THE BASEMENT MEMBRANE ZONE: MAKING THE CONNECTION

American Academy of Dermatology

Study Notes

THE BASEMENT MEMBRANE ZONE: MAKING THE CONNECTION

Study Guide

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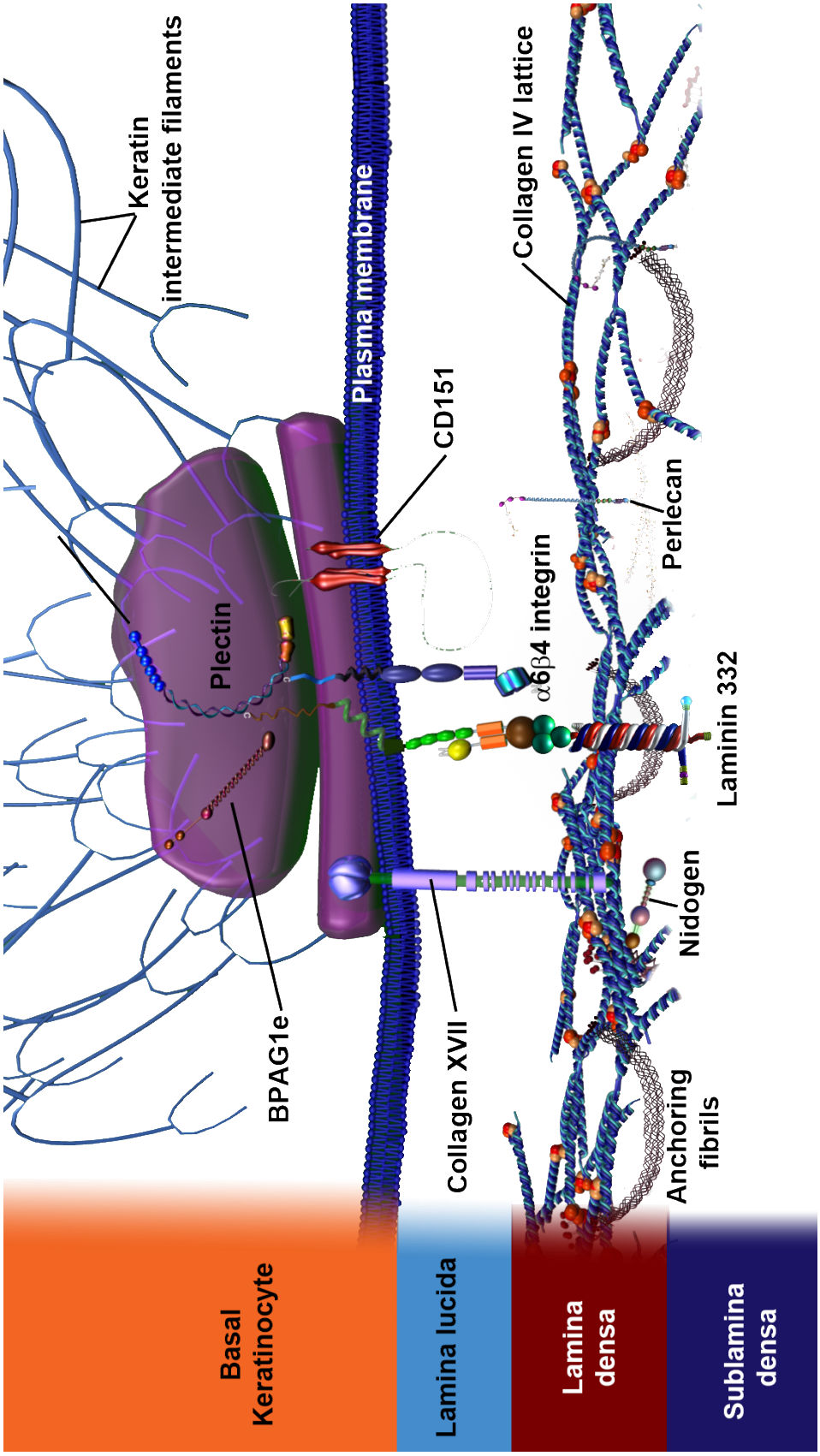
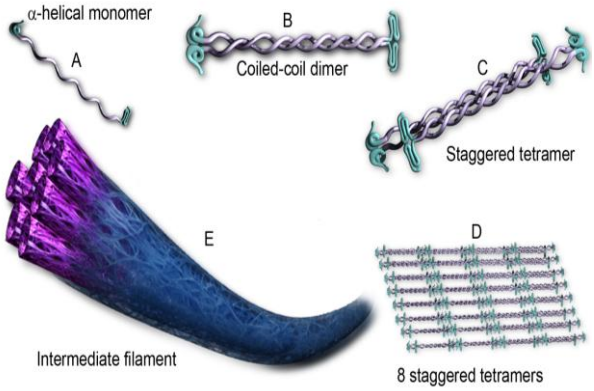
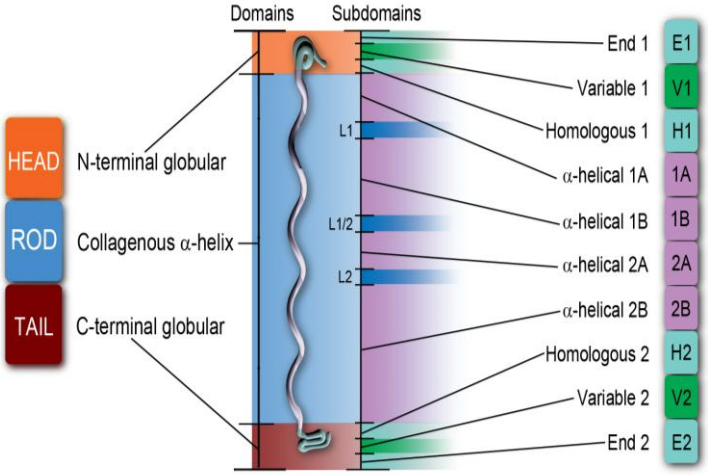


