Diagram, engineering drawing

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Fig. 2. (A) Infection duration depends on the strength of negative and positive (chronicity-promoting and clearance-promoting) feedbacks. (B-D) When negative feedbacks are relatively strong, the parasite is always cleared rapidly, with higher doses leading to shorter durations due to the promotion of a Th2 response. (E-G) When clearance-promoting feedbacks are strong, low doses of parasites can become chronic by not provoking the Th2 positive feedback loop, whereas high doses are cleared. (H-J) When chronicity-promoting feedbacks are strong, high doses of parasites can become chronic by provoking the Th1 positive feedback loop, whereas low doses are cleared.

A picture containing looking, sitting, computer, computer

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Fig. 3. A bolus dose of parasites can be cleared rapidly whereas a trickle dose can become chronic. The low initial dose sets the immune response on a trajectory towards quiescence that is not activated as additional parasites are trickled into the system. The immune system becomes “trapped” at a low activation state.

Chart, histogram

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Fig. 4. Hypotheses for shifts to chronicity in rewilded mice. This can be achieved if rewilding causes an initial bias towards Th1 due to a higher baseline level of exposure to Th1-promoting micobes. This makes it easy for the parasite to immunomodulate, leading to a high Th1 response that suppress the Th2 response. Alternatively, rewilding could weaken clearance-promoting feedback loops by weakening the stimulation of the Th2 response by parasites or by reducing positive Th2 self-stimulation. This leads to a general weakening of the immune response that prevents it from being able to clear the parasite.