Helminth infection modifies the lung macrophage responses that is associated with early susceptibility to gammaherpesvirus concurrent infection in C57BL/6 mice

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Parasitic helminths can imprint innate cells such as lung macrophages for accelerated clearance in a secondary infection. However, it is unknown how helminth-induced macrophage changes in the lung affect the response to concurrent bystander infection with viruses. Here, we have examined the lung macrophage responses after Schistosoma mansoni egg-induced inflammation or Nippostrongylus brasiliensis infection and observed a severe expansion of CD11b+ interstitial macrophages while siglec-F+ alveolar macrophages were reduced. Interestingly, expansion of interstitial macrophages was more pronounced in C57BL/6 compared to BALB/c mice and we observed a strong upregulation of the M(IL-4) alternative activation marker YM1 in interstitial macrophages of C57BL/6 that was less pronounced in BALB/c mice. We then examined the susceptibility of both mouse strains to murid gammaherpesvirus 4 (MuHV-4) infection and observed that helminth exposure rendered C57BL/6 mice highly susceptible to MuHV-4 acute infection whereas BALB/c mice controlled viral infection earlier as previously published by our group through the expansion of “virtual” memory CD8+ T cells (TVM) (Rolot et al., 2018. Nat Commun. 2018 Oct 30;9(1):4516). We further confirmed the role of IL-4-induced TVM by helminth in the CD8-mediated control of MuHV-4 in both C57BL/6 and BALB/c strains, suggesting that the increased early susceptibility of C57BL/6 mice to MuHV-4 does not affect the induction of enhanced effector CD8+ T cell responses. Finally, we observed increased proportions of MuHV-4-infected macrophages 4 days after viral infection when C57BL/6 mice were exposed to helminths, suggesting that helminth infection modifies the lung macrophage niche to become more permissive to MuHV-4 infection.

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