Intermediate Filamments, Type I & II

- **Classification:** Cytoskeletal protein
- **Molecular weight:** 40-64 kDa.
- **Location:** Basal keratinocyte.
- **Function(s):**
  a. Structural/mechanical integrity.
  b. Organizing cytoplasmic architecture.
  c. Intracellular signaling.
  d. Regulation of transcription.
- **Disease associations:**
  a. Dominant epidermolysis bullosa simplex (DEBS) [K5, K14].
  b. REBS [K14].
  c. EBS, Köebner type [K5, K14].
  d. EBS, Weber-Cockayne type [K5, K14].
  e. EBS, Dowling-Meara type [K5, K14].
  f. EBS with mottled pigmentation [K5, K14].
  g. EBS with migratory circinate erythema [K5].
  h. EBS with severe palmoplantar hyperkeratosis [K5].
  i. Dowling-Degos disease [K5]
  j. Epidermolytic hyperkeratosis [K1,K10]
  k. Epidermolytic PPK [K1, K5, K9,K10, K16].
  l. Diffuse non-epidermolytic PPK [K1].
  m. Focal non-epidermolytic PPK [K6c, K16].
  n. Ichthyosis hystrix, Curth-Mackin type [K1].
  o. Cyclic ichthyosis with epidermolytic hyperkeratosis [K1, K10]
  p. Greither's syndrome [K1].
  q. Striate palmoplantar keratoderma [K1].

