

## **The Immune State of Wild Mice, *Mus musculus domesticus***

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Most of what we know about mammalian immunology – and so immunoparasitology – is based on studies of laboratory rodents. In contrast, the immune state of wild animals is largely unknown. To properly understand parasites, we need to know the actual immune environment in which they live and evolve in the wild.

We have investigated the immunobiology of wild house mice – the same species as the laboratory mouse – as an example of a wild mammal, characterising their adaptive humoral, adaptive cellular and innate immune state.

We find that wild mouse cellular immune systems are in a highly activated (primed) state, compared with those laboratory mice. We find that wild mice have a population of highly activated myeloid cells not present in laboratory mice. In contrast to the activated cellular state, we find that *in vitro* cytokine responses to pathogen-associated ligands are generally lower in cells from wild mice, probably reflecting the importance of maintaining immune homeostasis in the face of intense antigenic challenge in the wild.

We have also discovered how immune variation is structured among mouse populations, finding that there can be extensive immune discordance among neighbouring populations. Finally, we have identified the principal factors that underlie the immunological differences among mice, showing that individuals' body condition promotes, and age constrains, immune state, while factors such as microparasite infection and season are comparatively unimportant.

Together these results reveal the actual immune environment that parasites experience during their daily lives. These results raise questions about the utility of laboratory rodent models in immunoparasitological research.