IL-13Rα2 IS CRUCIAL FOR DC SUBSET ACTIVATION FOLLOWING VIRAL VECTOR VACCINATION

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Introduction: When developing vaccines against chronic pathogens such as HIV-1, route of delivery, vaccine vector combination and cytokine milieu play an important role in modulating vaccine efficacy. Specifically, intranasal recombinant Fowlpox virus (rFPV) vaccination induced lower IL-13 production by ILC2, resulting in recruitment of $CD11b^+$ conventional DCs, responsible for high avidity $CD8^+$ T cell immunity. In contrast, recombinant Vaccinia Virus (rVV) and Modified Vaccinia Ankara (rMVA) viral vectors that induced elevated IL-13 production by ILC2, recruited $CD11b^-$ $CD103^+$ DCs, associated with low avidity CD8 T cells. Thus, in the current study we further dissected the different DC subsets recruited to the vaccination site following pox viral and non-pox viral vaccination.

Methods: Mice n=5 per group were immunised intransally with $1x10^7$ pfu rFPV, rVV, rMVA, and $2x10^7$ pfu adenovirus, 5×10^6 TCID50 rhinovirus. 24-48h post vaccination lungs were harvested, single cell suspensions were prepared and multi-colour flow cytometry was performed to identify the DC subsets and IL-4/IL-13 receptors.

Results: Compared to i.n. rFPV vaccination, recombinant adenovirus and rhinovirus vaccinations were shown to recruit reduced $CD11b^+$ conventional DCs, and elevated numbers of plasmacytoid DCs to the lung mucosae. Furthermore, i) 24h post viral vector vaccination, enhanced IL-13Rα2 expression was observed on lung DC subsets and ii) over time the IL-13Rα2 densities on DCs, were differentially regulated according to the vaccine vector used, resulting in diverse adaptive immune outcomes.

Conclusion: We have for the first time shown that DC phenotype and the IL-13Rα2 regulation is vaccine vector dependent. Out of IL-4/IL-13 receptors, high affinity IL-13Rα2 is the dominant receptor regulating initial DC function at the vaccination site.

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