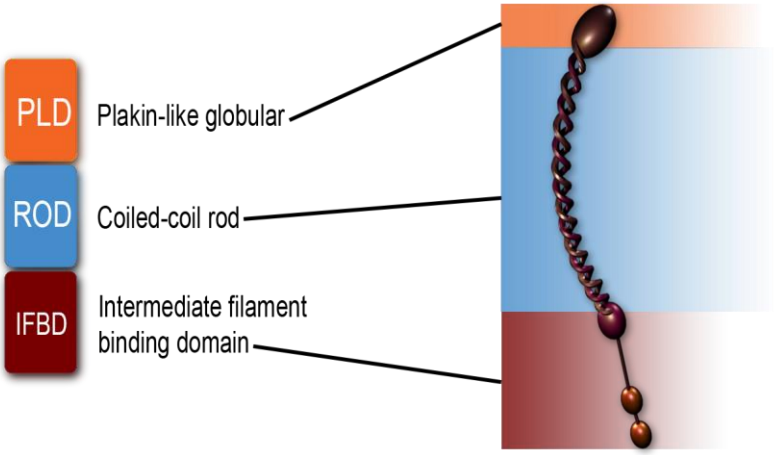


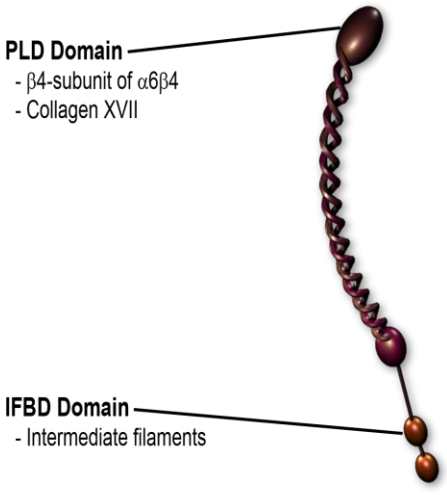


IF binds:
- Plectin
- BPAG1

BPAG1e

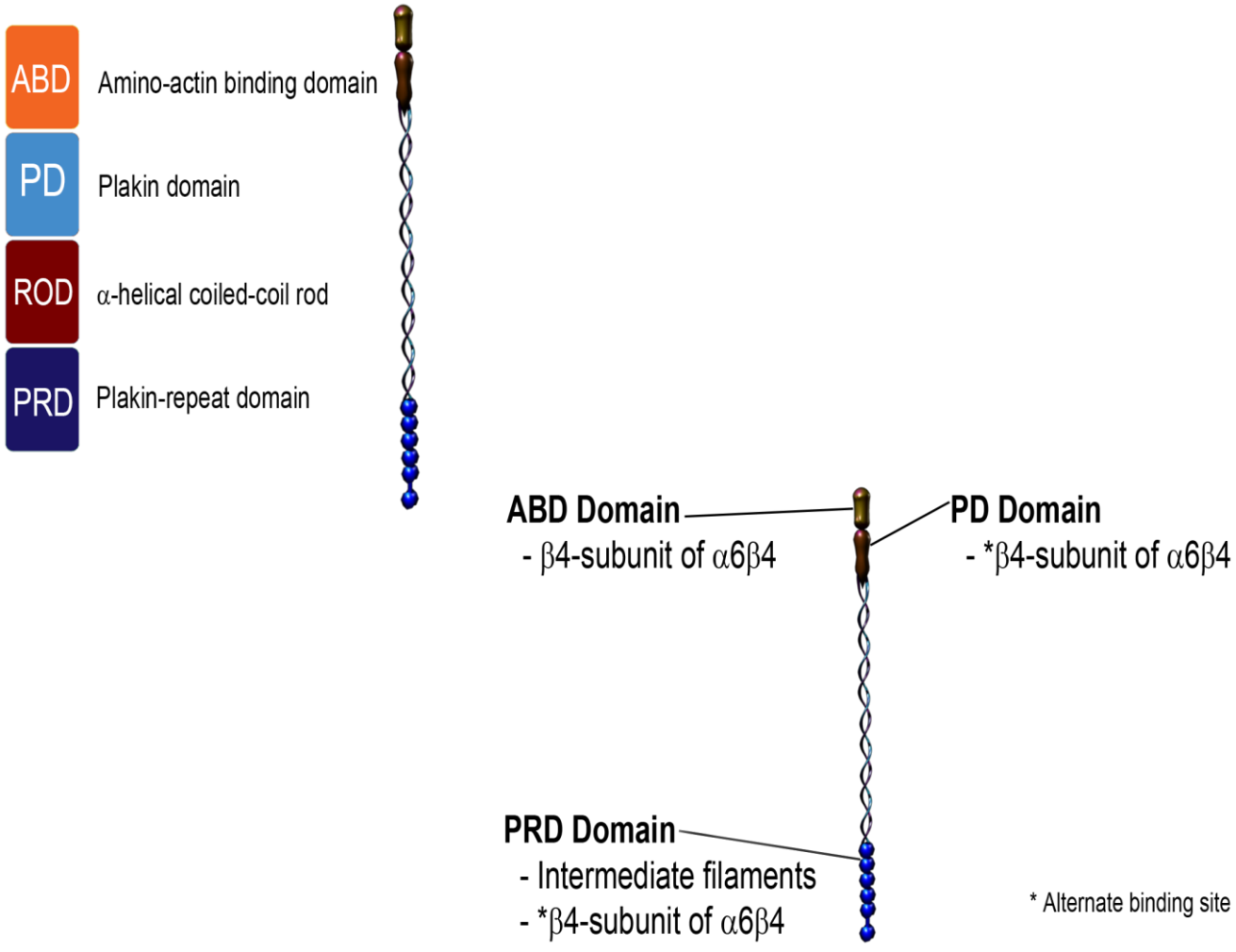
- **Classification:** Plakin family of proteins.
- **Molecular weight:** 230 kDa
- **Location:** Basal keratinocyte, HD (inner plaque).
- **Function(s):**
  a. Structural/mechanical integrity.
  b. Component of hemidesmosome (type I).
  c. Signaling (via β4 integrin binding) for epidermal migration and cell polarity.
- **Disease associations:**
  - Bullous pemphigoid.
  - Paraneoplastic pemphigus.





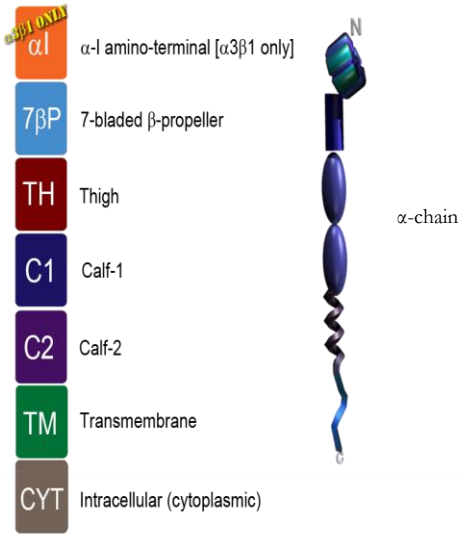
Plectin

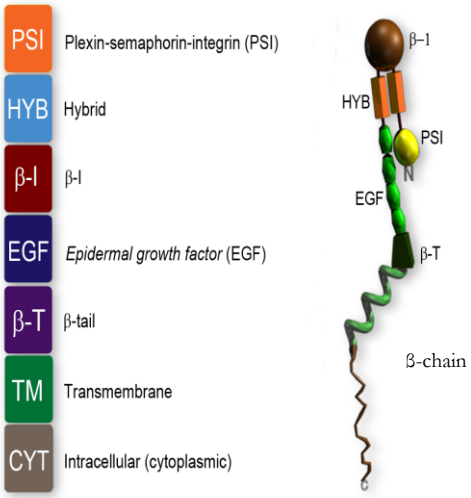
- **Classification:** Plakin family of proteins.
- **Molecular weight:** 450-533 kDa.
- **Location:** Basal keratinocyte, HD (inner plaque).
- **Function(s):**
  a. Structural/mechanical integrity of hemidesmosomes.
  b. Linkage of intracellular cytokeratin proteins.
  c. Scaffold for signaling proteins.
- **Disease associations:**
  a. Epidermolysis bullosa simplex with muscular dystrophy.
  b. Epidermolysis bullosa simplex with pyloric atresia.
  c. Epidermolysis bullosa simplex Ogna variant.
  d. Paraneoplastic pemphigus.
  e. Bullous pemphigoid.

