CD11c^{+} Cells Primed With Unrelated Antigens Facilitate An Accelerated Immune Response To Influenza Virus In Mice

- Recent evidence suggests that an individual's unique history and sequence of exposures to pathogens and antigens may dictate downstream immune responses to disparate antigens.
- i.n. delivery of nonreplicative virus-like particles (VLPs), which bear structural but no antigenic similarities to respiratory pathogens, acts to prime the lungs of both C56BL/6 and BALB/c mice, facilitating heightened and accelerated primary immune responses to high-dose influenza challenge, thus providing a nonpathogenic model of innate imprinting.
- Responses correspond closely to those observed following natural infection with the opportunistic fungus, *Pneumocystis murina*, and are characterized by accelerated antigen processing by DCs and alveolar macrophages, an enhanced influx of cells to the local tracheobronchial lymph node, and early upregulation of T-cell co-stimulatory/adhesion molecules.
- Pre-exposure to VLPs or *Pneumocystis* eliciting DC response and lung repopulation by Ly-6C^{+} precursors during influenza , relies on CCR2 expression.
- Immune imprinting 72 h after VLP-priming, or 2 weeks after *Pneumocystis*-priming is CCR2-mediated and results from the enhanced antigen processing, maturation, and trafficking abilities of DCs and alveolar macrophages, which cause accelerated influenza-specific primary immune responses and result in superior viral clearance.

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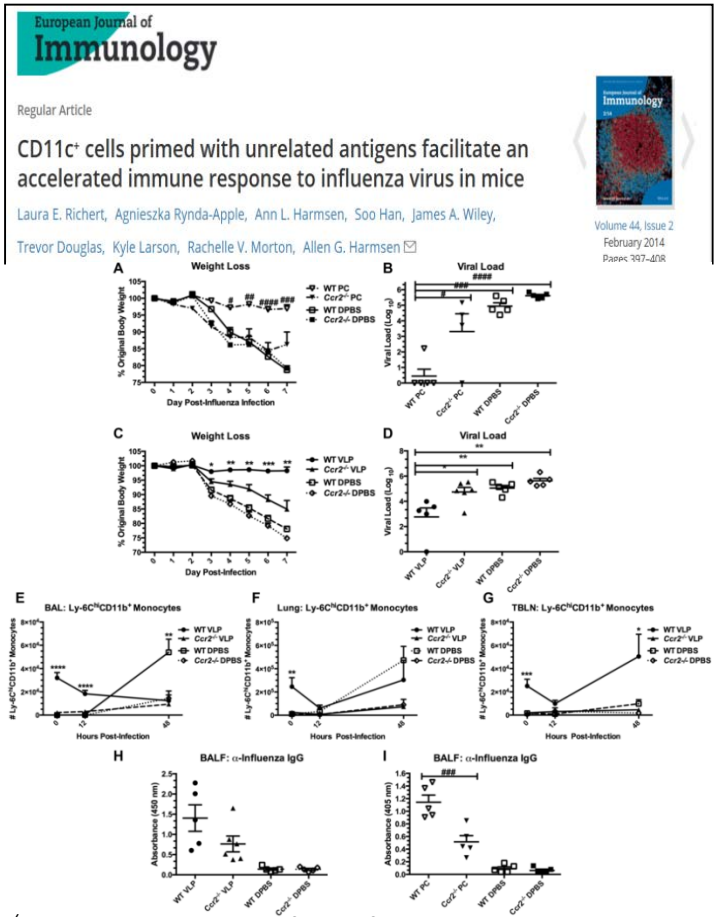

Ccr2$^{-/-}$ mice are not protected from influenza virus via prior exposure to VLPs or *Pneumocystis* infection. C57BL/6 (WT) or *Ccr2*$^{-/-}$ mice were infected with *Pneumocystis* (PC), or exposed to VLPs, or vehicle (DPBS). Upon rechallenge with either PR8 or VLP, cells isolated from BAL (E), lung homogenate (F), and TBLN (G) were stained for Ly-6C^{+}CD11b^{+} and analyzed by flow cytometry. Granulocytes were gated using forward and side scatter plots and the resultant CD11c$^{lo/int}$ cells were gated on and analyzed for their expression of Ly-6C and CD11b. Cell-free lavage fluid (BALF) was analyzed by ELISA to determine the concentration of anti-influenza IgG (H, (1:2 dilution), I (neat)).