Activity and subcellular distribution of cathepsins in primary human monocytes

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Cathepsins (Cat) in antigen presenting cells (APC) control antigen processing as well as major histocompatibility complex class II transport and function. The set of active Cat and the subcellular architecture of the class II antigen presentation compartment are largely unknown in primary human APC, including peripheral blood monocytes. We used novel chemical tools to visualize Cat in an activity-dependent manner. Primary human monocytes contained active CatS, -B, and -H, while CatL was absent. Expression and activity patterns of Cat in human myelo-monocytoid cell lines were distinct from those found in primary cells. On a subcellular scale, the bulk of active Cat was concentrated in lysosomes in primary monocytes. In late endosomes, only active CatS was found in sizable amounts, colocalizing with C-terminal processing of the class II invariant chain and with cystatin C, the major endogenous Cat inhibitor. Late endosomes of human peripheral blood monocytes contain a well-controlled proteolytic machinery distinct from lysosomes, which is likely to play a key role in class II function.

type: journal paper/review (English)
date of publishing: 2-2003
journal title: Journal of leukocyte biology (73/2)
ISSN print: 0741-5400
pages: 235-42