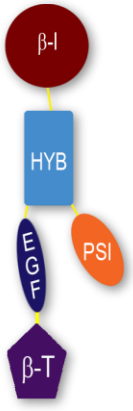


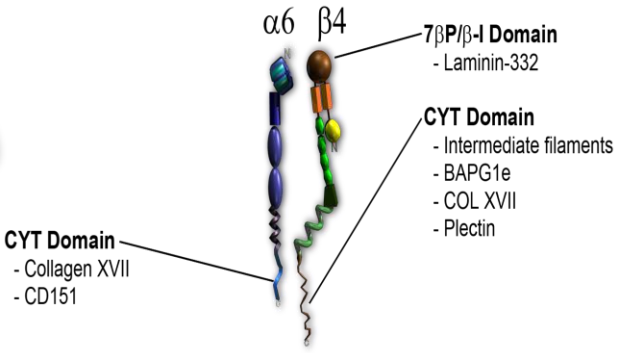
Integrins

- **Classification:** Integrins (α6β4, α3β1)
- **Molecular weight:** 260-360 kDa
- **Location:** Basal keratinocyte, HD (outer plaque), lamina lucida.
- **Function(s):**
    a. Structural/mechanical integrity.
    b. Epidermal homeostasis (adhesion, differentiation, proliferation).
    c. Cellular signaling.
    d. Hair growth.
- **Disease associations:**
    a. Junctional epidermolysis bullosa with pyloric atresia (Itga6, Itgb4).
    b. Psoriasis (Itgb1).





