Expanded View Figures

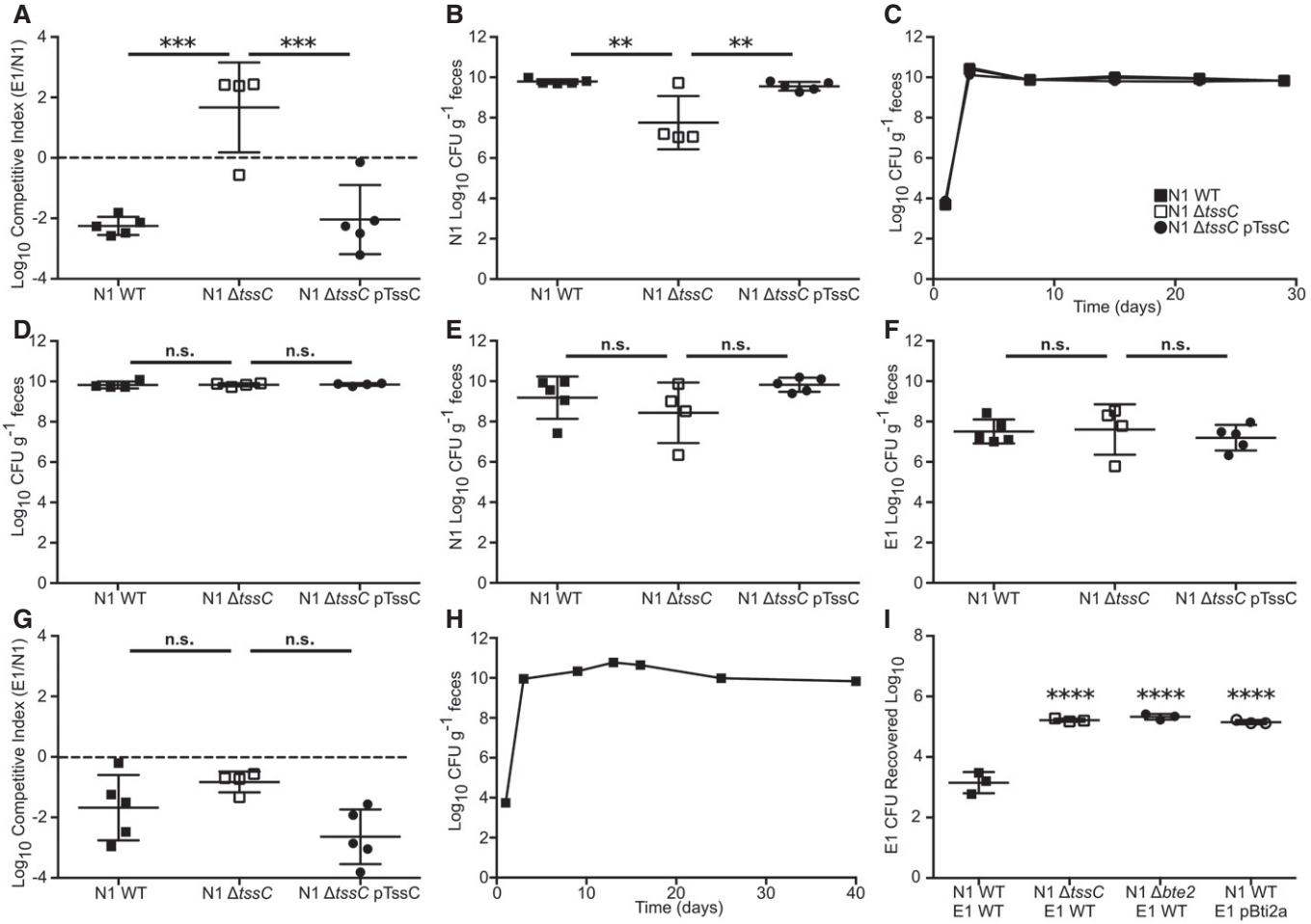

Figure EV1. The N1 T6SS is required for strain dominance of E1 both *in vivo* and *in vitro*.

A, B SPF mice were co-colonization with E1 WT and N1 WT (n = 5), T6SS mutant (Δ*tssC*, n = 4), or complemented (Δ*tssC* pTssC, n = 5). Fecal CFU was monitored for 4 weeks post-colonization. N1 clone fecal CFU was compared between groups at the 4-week time point (A) and the competitive index of E1 over N1 was determined for each mouse (B).

C, D Mice (n = 4) were mono-colonized with N1 WT, T6SS mutant (Δ*tssC*), or complemented (Δ*tssC* pTssC), and fecal CFU was determined for 4 weeks (C). Comparison of fecal CFU was made between groups after 4 weeks (D).

