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CD99 form complex with CD81, MHC molecules and translocate into immunological synapes

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Abstract

CD99, a leukocyte surface glycoprotein, is broadly expressed in many cell types. CD99 is expressed as two distinct isoforms, a long form and a short form. CD99 has been demonstrated to play a key role in several biological processes, including the regulation of T cell activation. However, the molecular mechanisms by which CD99 participates in such processes are unclear. As CD99 contains a short cytoplasmic tail, it is unlikely that CD99 itself takes part in its multi-functions. Association of CD99 with other membrane proteins has been suggested to be necessary for exerting its functions. In this study, we analyzed the association of CD99 with other cell surface molecules involved in T cell activation. We demonstrate the association of MHC class I, MHC class II and tetraspanin CD81 with CD99 molecules on the cell surface. Association of CD99 with its partners was observed for both isoforms. In addition, we determined that CD99 is a lipid raft-associated membrane protein and is recruited into the immunologic synapse during T cell activation. Upon T cell activation, CD99 engagement can inhibit T cell proliferation. We speculate that the CD99-MHC-CD81 complex is a tetraspanin web that plays an important role in T cell activation.