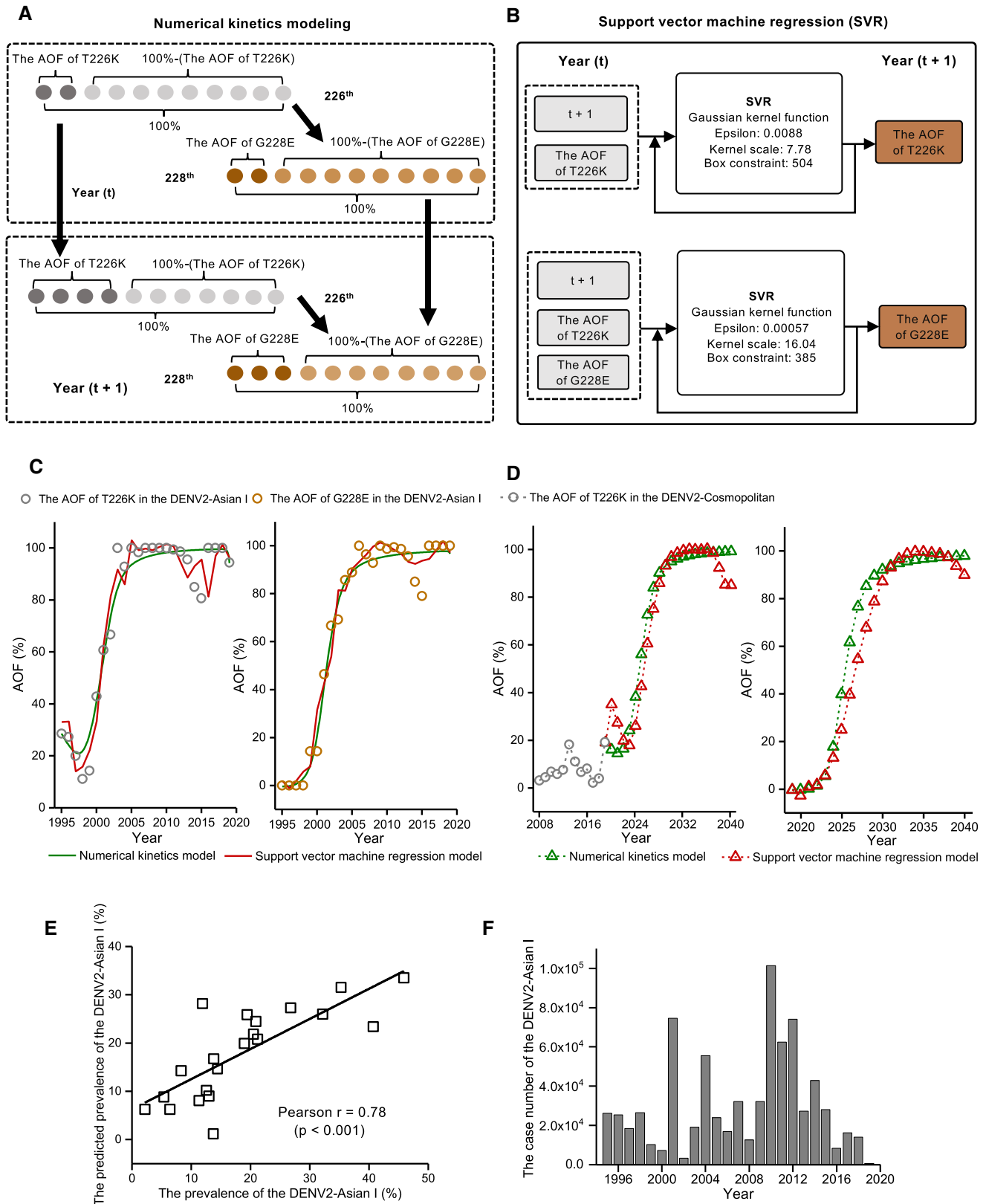


Figure EV5.