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Title: Neonatal lungs are characterized by the presence of high numbers of CD11b+Ly6Chigh myeloid derived suppressor cells that potentiate rather than suppress sensitization to house dust mite

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Body: Allergic asthma most often develops during childhood, when both the immune and the respiratory system are still in an immature state. In this study we investigate immune cell development and the immune reactions to house dust mite (HDM) in lungs of neonatal mice. We find high percentages of granulocytic CD11b+Ly6G+ and monocytic CD11b+Ly6G-Ly6Chigh cells (20 and 10% of alive cells at day +1 resp) in the spleen and lungs of neonatal mice. Both cell types start entering the lungs a few hours before birth, a process that continues until two weeks after birth. The homing process to the lungs is independent of GM-CSF or TLR4. Upon entering the lung neonatal CD11b+Ly6Chigh, but not CD11b+Ly6G+ cells gain suppressive capacity. This suppressive capacity, as measured by suppression of T cell proliferation in vitro, is arginase-1 dependent. Neonatal lung CD11b+Ly6Chigh cells can therefore be classified as myeloid derived suppressor cells. The cells do not proliferate locally, but keep entering the growing lungs until the age of two weeks. Within the first week the Ly6G+ cells become apoptotic and the Ly6Chigh cells differentiate into dendritic cells and M1 and M2 macrophages. M2-macrophages, consequently peak in numbers between 7 and 14 days after birth. The high frequency of suppressive CD11b+Ly6Chigh cells in the neonatal lung do not suppress but rather potentiate sensitization to house dust mite by differentiating into ST2 expressing CD11b+ dendritic cells.