Ly6Chi monocytes are key orchestrators of gammaherpesvirus lifecycle

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Introduction
Gammaherpesviruses (γHVs) represent highly prevalent human viruses as the best studied γHVs, Epstein-Barr virus and the Kaposi's Sarcoma-associated Herpesvirus, infect respectively some 90% and up to 40% of human populations. Through coevolution with their hosts, γHVs have developed numerous mechanisms to control the immune response and successfully persist in the host in a symbiotic relationship. Thus, pulmonary infection with Murid herpesvirus 4 (MuHV-4), a γHV infecting mice, induces the replacement of alveolar macrophages by inflammatory monocytes (Ly6Chi MOs) that confer protection against allergic asthma. The objective of this study was to decipher the importance of Ly6Chi MOs in MuHV-4 lifecycle.

Materials and methods
Female BALB/c, C57BL/6 wild-type, IL10-/- or CCR2-/- mice were infected with 1*104 P.F.U. of MuHV-4. CCR2+ MOs were systemically depleted by using the rat anti-mouse CCR2 antibody MC-21 (Mack et al., 2001). Mice were in vivo imaged with an IVIS Spectrum instrument (PerkinElmer) and weighed until euthanasia. Eight days post infection, blood, lungs and bronchoalveolar lavages were harvested to perform flow cytometry stainings.

Results
Our results show that, at early time points after MuHV-4 infection, recruitment of Ly6Chi MOs is associated with reduced viral replication, clinical signs, and neutrophilic infiltration in lung and with enhanced NK and CD8 T cells responses. Moreover, these recruited Ly6Chi MOs produced high levels of IL-10 suggesting regulatory properties.

Conclusion
These results highlight that Ly6Chi MOs are key orchestrators of immune response following γHV infection. Recruitment of Ly6Chi MOs is beneficial for the host by reducing virus replication and limiting tissue damages.

Keywords : Gammaherpesvirus/monocyte/NK/CD8/immune evasion
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