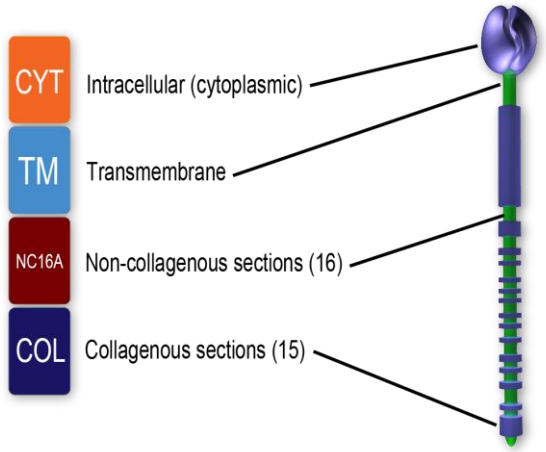


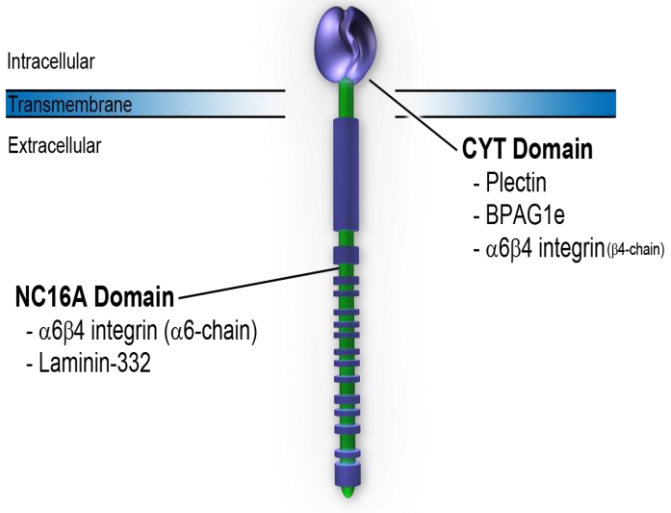


Collagen XVII

Classification: Transmembrane collagen

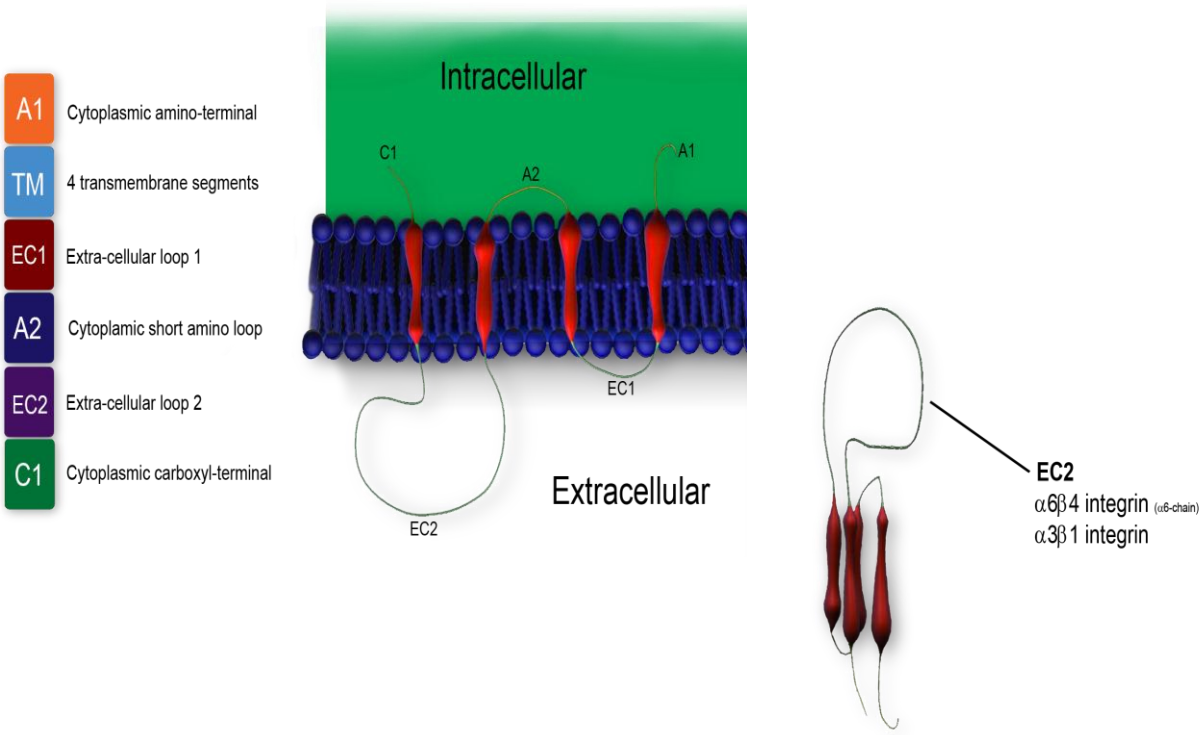
- **Molecular weight:** 180 kDa
- **Location:** Basal keratinocyte, HD (outer plaque), lamina lucida, lamina densa.
- **Function(s):**
    a. Structural/mechanical integrity.
    b. Basal cell adhesion/migration.
    c. Tooth enamel formation.
- **Disease associations:**
    a. Bullous pemphigoid.
    b. Generalized atrophic benign epidermolysis bullosa (GABEB)
    c. Junctional epidermolysis bullosa (JEB-other)(COL17A1).
    d. Linear IgA bullous dermatosis.





