



VIRULENCE DYNAMICS OF FRIEND VIRUS COMPLEX IN WILD-DERIVED MICE DIFFERS BY SEX

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Friend Virus Complex (FVC) is a murine specific retrovirus commonly utilized in immunological and tumorigenesis studies. However, as these studies tend to use only female rodents, virulence patterns in males are poorly understood. In order to gain a better understanding of virulence dynamics of FVC we infected wild-derived, outbred *Mus* with FVC in both caged trials and semi-natural enclosures. Using a highly virulent strain of FVC, the primary symptomatic presentation is rapid spleen enlargement. In caged trials, 15 sibling pairs (15 males and 15 females) were infected with FVC via intraperitoneal injection. Infections lasted 12 days and mice were subsequently sacrificed. Infected female mice had spleens 3.46 times larger than males (Figure 1A; Mann-Whitney; $n = 28$, $W = 158.5$, $P = 0.005$), but this did not correspond with significantly higher viral titers per spleen (Figure 1B; t-test; $t = 1.97$, $P = 0.060$). Although there was a direct correlation of viral titers and spleen weight in males (LM; $r^2 = 0.45$, $f = 12.77$, $P = 0.003$), this correlation was not observed in females (LM; $r^2 = 0.03$, $f = 1.32$, $P = .276$; Figure 1C). In semi-natural enclosures, index animals (infected via intraperitoneal injection) had larger spleens (Figure 1D; Tukey; $N_{\text{infected}} = 75$, $P < 0.05$) and greater viral titers (Figure 1E; Tukey; $P < 0.01$) than contact animals (infected via natural transmission) in both sexes. A trend was observed that contact males have higher titers than contact females (Figure 1E; Tukey; $P < 0.10$). Similar to caged trials, males displayed a correlation between viral titers and spleen mass (LM; $r^2 = 0.59$, $F_{1,19} = 27.4$, $P < 0.0001$), but this relationship was not observed in females (LM; $r^2 = 0.03$, $F_{1,27} = 0.70$, $P = 0.411$; Figure 1F). The increased virulence exhibited by female mice during FVC infection and the lack of correlation between viral titers and spleen size of female mice collectively suggest female mice may act as a spill over host. Conversely, male mice display a direct correlation between viral titers and spleen size, and these data suggest FVC is adapted to a male host environment.