E–G SPF mice were co-colonized with E1 and N1 WT (n = 5), T6SS mutant (Δ*tssC*, n = 4), or complemented (Δ*tssC* pTssC, n = 5). Fecal CFU at 1 day post co-colonization was determined for N1 (E) and E1 (F) and competitive index of E1 over N1 was calculated for each mouse (G).

H SPF mice (n = 4) were mono-colonized with E1 and fecal CFU determined over time.

I *In vitro* competitions were performed between E1 WT and N1 WT, N1 Δ*tssC*, or N1 Δ*bte2*, or between E1 Bti2a and N1 WT (n = 3 competitions). Recovered CFU of E1 was quantified after each competition, and statistical difference from E1 WT recovered after competition with N1 WT was determined.

Data information: Results are representative of three independent experiments. Data are presented as mean ± SD (A, B, D–G, I) or mean ± SEM (C and H). A dashed line denotes equal recovery of competitors. n.s., not significant; $^{**}P < 0.01$, $^{***}P < 0.001$, $^{****}P < 0.0001$. Statistical significance was determined by one-way ANOVA, Tukey's multiple comparisons test (A, B, D–G, I).

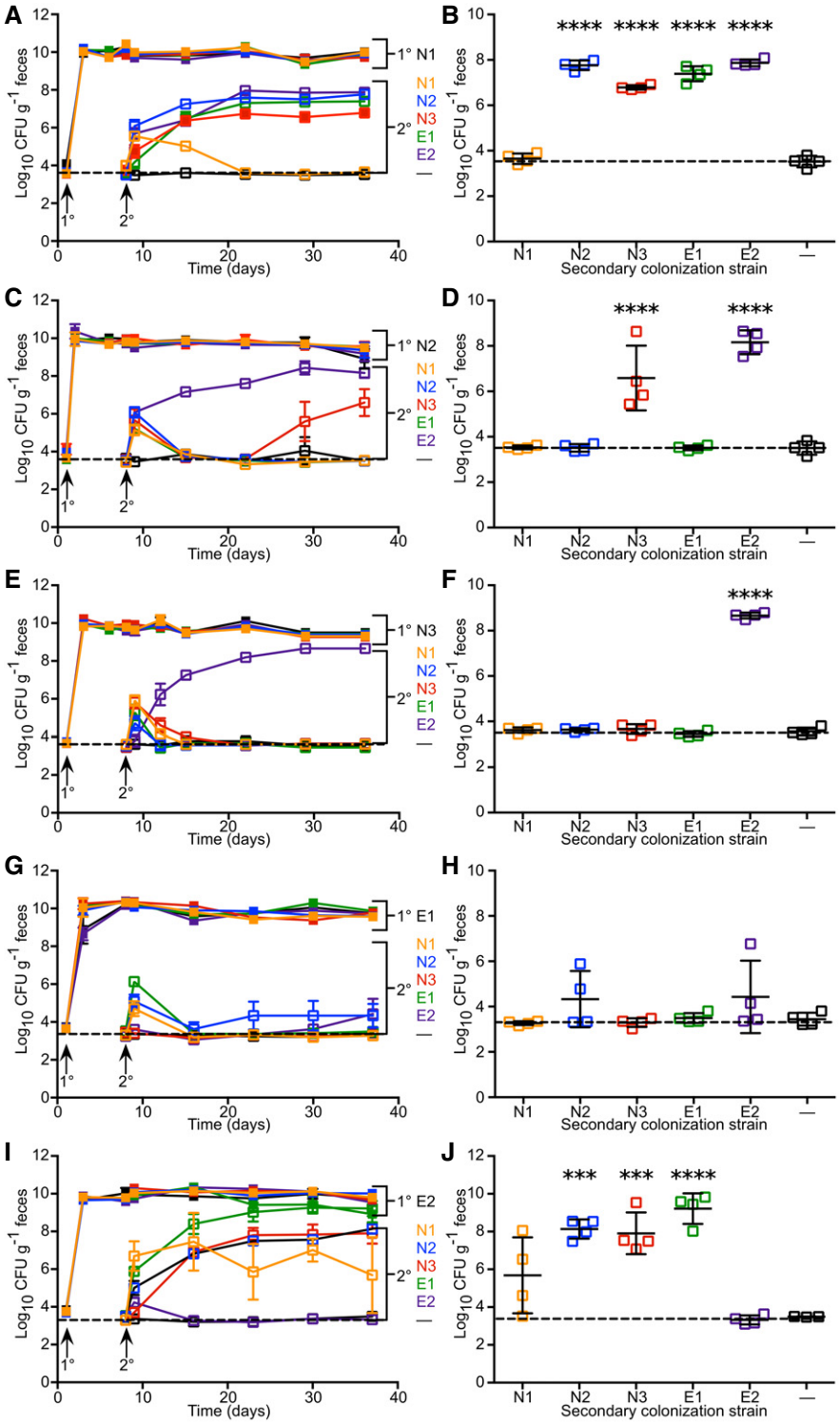

Figure EV2. Successful *B. fragilis* secondary challenge is strain-dependent.