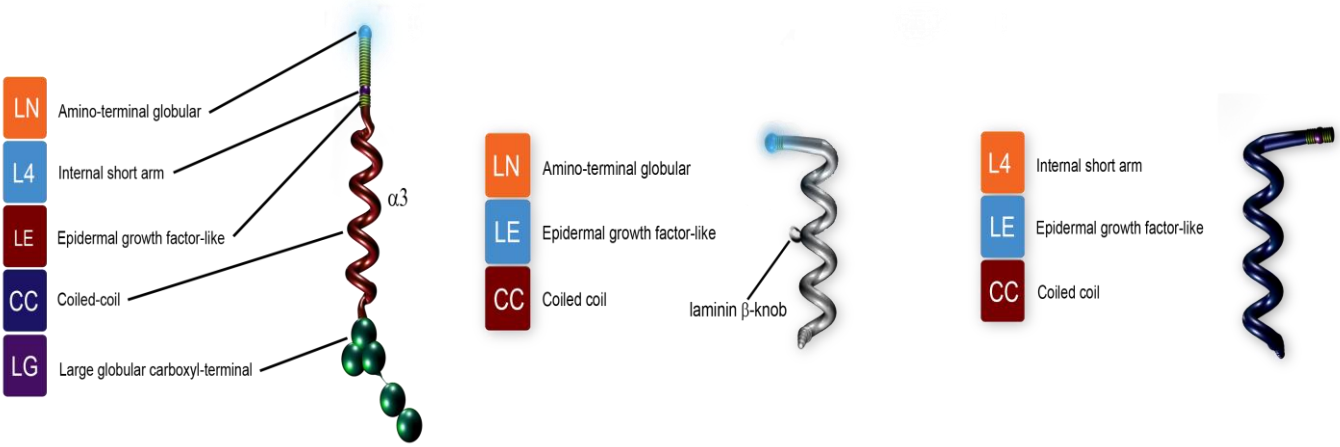
CD151

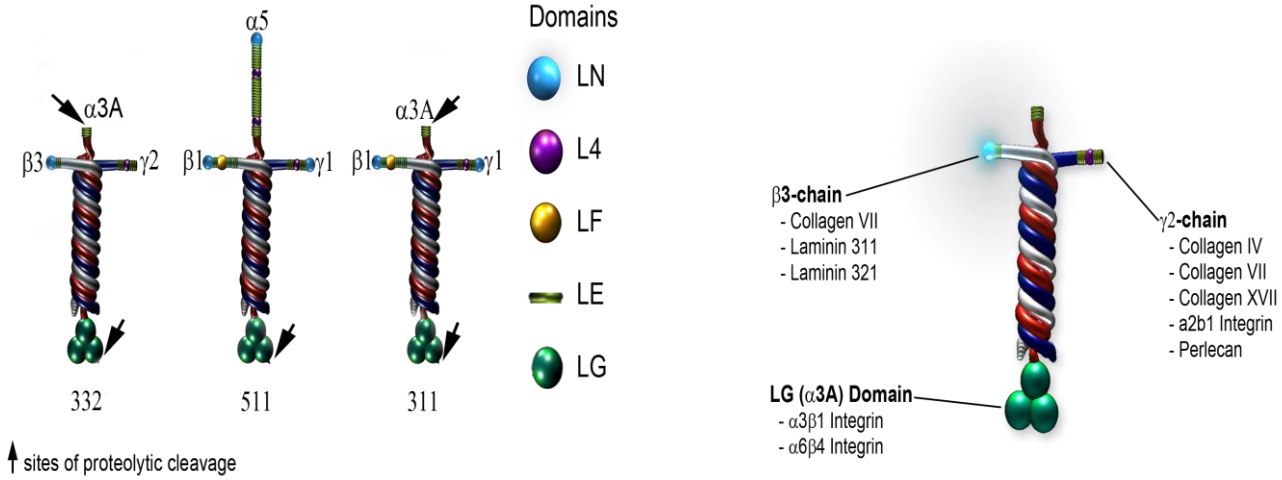
- **Classification:** Tetraspanin (cell surface proteins)
- **Molecular weight:** 29 kDa
- **Location:** Basal keratinocyte and lamina lucida.
- **Function(s):**
    a. Structural/mechanical integrity.
    b. Mediation of transmembrane signal transduction.
    c. Mediation of cellular:
        i. Development.
        ii. Activation.
        iii. Growth.
        iv. Motility (i.e. invasion and metastasis of cancer cells).
    d. Potential tumor marker (breast, liver).
    e. Regulation of integrin function.
- **Disease associations:**
    a. Nephropathy with pretibial epidermolysis bullosa and deafness.
    b. Hereditary nephritis.
    c. B-thallassemia minor.
    d. Gingival squamous cell cancer.
    e. Merkel cell carcinoma.
    f. Pancreatic cancer.
    g. Ductal breast carcinoma.
    h. Prostate cancer (adenoma)
    i. Hepatocellular cancer.
    j. Lung cancer.



Laminins (332, 311, 511)

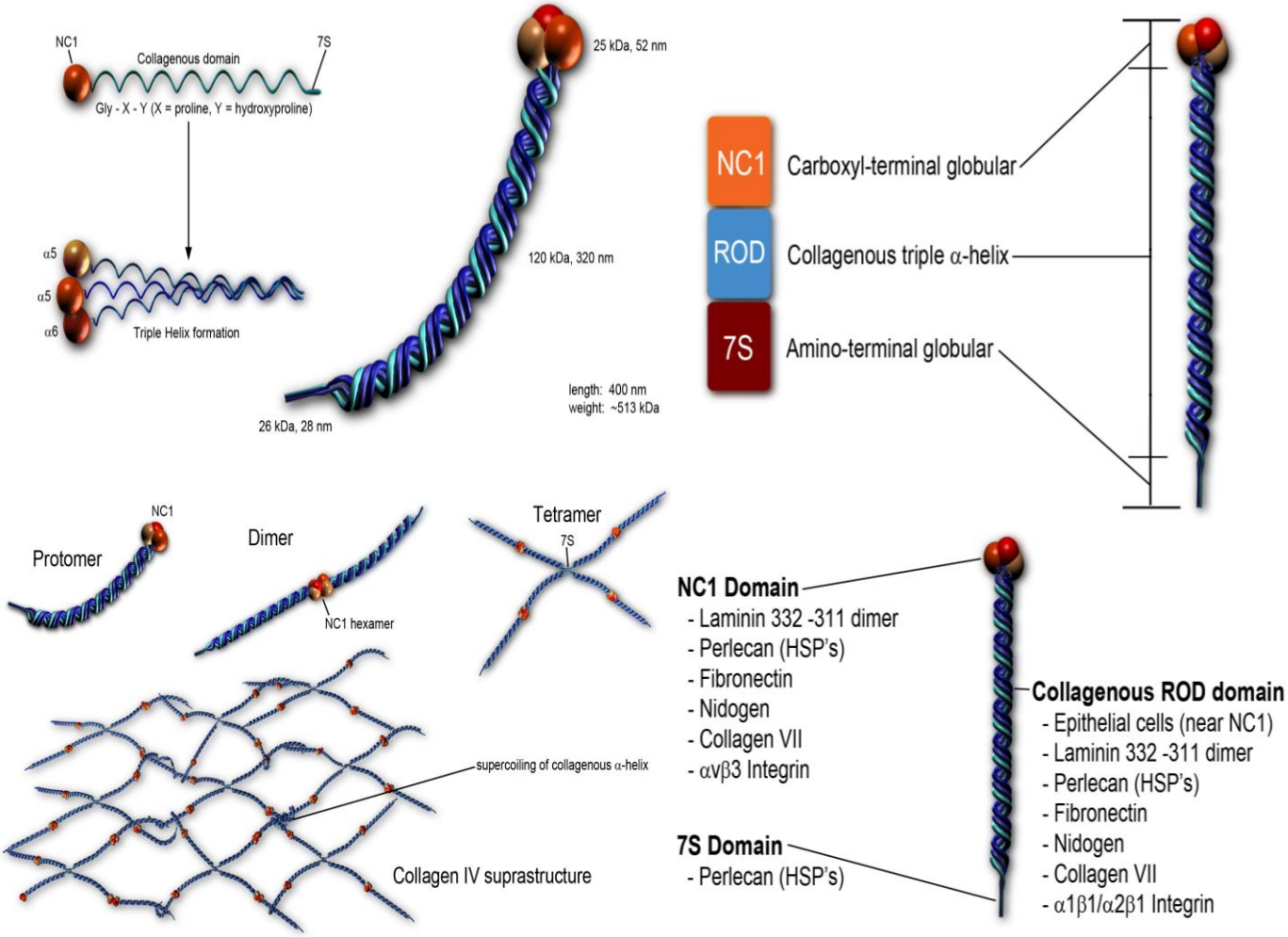
- **Classification:** Laminin family
- **Molecular weight:** ≈ 900 kDa
- **Location:** Lamina lucida and lamina densa.
- **Function(s):**
  a. Structural/mechanical integrity.
  b. Embryogenesis/organogenesis
  c. Tissue morphogenesis (e.g. Hair follicle)
  d. Regulation of cellular functions (e.g. proliferation, differentiation).
  e. Tumorigenesis.
- **Disease associations:**
  - Junctional epidermolysis bullosa (LAMC2)
  - Herlitz type junctional epidermolysis bullosa (LAMA3, LAMB3)
  - Larygoonychocutaneous syndrome (LAMA3).
  - Generalized atrophic benign epidermolysis bullosa (LAMB3)
  - Squamous cell cancer.
  - Breast cancer.





