

Nematode-virus co-infection has a variable impact on the resistance and tolerance to *H. polygyrus* in genetically diverse mice.

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To combat infection, hosts develop two defence strategies: resistance, which is their ability to clear out the pathogen and tolerance, their ability to reduce the impact of the pathogen on their fitness. The aim of the study was to characterise the phenotypic variation of host resistance and tolerance to *Heligmosomoides polygyrus* in genetically diverse mice during co-infection (*H. polygyrus* and Theiler's murine encephalomyelitis virus). Three strains of mice were used: SJL mice (resistant to *H. polygyrus* but susceptible to TMEV), BALB/c mice (intermediate susceptible to both pathogens), and C57BL/6 (susceptible to *H. polygyrus* but resistant to TMEV). Mice of each strain were infected with either a single (*H. polygyrus*) or two pathogens (*H. polygyrus* and TMEV) or were sham infected ($n=15$). Both pathogens were administered at the subclinical level (200 L₃ *H. polygyrus* in 0.2ml water and an avirulent TMEV at 10⁶ pfu in 0.2 ml DMEM). Mice were euthanised at 14 dpi and 42 dpi to represent nematodes establishment period and nematodes clearance period. In the susceptible to *H. polygyrus* C57BL/6 mice, average daily gain (ADG 0.08 g/day) and FI (0.07g/day) was higher in Co-inf compared to Par, Vir, and Sham at 14 dpi ($P<0.001$). However, in the BALB/c mice, co-infection treatment resulted in 20% lower ADG compared to mice receiving *H. polygyrus*-only ($P=0.034$); 10% of ADG loss was observed in the resistant to *H. polygyrus* SJL mice ($P<0.001$). When compared to *H. polygyrus*-only infected C57BL/6 mice, co-inf resulted in 15% lower EIC ($P<0.001$), and 20% worm counts ($P<0.05$), whereas Co-inf BALB/c mice showed 5% elevated EIC ($P<0.001$) and 10% worm counts ($P<0.05$) compared to *H. polygyrus*-only mice. Co-inf did not have any impact on resistance traits in SJL mice. The trend was the same for all parasitological measurements at 42 dpi. Compared to *H. polygyrus* only SJL mice, Co-inf mice were 5% more tolerant ($P<0.05$). Co-inf C57BL/6 mice tended to be more tolerant ($P=0.058$) whereas Co-inf BALB/c mice tended to be less tolerant than their *H. polygyrus* only counterparts ($P=0.051$). Our data showed that the impact of co-infection with two intestinal pathogens resulted in significant variation on host resistance and tolerance to *H. polygyrus* in three inbred mouse strains. Contrary to expectation, mice susceptible to *H. polygyrus* benefited most from co-infection, as their resistance was improved compared to *H. polygyrus*-only counterparts. On the other hand, mice already resistant to *H. polygyrus* improved their tolerance following co-inf, compared to *H. polygyrus* only mice. The underlying mechanisms of these co-infection phenotypes are currently investigated.

Keywords: Mice, Genetic resistance, Infection tolerance, Co-infection, Nematodes, *Heligmosomoides polygyrus*