A–J Mice (n = 4 per group) were initially colonized with N1 (A and B), N2 (C and D), N3 (E and F), E1 (G and H), or E2 (I and J) followed by secondary challenge by all strains or a mock inoculum at 1 week post-primary colonization. Fecal CFU of primary and secondary strains were monitored for 4 weeks post-secondary challenge (A, C, E, G, and I). At the last time point, the secondary challenge strain was tested for statistical significance above the mock-inoculated group (B, D, F, H, and J).

Data information: Results are representative of at least two independent experiments. Data are presented as mean ± SEM (A, C, E, G, and I) or mean ± SD (B, D, F, H, J). Limit of detection is denoted by a dashed line. ***$P < 0.001$, ****$P < 0.0001$. Statistical significance was determined by one-way ANOVA, Tukey's multiple comparisons test (B, D, F, H, and J).

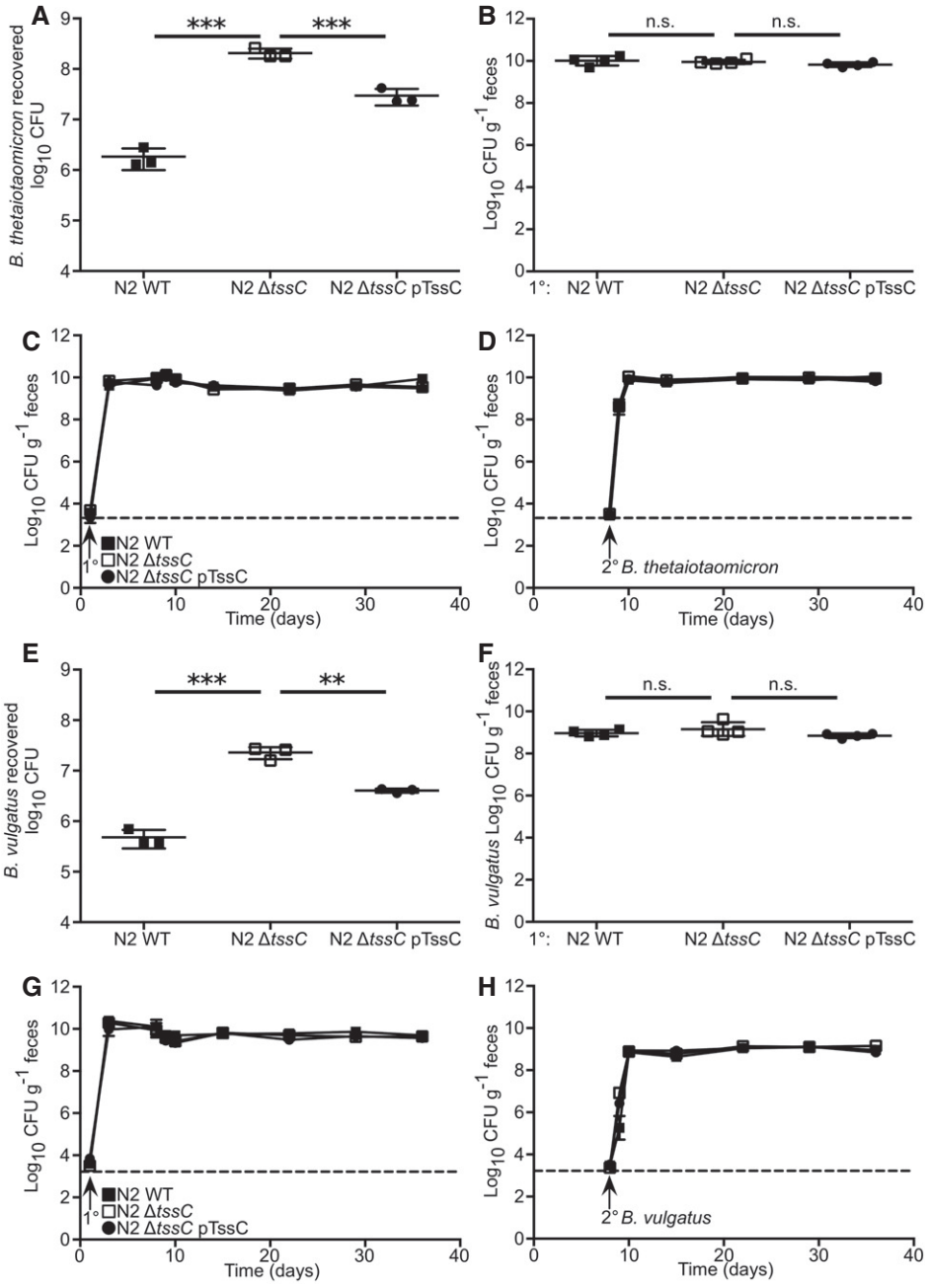

Figure EV3. T6SS-dependent colonization resistance does not extend to related *Bacteroides* species *in vivo*.

