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# Intercellular adhesion molecules (ICAMs)

Intercellular adhesion molecules are a subset of the immunoglobulin superfamily that share the ability to interact with β2 integrins. There are now five members of this family of which three have been characterized in many studies dating back to the identification of ICAM-1 as an LFA-1 ligand in 1986. This chapter will describe the unique structural and functional features of each ICAM and a general discussion of the LFA-1 binding surface in ICAMs which is defined by the recent crystal structure of ICAM-2.

## ICAM-1 (CD54)

### Protein properties

ICAM-1 is a cellular ligand for the leukocyte integrins LFA-1 (integrin $\alpha L\beta 2$) and Mac-1 (integrin $\alpha M\beta 2$) through distinct binding sites. ICAM-1 is a type I transmembrane glycoprotein of 85 000–110 000 Da with a polypeptide of 55 000 Da[1] composed of five tandem Ig-like domains, a transmembrane domain, and a short cytoplasmic tail[2] that binds α-actinin[3] (Fig. 1). LFA-1 binds to domain 1 of ICAM-1,[4] while Mac-1 binds to domain 3 of ICAM-1 in a manner that is partially obstructed by a natural *N*-linked oligosaccharide.[5] ICAM-1 is also a receptor for the major group of rhinoviruses (cold viruses) and is the receptor for *Plasmodium falciparum* (malaria) infected erythrocytes.[6–8] LFA-1, rhinovirus, and *Plasmodium falciparum* bind to overlapping, but non-identical parts of ICAM-1 domain 1.[4,9] Rotary shadowing electron microscopy indicates that there is a bend between domains 3 and 4.[4,10] Human and mouse ICAM-1 form dimers on the cell surface that depend on the transmembrane domains and normal presentation of domain 4.[11,12] (unpublished observations). These dimers have a profound advantage for binding purified LFA-1, but the advantage of dimerization has been more difficult to assess in cell–cell adhesion.[11]

ICAM-1 is expressed on endothelial cells, some epithelial cells, and is present in an intracellular pool in mono-

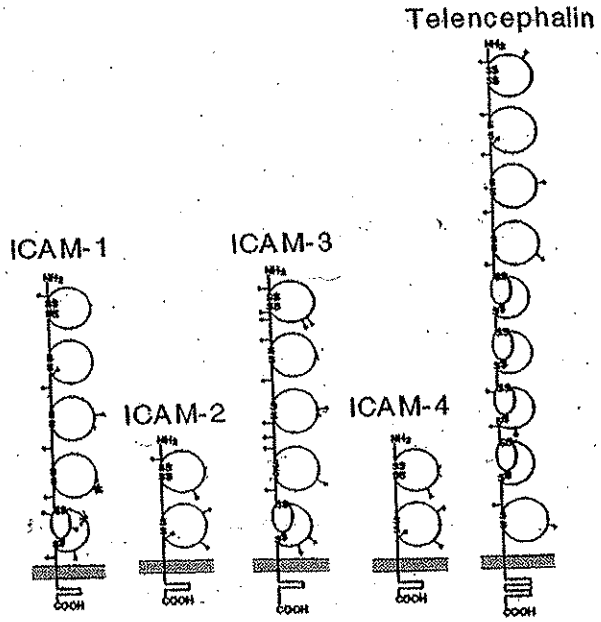


**Figure 1.** Schematic of interacullular adhesion molecules. The Ig-like domains are indicated as disulphide-linked loops. The glycosylation sites are indicated as lollipops. Glycosylation patterns are for mouse ICAM-1, ICAM-2 and telencephalin, and human ICAM-3 and ICAM-4.

Telencephalin is a 130 000 Da glycoprotein consisting of nine Ig-like domains, a transmembrane domain, and a short cytoplasmic tail.[56] Telencephalin is expressed on the soma and dendritic projections, but not axons, of neurones in the central nervous system. The first five Ig-like domains are 50 per cent similar to ICAM-1 and ICAM-3. Soluble recombinant telencephalin and telencephalin expressed on L-cells mediated adhesion of LFA-1-expressing cells in a divalent cation, energy, and activation dependent manner that was blocked by anti-LFA-1 mAb.[57] Telencephalin is well positioned in the central nervous system to play a role in leukocyte/neurone interactions.

## Antibodies

ICAM-4 and telencephalin are recognized by polyclonal antisera.

## Genes

Human ICAM-4 cDNAs have been cloned and expressed[54,56] (X93093). Telencephalin cDNAs have been obtained for human[56] (AA421394), rabbit[56] (L13199) and mouse (MMU06483) and the human form has been expressed.[57]

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