Imaging the host response in lungs to pathogens

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Using intravital imaging of the lungs in mice we have characterized the innate immune response. Under basal conditions, we identified a significant population of neutrophils constantly patrolling the lung capillaries while alveolar macrophages patrolled the alveoli. Adding a molecule like LPS increased the migration pattern of neutrophils as if they were searching for pathogens. Intravenous administration of intact bacteria resulted in the pathogens binding to the lung endothelium and neutrophils rapidly phagocytosing the microbes. The molecular mechanism responsible for recruiting more neutrophils did not involve integrins and was dependent on novel adhesion molecules. Molecules like dipeptidase-1 (DPEP-1) helped recruit neutrophils into the lung capillaries and prevented untoward damage in response to certain insults. Similarly, addition of bacteria into the alveoli resulted in very rapid sequestration of the pathogens by alveolar macrophages crawling from alveolus to alveolus. The crawling behavior was absolutely essential for the alveolar macrophages to eradicate the pathogens. This happened so quickly that essentially no neutrophils infiltrated the lung. However, if we exceeded a threshold of about 1 million bacteria, then neutrophils did enter the alveoli in an attempt to help the alveolar macrophages eradicate the pathogens. If the alveolar macrophages were unable to crawl than the neutrophils came into the alveoli at much lower concentration of bacteria suggesting that free bacteria attracted the neutrophils. Addition of virus resulted in a profound paralysis of the alveolar macrophages and now addition of bacteria as a secondary infection resulted in much worse infections and increased mortality. Clearly, the two compartments of the lung have different immune cells responsible for eradicating bacteria, but in over-whelming infection the neutrophils leave the vascular compartment and help the alveolar macrophages.