

Recent advances in cell adhesion molecules and extracellular matrix proteins: potential clinical implications

Shaker A. Mousa and David A. Cheresh

The roles of cell adhesion molecules (CAMs) and extracellular matrix proteins (ECMs) in various pathological processes leading to both acute and chronic disease states have recently been documented. The authors report on the development of various therapeutic and diagnostic candidates based on the key role of CAMs in a range of diseases, and discuss the structure-function aspects of cell adhesion and signaling of the different CAMs/ECMs.

Several physiological processes, including cell activation, migration, proliferation and differentiation, require direct contact between cells or extracellular matrix proteins. Cell-cell and cell-matrix interactions are mediated through several different families of cell adhesion molecules (CAMs), including the selectins, the integrins, the cadherins and the immunoglobulins. Newly discovered CAMs, together with the discovery of new roles for integrins, selectins and immunoglobulins in certain disease states, provide great opportunities for the development of therapeutic, and perhaps diagnostic, modalities¹.

Intensified R&D efforts, directed at manipulating CAM activity through the use of monoclonal antibodies, peptides, peptidomimetics and nonpeptide small molecules, continue

to broaden the scope of key clinical applications (Table 1). This article focuses on current advances in the discovery and development of novel anti-CAM agents for potential therapeutic and diagnostic applications.

Roles of CAMs in disease states

Cell adhesion molecules play highly significant roles both in normal and in various pathophysiological disease states. For this reason, the selection of a specific and relevant CAM to target a certain disease condition without interfering with other normal cellular functions is a very important prerequisite for ultimate success in developing truly active and safe therapeutic strategies²⁻⁷. Recent breakthroughs with animal models, the latest advances in the understanding of the signaling pathways, transcriptional regulation and the structure-function aspects of CAMs, as well as the role of CAMs and extracellular matrix proteins (ECMs) in cellular migration, spreading, proliferation and survival, have highlighted the potential for novel strategies based on CAM function.

There have been exciting advances in understanding several CAMs; most notably, the $\alpha_5\beta_1$, $\alpha_6\beta_1$, $\alpha_4\beta_1$ and $\alpha_9\beta_1$ integrin receptors and their direct relationships to different disease states represent tremendous therapeutic and diagnostic opportunities¹⁻⁸. Potential roles for specific CAMs in different disease states, including cardiovascular, cancer, inflammatory, ocular, pulmonary, bone, central nervous system, kidney and gastrointestinal system disorders, have been suggested, including the following examples:

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