CD43 in T cell–DC conjugate formation?

HERMANN J. ZILTENER[1,2] AND DOUGLAS A. CARLOW[1]

[1]The Biomedical Research Center and [2]The Department of Pathology and Laboratory of Medicine, University of British Columbia, Vancouver, BCV6T-1Z3, Canada. (hermann@brc.ubc.ca)

In an analysis of antigen-independent interactions between naïve T cells and dendritic cells (DCs), Revy *et al.*[1] reported that higher frequencies of CD4$^+$ *versus* CD8$^+$ T cells developed productive interactions with DCs, as measured by calcium fluxing. To account for the observed difference between CD4$^+$ and CD8$^+$ T cells, the authors applied a panel of monoclonal antibodies (mAbs) to CD2, CD3, CD4, CD8, CD11a, CD28, CD43 and CD45 to determine whether distinct expression of cell surface molecules might be responsible. Only one mAb, 1B11, showed significant differential binding on CD8$^+$, but not CD4$^+$, T cells. This led the authors to conclude that the selective expression of a highly glycosylated, repulsive molecule, CD43, on CD8$^+$ T cells could explain the lower frequency of CD8$^+$ T cell–DC conjugates. This conclusion is based on two sets of observations: reactivity of 1B11 with the high molecular weight glycoform of CD43 arising from O-glycan branching that can occur in activated T cells[2] and various studies that describe an anti-adhesive function of CD43.

We would like to point out that 1B11 has dual specificity and that the 1B11 reactivity Revy *et al.* identified and used to implicate CD43 in affecting CD8$^+$ T cell–DC conjugates is retained in CD43$^{-/-}$ mice and is therefore not due to CD43[3]. We have published strong evidence that this CD43-independent binding by 1B11 is mediated by a hyposialylated form of CD45RB that is expressed preferentially on naïve CD8$^+$ T cells[3,4]. Either an endogenous neuraminidase reportedly expressed by CD8$^+$ T cells[5,6] or reduced sialyltransferase activity may be responsible for the expression of hyposialylated CD45RB on CD8$^+$ T cells.

Although the overall findings by Revy *et al.* on synapse formation remain uncontested, their explanation involving CD43 is misleading and should be clarified to avoid further confusion. Nevertheless, their study, together with the aforementioned insights into 1B11 reactivity, offer an opportunity to reconcile these data. Specifically, there are indeed sialic acid–dependent adhesion systems[7] that may be compromised in hyposialylated CD8$^+$ T cells and thereby account for the reduction in conjugate frequencies between CD8$^+$ T cells and DCs. Thus the basis for differential T cell–DC conjugate formation may be related more to lack of such pro-adhesive interactions than to anti-adhesive influences of CD43.

1. Revy, P., Sospedra, M., Barbour, B. & Trautmann, A. *Nature Immunol.* **2**, 925–931 (2001).
2. Jones, A. T. *J. Immunol.* **153**, 3426–3439 (1994).
3. Carlow, D. A., Ardman, B. & Ziltener, H. J. *J. Immunol.* **163**, 1441–1448 (1999).
4. BDPharMingen. Product Information. *PharMingen Technical Data Sheet*. (www.pharmingen.com/pdfs/09691A558760.pdf)
5. Landolfi, N. F., Leone, J., Womack, J. E. & Cook, R. G. *Immunogenetics* **22**, 159–167 (1985).
6. Galvan, M., Murali-Krishna, K., Ming, L. L., Baum, L. & Ahmed, R. *J. Immunol.* **161**, 641–648 (1998).
7. Crocker, P. R. & Varki, A. *Trends Immunol.* **22**, 337–342 (2001).

Response

ALAIN TRAUTMANN

Institut Cochin de Genetique Moleculaire, Laboratoire d'Immuno-Pharmacologie, Centre National de la Recherche Scientifique (CNRS) UPR 415, ICGM, Bat Gustave-Roussy, 22 rue Mechain, Paris 75014, France. (trautmann@cochin.inserm.fr)

We have shown that the formation of an immunological synapse at the interface between a T cell and a DC was not initiated by antigen recognition, as functional synapses formed in the absence of exogenously added antigen and even in the absence of MHC[1]. In addition, we noticed that these synapses formed more easily with CD4$^+$ than with CD8$^+$ T cells, which specifically express a molecule recognized by the mAb 1B11. We suggested, therefore, a possible causal link between these two facts. We consider that 1B11 recognizes a hyperglycosylated form of CD43, whereas Ziltener and Carlow think that it recognizes an hyposialylated form of CD45RB.

Without any ambiguity it has been shown that 1B11 can recognize CD43[2–5], including at the surface of primary T cells in nonimmunized mice[2]. Ziltener and colleagues have shown that 1B11 can also bind to CD45RB, a likely reason why T cells from CD43-deficient mice are still 1B11-positive[6]. In a resting T cell, there is an ambiguity concerning the fraction of 1B11-labeling that is due to CD43 or to CD45RB. Before being detected by 1B11, CD45RB epitopes must be uncovered by neuraminidase treatment, as observed with either intact cells or in immunoprecipitates[6].

From this finding, we concluded that the epitope recognized by 1B11 in untreated naïve CD8 T cells was most probably CD43, and not CD45RB. Admittedly, this conclusion deserves to be challenged by additional experiments. It would also be worth examining whether the presence of the molecule recognized by 1B11 (whether it be CD43 or CD45RB) is directly responsible for the relative difficulty with which CD8$^+$ T cells form functional synapses with DCs, or whether this 1B11 labeling is only a neutral indicator of a different state of glycosylation.

1. Revy, P., Sospedra, M., Barbour, B. & Trautmann, A. *Nature Immunol.* **2**, 925–931 (2001).
2. Bagriacik, E. U., Armstrong, M. D., Okabe, M. & Klein, J. R. *Int. Immunol.* **11**, 1651–1662 (1999).
3. Ellies, L. G., Jones, A. T., Williams, M. J. & Ziltener, H. J. *Glycobiology* **4**, 885–893 (1994).
4. Jones, A. T. *et al. J. Immunol.* **153**, 3426–3439 (1994).
5. Tsuboi, S. & Fukuda, M.. *EMBO J.* **16**, 6364–6373 (1997).
6. Carlow, D. A., Ardman, B. & Ziltener, H. J. *J. Immunol.* **163**, 1441–1448 (1999).