PublisherInfo		
PublisherName	:	BioMed Central
PublisherLocation	:	London
PublisherImprintName	:	BioMed Central

Critical role of a stimulator/responder ratio between dendritic cells and CD4+ T cells for Th2 polarization

ArticleInfo		
ArticleID	:	143
ArticleDOI	:	10.1186/ar-2000-66853
ArticleCitationID	:	66853
ArticleSequenceNumber	:	100
ArticleCategory	:	Paper Report
ArticleFirstPage	:	1
ArticleLastPage	:	3
ArticleHistory	:	RegistrationDate : 2000–10–9 OnlineDate : 2000–10–9
ArticleCopyright	:	Current Science Ltd2000
ArticleGrants	:	
ArticleContext	:	130753311

Petya Dimitrova,[Aff1]

Aff1 University of Erlangen, Germany

Keywords

CD4$^+$ T cells, dendritic cells, stimulator/responder ratio, Th2 polarization

Context

Based on origin and nature of stimulation during maturation, dendritic cells (DCs) can differentiate into either DC type 1 (DC1) or DC type 2 (DC2) that induce Th1 or Th2 responses, respectively. It has previously been suggested that human monocyte-derived DCs develop into DC1, secrete high amounts of interleukin (IL)-12 in response to pathogens or pathogen-derived signals and thus promote Th1 differentiation. In this paper, the ability of human myeloid dendritic cells to induce polarized Th1 or Th2 cell differentiation was investigated.

Significant findings

At a low DC:T cell ratio, type I mature dendritic cells favored Th2 differentiation of naive CD4$^+$T cells regardless of the nature of stimulation during DC maturation. By contrast, at high stimulation/ responder ratios, a mixed Th1/Th2 response was induced. Th2 commitment was enhanced by upregulation of costimulatory molecules such as B7 or OX40 on dendritic cells.

Comments

The ratio of DCs to naive CD4$^+$ T cells was critical for T cell differentiation. One possible explanation for these results would be that limited DC:CD4$^+$ T cell interactions exhausted DCs to produce less IL-12 and therefore induced Th2 differentiation of CD4$^+$ T cells. The addition of neutralizing anti-IL-4 or IL-4 receptor antibodies did not influence the initiation of Th2 response and suggested that other, IL-4-independent factors were involved in Th2 differentiation. Blockade of CD28 and OX40L costimulation by CTLA4-Ig or anti-OX40L antibodies inhibited IL-4 and IL-5 production

from $CD4^+$ T cells without a concomitant shift to Th1 effectors and provided further evidence for a determinative role of costimulatory signals in Th2 differentiation. In conclusion, the stimulator/responder ratios and costimulation via CD28 and OX40L pathways are important factors that modulate the polarizing capacity of DC1s in promoting Th differentiation.

Methods

Purification and generation of DCs from human peripheral blood, differentiation of effector T cells by DCs in coculture experiments (MLR),

References

1. Tanaka H, Demeure CE, Rubio M, Delespesse G, Sarfati M: Human monocyte-derived dendritic cells induce naive T cell differentiation into T helper cell type 2 (Th2) or Th1/Th2 effectors: role of stimulator/responder ratio. J Exp Med. 2000, 192: 405-411.