A *B. thetaiotaomicron* recovered after *in vitro* competition (n = 3 competitions) with N2 WT, N2 Δ*tssC*, or N2 Δ*tssC* pTssC.

B–D SPF mice (n = 4) were sequentially colonized with N2 WT, N2 Δ*tssC*, or N2 Δ*tssC* pTssC strains, followed by secondary challenge of *B. thetaiotaomicron* 1 week after primary colonization. Four weeks post-secondary challenge, fecal CFU was determined for *B. thetaiotaomicron* (B). Fecal CFU for primary (C) and secondary strains (D) were determined for 4 weeks post-secondary challenge.

E *B. vulgatus* recovered after *in vitro* competition with N2 WT, N2 Δ*tssC*, or N2 Δ*tssC* pTssC.

F–H SPF mice (n = 4) were sequentially colonized with N2 WT, N2 Δ*tssC*, or N2 Δ*tssC* pTssC followed by secondary challenge with *B. vulgatus* 1 week after primary colonization. Four weeks post-secondary challenge, fecal CFU was determined for *B. vulgatus* (F). Fecal CFU for primary (G) and secondary strains (H) were determined for 4 weeks post-secondary challenge.

Data information: Results are representative of three independent experiments. Data are presented as mean ± SEM (C, D, G, and H) or mean ± SD (A, B, E, and F). Limit of detection is denoted by a dashed line. n.s., not significant; $^{**}P < 0.01$, $^{***}P < 0.001$. Statistical significance was determined by one-way ANOVA, Tukey's multiple comparisons test (A, B, E, and F).

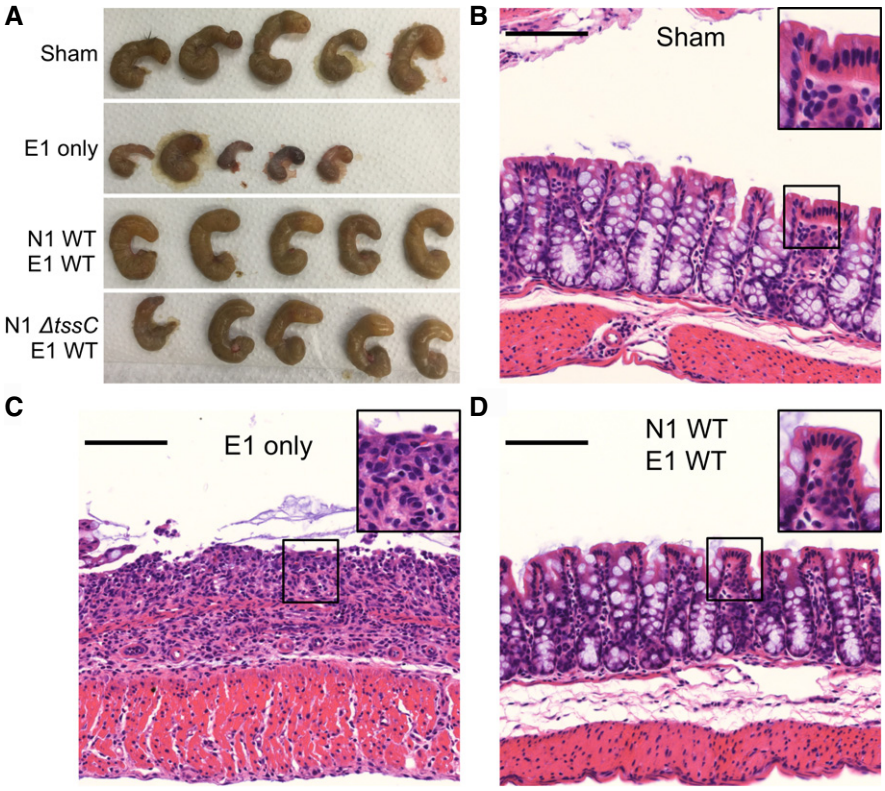

Figure EV4. N1 protects from ETBF-mediated intestinal damage via competition with E1 in DSS-treated mice.

A–D Mice pre-treated with DSS were inoculated with no organisms (sham), E1 only, E1 with N1 WT, or E1 with N1 Δ*tssC*. Gross examination of ceca (A, n = 5 per group) and histopathological examination of colonic tissue (B–D, n = 5 per group) were performed after intestinal dissection. Scale bars (B–D) denote 100 μm (main image) and 200 μm (inset). Results are representative of three independent experiments.