

PubMed Results

Item 1 of 1

1. J Immunol. 2010 Sep 15;185(6):3217-26. Epub 2010 Aug 23.

The cystine/glutamate antiporter regulates dendritic cell differentiation and antigen presentation.

[D'Angelo JA](#), [Dehlink E](#), [Platzer B](#), [Dwyer P](#), [Circu ML](#), [Garay J](#), [Aw TY](#), [Fiebiger E](#), [Dickinson BL](#).

Department of Microbiology, Immunology, and Parasitology, Louisiana State University Health Science Center, New Orleans, LA 70112, USA.

Abstract

The major cellular antioxidant glutathione is depleted during HIV infection and in obesity. Although the consequence of glutathione depletion on immune function is starting to emerge, it is currently not known whether glutathione dysregulation influences the differentiation and maturation of dendritic cells (DCs). Moreover, the effect of glutathione depletion on DC effector functions, such as Ag presentation, is poorly understood. Glutathione synthesis depends on the cystine/glutamate antiporter, which transports the rate-limiting precursor cystine into the cell in exchange for glutamate. In this paper, we present a detailed study of antiporter function in DCs and demonstrate a role for the antiporter in DC differentiation and cross-presentation. We show that the antiporter is the major mechanism for transport of cystine and glutamate and modulates the intracellular glutathione content and glutathione efflux from DCs. Blocking antiporter-dependent cystine transport decreases intracellular glutathione levels, and these effects correlate with reduced transcription of the functional subunit of the antiporter. We further demonstrate that blocking antiporter activity interferes with DC differentiation from monocyte precursors, but antiporter activity is not required for LPS-induced phenotypic maturation. Finally, we show that inhibiting antiporter uptake of cystine interferes with presentation of exogenous Ag to class II MHC-restricted T cells and blocks cross-presentation on MHC class I. We conclude that aberrant antiporter function disrupts glutathione homeostasis in DCs and may contribute to impaired immunity in the diseased host.

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