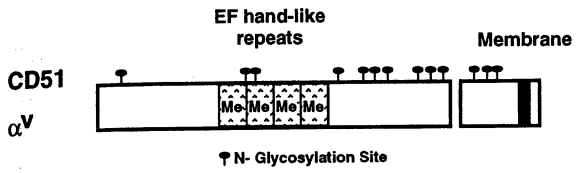
lymphocytes in the apical light zone and mantle zone of the follicle expressed the antigen at much greater levels than those within the dark zone of the follicle. Minimal expression was detected in the interfollicular zone. The antigen detected by S276 (Mo2PT501), probably CD48, was also restricted to lymphoid cells, but was expressed by all lymphoid subsets seen in the tonsil and colon as well as by intraepithelial lymphoid cells.

The mAb in Subpanels 7 and 8 therefore appear to identify a wide range of different integrin and non-integrin receptor molecules. Expression of each integrin subunit is regulated in a cell-type and differentiation-dependent manner.

AS7/8.2 CD51 (α^V) and CD51/CD61 complex cluster report

DENNIS A. WONG and TIMOTHY A. SPRINGER



CD51 is α^V, an integrin α chain [1]. While it is common for β chains to associate with multiple α subunits, CD51 is unique in its ability to associate with five different integrin β chains. In combination with CD61 (β_3), CD51 is the classic RGD-dependent vitronectin receptor, and combined with β_5 also appears to bind vitronectin [2,3]. When associated with β_1 or β_6, it binds the RGD sequence in fibronectin [4,5]. α^V has also been shown to be associated with the newest integrin β chain, β_8 [6]. CD51 was clustered in the Fourth Workshop with four monoclonal antibodies (mAb), 13C2, 23C5, NKI-M7, and NKI-M9. On the basis of flow cytometry, immunoprecipitation, and enzyme-linked immunosorbent assay (ELISA) results, S236 (AMF7), S245 (13C2), and S262 (LM142) in this Workshop have been clustered to CD51. Two mAb, S246 (23C6) and S263 (LM609), bind to the CD51/CD61 complex and do not recognize CD51 or CD61 complexed with other subunits.

Molecular cloning

The predicted amino acid sequence of CD51 [7] has 1048 residues. Its structure is typical of cleaved integrin α chains (introductory diagram). The molecule is post-translationally cleaved into a heavy chain and light chain. The heavy chain contains four cation-binding domains, while the light chain contains the hydrophobic transmembrane domain and a short cytoplasmic tail. There are 13 potential N-linked glycosylation sites. Structurally, it is most closely related to the other cleaved integrin α chains, particularly α^5, α^8, and α^{IIb}. The gene has been localized to chromosome 2q31–q32 [8,9].

Immunochemistry

The heavy chain and light chain are disulfide-linked. CD51 runs as a 125/24 kDa protein by sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) under reducing conditions and a 150-kDa protein under non-reducing conditions. Antibodies clustered to CD51 and to the CD51/CD61 complex in this Workshop immunoprecipitate $\alpha^V\beta_3$ from osteoclasts [Wesbitt and Horton AS7/8.9], the B-cell line, JY [see Wong and Springer AS7/8] the rhabdomyosarcoma cell line, RD [Bodorova and Hemler, unpublished Workshop report], and peripheral blood mononuclear cells [Arroyo: Sánchez-Madrid; Krissansen and Print, unpublished Workshop reports]. The three CD51 clustered mAb also immunoprecipitated $\alpha^V\beta_5$ from the adenocarcinoma cell line A549 [see Wong and Springer AS7/8].

Cellular expression

The classic vitronectin receptor, $\alpha^V\beta_3$ is found on endothelial cells, some B cells, monocytes/macrophages,

platelets, oestoclasts, mast cells, and tumour cells [10,11]. In association with β_5, it is found on carcinoma cells, hepatoma cells, and fibroblasts [2,3]. Two cell lines, FG-2 and UCLA-P3, have been found to express $\alpha^V\beta_6$ [5]. During the Workshop, CD51 was found to be expressed in all stromal cells including fibroblastic, epithelial, hepatocytic, mesothelial, and endothelial cell lines. It was also present on JY, monocytic, and HMC-1 (mast cell) cells and weakly expressed on platelets. Immunohistochemistry showed staining in all organs, on epithelium, endothelium, fibroblasts, smooth muscle cells, and nerve tracts. While CD51 antibodies stain colon carcinoma and breast epithelial cells, CD51/CD61 complex antibodies did not stain these cells. These results suggest that α^V is associating with another β chain in those cells, probably β_5.

Function

The $\alpha^V\beta_3$ integrin complex binds vitronectin at the RGD sequence and is also known to bind fibrinogen, von Willebrand factor (vWF), thrombospondin, fibronectin, osteopontin, and collagen [1]. While $\alpha^V\beta_5$ has also been shown to bind vitronectin at the RGD site, $\alpha^V\beta_1$ and $\alpha^V\beta_6$ have only been shown to bind fibronectin [2–5]. As cell surface molecules, the α^V molecules appear to have become the targets of pathogens. $\alpha^V\beta_3$ and $\alpha^V\beta_5$ have been shown to promote adenovirus internalization but not virus attachment [12]. $\alpha^V\beta_5$ has been shown to bind to the Tat protein of HIV [13]. *Mycobacterium avium-intracellulare* may use $\alpha^V\beta_3$ to invade monocytes [14]. During this Workshop, S236 (AMF7) was shown to block macrophage recognition of apoptotic cells. [Flora and Gregory, AS7.9]. S262 (LM142) and S263 (23C6) inhibited T-cell proliferation to tetanus toxin peptide and allogeneic cells [Wyss-Coray and Pichler, unpublished Workshop report]. S236 (AMF7), S245 (13C2), S246 (23C6), and S263 (LM609) are reported by their donors to inhibit binding in adhesion assays but this was not tested during the Workshop.

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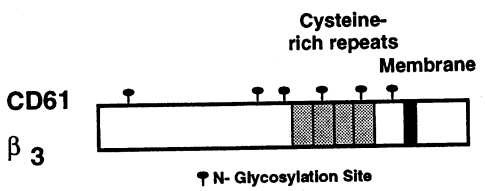
AS7/8.3 CD61 (β_3) cluster report

DENNIS A. WONG and TIMOTHY A. SPRINGER



CD61 is the integrin β_3 chain that was initially discovered as part of the heterodimer gpIIb/IIIa (CD41/CD61), a major glycoprotein found on platelets [1]. With the cloning of CD41/CD61 and the finding that the vitronectin receptor is $\alpha^V\beta_3$ (CD51/CD61), it became clear that CD41/CD61 and