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Cathepsins B and S Content in *Mycobacterium* ContainingCompartments in Human Macrophages and Dendritic cells

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Antigen-presenting cells (APC) such as macrophages and dendritic cells (DCs) play a pivotal role in tuberculosis pathogenesis. Macrophages are also key effector cells in mycobacteria killing. In order to survive inside the host immune cells mycobacteria developed different strategies. Among them blocking of phagosome-lysosome fusion and consequential reduced phagosome acidification assumes a crucial role allowing mycobacteria to escape acidic pH and destruction by proteolytic enzymes present in phagolysosomes. Since phagosome acidification varies between macrophages and DCs this may allow different kinetics of acquisition and activity for the enzymes involved.

The aim of the present study was to compare the distribution of two key cathepsins: the exopeptidase cathepsin B and the endopeptidase cathepsin S inside human monocyte derived macrophages and DCs infected with *Mycobacterium spp.* Infected immune cells were collected after 3 hours and 1 day post-infection and prepared either for immunofluorescence confocal microscopy or for immunogold electron microscopy on ultrathin cryo sections. In macrophages we did not observe significant co-localization between either BCG or *Mycobacterium tuberculosis* and cathepsins B or S indicating that phagosome-lysosome fusion was strongly hindered. Similar results were observed for *Mycobacterium tuberculosis* after infection of DCs. In DCs the acquisition of cathepsin B into the phagosomes containing BCG was different from the acquisition of cathepsin S. Cathepsin S content was decreased by 30% after 1 day of infection whereas cathepsin B content inside BCG-positive phagosomes was increased.

Our data indicate that cathepsins might be involved in differential mycobacterial persistence in macrophages compared to dendritic cells.

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