Indoleamine 2,3-dioxygenase 1 (IDO1): relationship between functions and intracellular localization

[1]A. Iacono,[2]F. Grassi,[3]A. Pompa,[3]F. De Marchis,[3]M. Bellucci,[1]G. Mondanelli,[1]U. Grohmann and[1]M.T. Pallotta.

[1]Department of Experimental Medicine, University of Perugia, Italy
[2]Institute for Research in Biomedicine, Bellinzona, Switzerland; Department of Medical Biotechnology and Translational Medicine, University of Milan, Milan, Italy
[3]Institute of Biosciences and Bioresources of Perugia - Italian National Council of Research,Perugia, Italy

Indoleamine 2,3-dioxygenase (IDO1), a tryptophan catabolizing enzyme, is recognized as an authentic regulator of immunity in several physiopathologic conditions. We recently demonstrated that IDO1 does not merely degrade tryptophan and produce immunoregulatory kynurenines, but it also acts as a signal-transducing molecule, independently of its enzymic function. In particular, in a microenvironment dominated by TGF-b, we found that IDO1 is involved in intracellular signaling events responsible for the self-amplification and maintenance of a stably regulatory phenotype in plasmacytoid dendritic cells (pDC_s), a DC subset. In the literature, IDO1 has been described as a protein with a cytoplasmic localization. However, no thorough analysis of modifications of this localization in different conditions has been performed so far. We here investigated the intra-cellular localization of IDO1 in pDC_s by means of confocal microscopy. Besides confirming the main cytoplasmic localization of the protein IDO1, we detected the presence of a significant amount of IDO1 in subcellular structures other than cytoplasm, particularly in cells treated with TGF-b. In particular, IDO1 appeared to be more concentrated in specific compartments closed to the inner face of the cellular membrane after in TGF-b–treated pDCs. In order to identify the intracellular compartments other than cytoplasm in which IDO1 can localize, we performed immunofluorescence experiments in pDC_s using antibodies specific for cell organelle markers, which indicated the co-localization of IDO1 and EEA1, a marker of early-endosomes in pDC_s treated with TGF-b.Thanks to these data, it is possible to assume the enzyme IDO1 has not exclusively a cytoplasmic localization, but there could be a balance between its localization in the cytosol and early endosomes, possibly related to two distinct IDO1-mediated (catalysis *vs.* signaling) tolerogenic mechanisms.