

The host-parasite interactions of *Toxoplasma gondii* in the mammalian hosts

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Abstract

Toxoplasma gondii is a zoonotic protozoan pathogen that causes toxoplasmosis, an infectious disease that affects all warm-blooded animals, including domestic animals, wild animals, and humans. Toxoplasmosis in domestic animals causes miscarriages or stillbirths, resulting in economic losses and posing a challenge in animal husbandry. *T. gondii* is thus an important pathogen that causes serious animal and public health issues, however, there is still no eradicated or preventative medicine. Therefore, efforts to develop novel treatments for toxoplasmosis and to understand the interaction between the host immune response and the parasite in host cells are essential. Here, we generated human cells lacking the interferon- γ (IFN- γ)-inducible gene, and showed that indole-2,3-dioxygenase 1 (IDO1) is required for the IFN- γ -induced anti-*T. gondii* response in human cells¹). Then, we focused on the *T. gondii* effector GRA15 and analyzed its virulence function and mechanism to antagonize the IDO1-mediated anti-*T. gondii* response by generating GRA15-deficient *T. gondii*. As a result, we showed that Interleukin-1 β (IL-1 β) is produced from monocytes in a *Toxoplasma* effector GRA15- and host Caspase-1 (CASP-1)-dependent manner. We further showed that inducible nitric oxide synthase (iNOS) and nitric oxide (NO) have an essential role in the *Toxoplasma* GRA15-dependent inhibition of the IDO1-induced anti-*T. gondii* response in human cells^{2,3}). Although immune responses in humans and domestic animals are not identical, the tryptophan-degrading enzyme IDO have been found in most mammalian species. Hence, the GRA15-dependent virulence mechanism may contribute to *T. gondii* infection in not only humans but also domestic animals. Studies to examine whether the GRA15-dependent virulence mechanism has an important role in *T. gondii* infection of domestic animals, and to identify chemical compounds that block iNOS expression or NO production could contribute to the development of novel anti-toxoplasmosis therapies for humans and domestic animals.

References

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