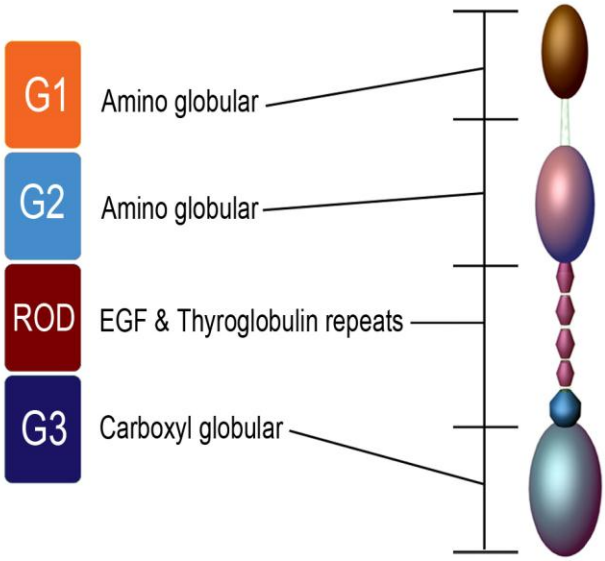
Collagen IV

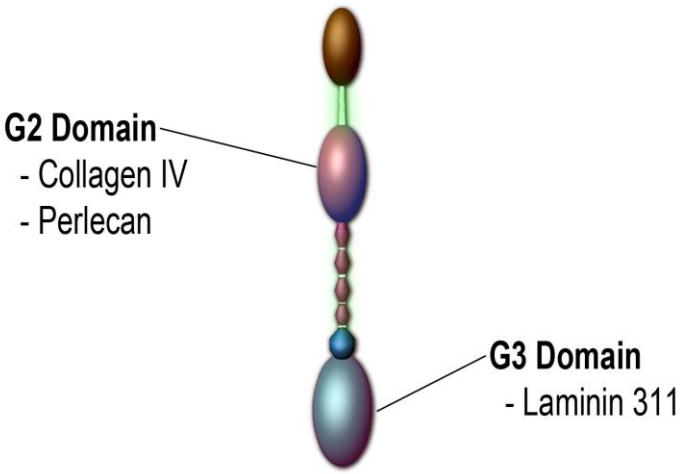
- **Classification:** Collagen
- **Molecular weight:** 513 kDa.
- **Location:** Lamina densa, subamina densa.
- **Function(s):**
  a. Structural/mechanical integrity.
  b. Forms three-dimensional lattice framework for structural support, making up the majority of the lamina densa.
  c. Tumorigenesis/invasive potential.
- **Disease associations:**
  - Porencephaly, familial [COL4A1].
  - Brain small vessel disease with hemorrhage [COL4A1].
  - Brain small vessel disease with Axenfeld-Rieger anomaly [COL4A1].
  - Angiopathy, hereditary, with nephropathy, aneurysms, and muscle cramps [COL4A1].
  - Alport syndrome (AR) [COL4A3, COL4A4].
  - Alport syndrome (AD) [COL4A3].
  - Hematuria, benign familial [COL4A3, COL4A4].
  - Leiomyomatosis, diffuse, with Alport syndrome [COL4A6].



