[S7-4] [10/11/2003(Sat) 11:10-11:40/ Grand Ballroom 104]

Targeting Cell-Cell and Cell-Matrix Interactions and Its Therapeutic Applications

In-San Kim

Cell & Matrix Biology Laboratory, Department of Biochemistry, Kyungpook National University Medical School

Cell-cell and cell-matrix interaction is clearly required for metazoans not only to hold their cells together but also to conduct more sophisticated biological processes. Each cell has adhesion molecules on its cell membrane to link extracellular matrix and adjacent cells to the intracellular cytoskeleton, and also to transduce signals. In complex metazoans, information is transmited from one cell to another by mechanisms such as direct intercellular communication, soluble signal molecules among distant cells, and local cellular environments formed by highly specialized extracellular matrix. The reciprocal dynamic interaction between cells and ECM is critical for embryonic development, wound repair, angiogenesis, inflammation, and tumor metastasis.

The fas-1 domain was first identified in Drosophila neuroadhesion molecule, fasciclin-1. It consists of about 100-140 amino acids containing two conserved motifs, H1 and H2 at N-terminus and C-terminus respectively. The fas-1 domain is evolutionary well conserved since it is found in proteins of bacteria, yeast, plants, C-elegance, Drosophilla, zebra fish and mammals. In human, four proteins, βig-h3, periostin, Fex-1(stabilin-1) and Fex-2 (stabilin-2) were identified to have the fas-1 domains. These proteins can be categorized into two groups, the secretory type and the membrane type. The first two proteins are secretory proteins having four fas-1 domains whereas the last two proteins are membrane proteins having seven fas-1 domains. The proteins in each group are highly homologous besides of the fas-1 domains. Although the biological functions of the fas-1 domain is not comprehensively understood, we have reported that the fas-1 domain has motifs mediating cell adhesion and migration through interacting with several integrins. We have identified a motif mediating epithelial cell adhesion and migration through interacting with the α3β1 integrin and a motif mediating mesenchymal cell adhesion and migration through interacting with the avb5/avb3 integrins. Therefore, we suggest that most proteins containing the fas-1 domains may function in cell-cell or cell-matrix interactions through interacting with integrins. The functions of each protein containing the fas-1 domains

are largely unknown. We found that the βig-h3 is expressed not only in the basement membrane of epithelial cells of many organs including lung and kindney but also in the vascular basement membrane suggesting the βig-h3 play important roles in several cell functions such adhesion, migration, invasion, differentiation, regeneration and angiogenesis. Evidence demonstrating the biological functions of βig-h3 including angiogenesis and inflammation will be shown. The functions of other three human proteins are almost unknown. The possible functions of these proteins will be also discussed.