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Angiopoietin-like 4 increases pulmonary tissue leakiness and damage during influenza pneumonia

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Excessive host inflammatory responses negatively impact disease outcomes in respiratory infection. Host-pathogen interactions during the infective phase of influenza are well studied, however little is known about the host's response during the repair stage. A better understanding of the host response during the pulmonary repair phase may facilitate innovative treatment strategies. To our knowledge, angiopoietin-like 4 (ANGPTL4) has not been studied in detail in influenza pneumonia, and study on this host response factor may open door to new intervention strategies. By injection of ANGPTL4 antibody or using transgenic mouse models, effect of ANGPTL4 was studied in mouse models infected with different strains of influenza virus. Mechanism of ANGPTL4 regulation and downstream effects in disease outcomes were analyzed. Here we show that influenza infection stimulated the expression of angiopoietin-like 4 (ANGPTL4) via a direct IL6-STAT3-mediated mechanism. ANGPTL4 enhanced pulmonary tissue leakiness and exacerbated inflammation-induced lung damage. The treatment of infected mice with neutralising anti-ANGPTL4 antibodies significantly accelerated lung recovery and improved lung tissue integrity. ANGPTL4-deficient mice also showed reduced lung damage and recovered faster from influenza infection when compared to their wild type counterparts. Retrospective examination of human lung biopsies from infection-induced pneumonia with tissue damage showed elevated expression of ANGPTL4 when compared to normal lung samples. These observations underscore the important role that ANGPTL4 plays in lung infection and damage, and may facilitate new therapeutic strategies for the treatment of influenza pneumonia.

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Phenotypic analysis of natural killer cells in acute dengue infection

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Background: Early activation of natural killer cells (NKs) has been shown to associate with protection in dengue mouse models, and higher NK numbers have been seen in patients with dengue fever (DF) as opposed to dengue haemorrhagic fever (DHF). Therefore, we set out to investigate the phenotype of NKs in acute dengue infection.
Methods: Activating and inhibitory receptors and natural cytotoxicity receptors of NK cells were phenotyped in 25 adult patients with confirmed dengue infection and 10 healthy individuals (HCs).
Results: Percentages of NK cells were significantly lower (p=0.0002) in the patients (mean 9.6, SD±3.1) than HCs (mean 4.96, SD±2.7). The CD56 bright population (CD56B) was significantly expanded in patients (p=0.0002), especially in those with DF. Expression of NKG2D was higher in both the CD56 dim and CD56B NKs in patients with DF when compared to those with DHF. NKG2A/CD94 expression was significantly lower in the CD56B in patients (p=0.005), but expression rates were higher in patients with DHF when compared to DF. There was no difference in NKp30 expression in NK cells from patients and HCs, however, NKp46 expression on NK cells was lower in patients, especially in the CD56B group (p=0.007). The NKs of the patients or HCs did not have any detectable expression of NKp44. The CXCR6 bearing tissue resident NK cells were significantly expanded (p< 0.0001) in patients compared to HCs.
Conclusion: Severe forms of dengue appear to associate with reduced expression of activation markers and increased expression of inhibitory markers on NK cells.