Nidogen (1 & 2)

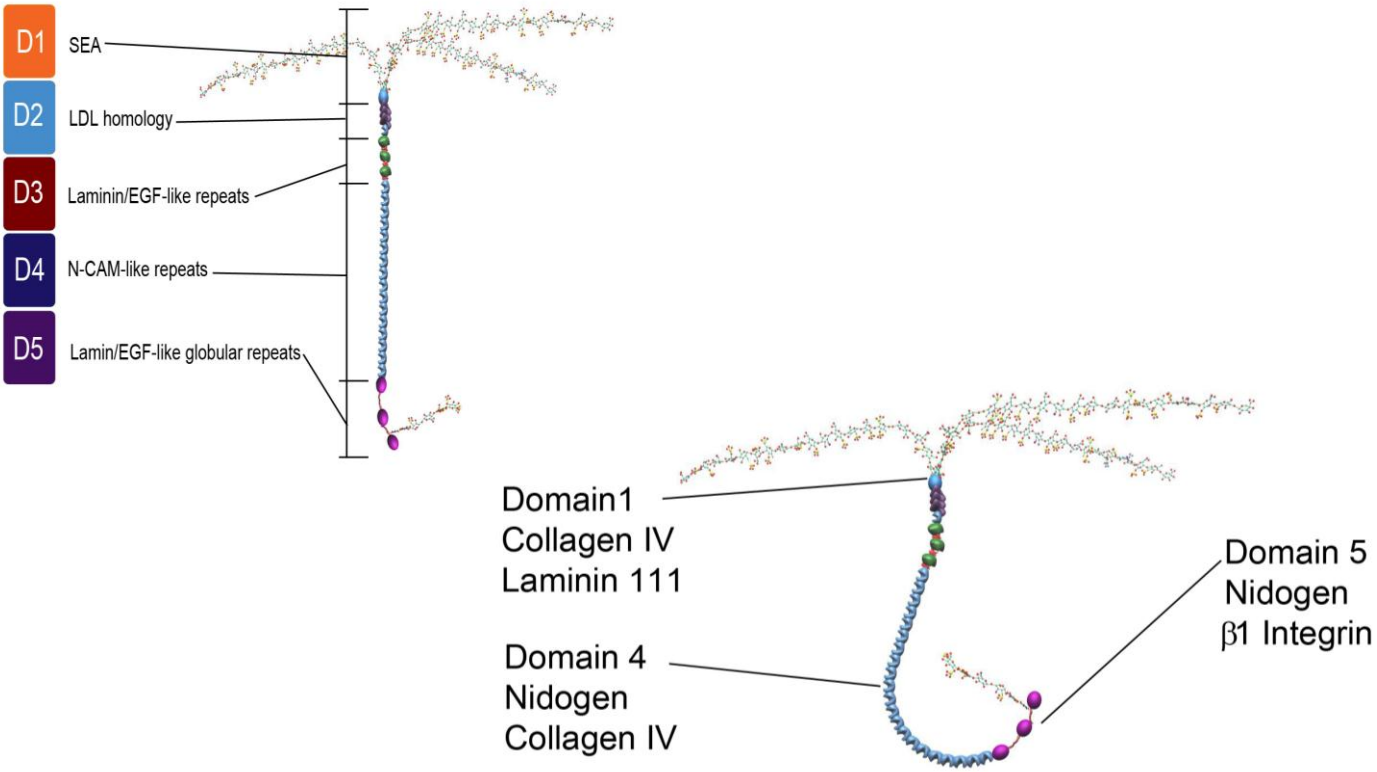
- **Classification:** Nidogen family
- **Molecular weight:** 150-200 kDa
- **Location:** Lamina Densa.
- **Function(s):**
    a. Structural/mechanical integrity.
    b. Biomarker for ovarian cancer.
- **Disease associations:**
    k. No genetic human disease.
    l. Ovarian cancer serum biomarker.





Perlecan

- **Classification:** Heparin Sulfate Proteoglycan
- **Molecular weight:** 680-770 kDa
- **Location:** Lamina Densa.
- **Function(s):**
    a. Structural/mechanical integrity.
    b. Epidermal morphogenesis.
    c. Regulation of tumor metastasis
    d. Regulation of angiogenesis (inhibition & stimulation)
    e. Regulation of fibrillogenesis
    f. Initiation of chondrogenesis
    g. Cellular signaling.
    h. Growth factor delivery.
    i. Role in developmental processes?
- **Disease associations:**
    a. Dyssegmental dysplasia (MIM#224410).
    b. Schwartz-Jampel syndrome, type I (MIM#255800).
    c. Diabetes.
    d. Atherosclerosis.
    e. Arthritis.
    f. Alzheimer's disease.
    g. Malignancy (oral, pancreatic, liver, colon, breast).



Collagen VII

- **Classification:** Collagen
- **Molecular weight:** 290 kDa (*Anchoring fibril ~870 kDa*).
- **Location:** Lamina densa, subamina densa.
- **Function(s):**
    a. Structural/mechanical integrity.
- **Disease associations:**
    h. Epidermolysis bullosa, pretibial.
    i. Epidermolysis bullosa dystrophica, AD
    j. Epidermolysis bullosa dystrophica, AR
    k. Epidermolysis dystrophica, Bart type.
    l. Epidermolysis dystrophica inversa.
    m. Epidermolysis bullosa pruriginosa
    n. Epidermolysis vullosa dystrophica localisata variant
    o. Transient bullous dermolysis of newborn (DEB)
    p. Bullous lupus erythematosus.
    q. Potential role in RDEB squamous cell cancer tumorigenisis