We now know that tissue-resident macrophages, such as alveolar macrophages, are not hemapoetically-derived but represent self-maintaining macrophage lineages that emerge during embryogenesis. Our appreciation of the divergent responses of alveolar macrophages and monocyte-derived macrophages to insult and infection is still emerging. We will look at the unique characteristics of these cells in the context of both *Mycobacterium tuberculosis* and HIV-1 infections *in vivo*.