INTERMEDIATE FILAMENT

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Q.What are the intermediate filaments? State their role as cytoskeleton. How its functional significance differs from others?

This component of cytoskeleton intermediates between actin filaments (about 7 nm in diameter) and microtubules (about 25 nm in diameter). In contrast to actin filament and microtubule the intermediate filaments are not directly involved in cell movements, instead they appear to play basically a structural role by providing mechanical strength to cells and tissues. (**Figure 1:** Structure of intermediate filament proteins- intermediate filament proteins contain a central α-helical rod domain of approximately 310 amino acids (350 amino acids in the nuclear lamins). The N-terminal head and C-terminal tail domains vary in size and shape.

Q.How intermediate filaments differ from actin filaments and microtubules in respect of their components?

Actin filaments and microtubules are polymers of single types of proteins (e.g; actin tubulins), whereas intermediate filaments are composed of a variety of proteins that are expressed in different types of cells (as given in the tabular form)

Type	Protein	Size (kd)	Site of expression
I	Acidic keratin	40-60	Epithelial cells
II	Neutral or basic keratin	50-70	Do
III	Vimentin Desmin Periferin	54 53 57	Fibroblasts, WBC and other cell types Muscle cells Peripheral neurons
IV	Neurofilament proteins NF-L NF-M NF-H	 67 150 200	 Neurons Neurons Neurons
V	Nuclear lamins	60-75	Nuclear lamina of all cell types
VI	nestin	200	Stem cells, especially of the central nervous system

Q.How do intermediate filaments assemble? (**Figure 2**)

The central rod domains of two polypeptides wind around each other in a coiled-coil structure to form dimmers. Dimers then dissociate in a staggered antiparallel fashion to form tetramers.

Tetrameres associate end- to- end to form protofilaments and laterally to form filaments. Each filaments contains approximately 8 protofilaments would around each other in a ropelike structure.

Q.What are the advantages of intermediate filaments? Mention its role in cell division.

(i)They are more stable than actin filaments or microtubules and do not exhibit the dynamic behaviour associated with these other chemicals of the cytoskeleton (e.g; the treadmilling of actin filaments illustrated in previous note).

(ii)Intermediate filament proteins are frequently modified by phosphorylation which can regulate their assembly and disassembly within the cell.

(iii)Phosphorylation of nuclear lamins results in disassembly of the nuclear lamina and breakdown of the nuclear envelope during **mitosis**.

Q.State the pattern of intracellular organization of intermediate filaments.

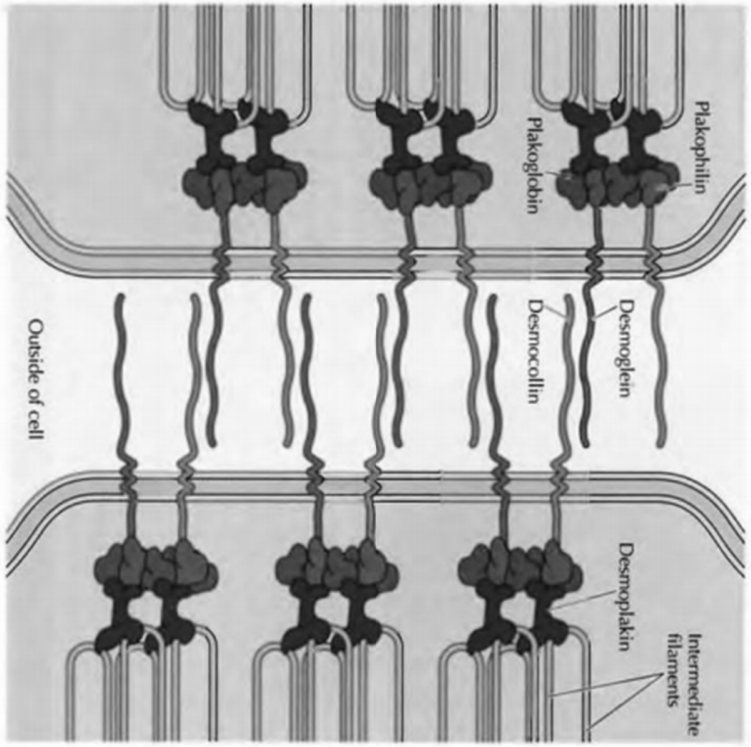
Intermediate filaments form an elaborate network in the cytoplasm of most cells, extending from a ring surrounding the nucleus to the plasma membrane. **Keratin** and **Vimentin** filaments attach to the nuclear envelope, apparently serving to position and anchor the nucleus within the cell.
These intermediate filaments can also associate the other elements of the cytoskeleton, actin filaments and microtubules.

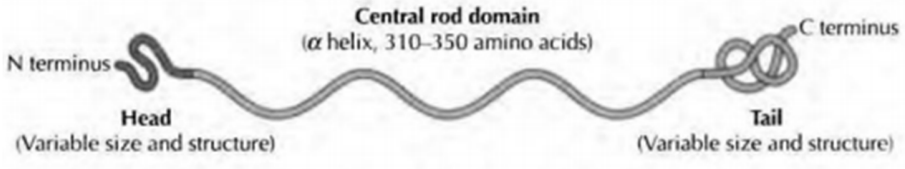
Role of intermediate filaments in DESMOSMES and HEMIDESMOSMES

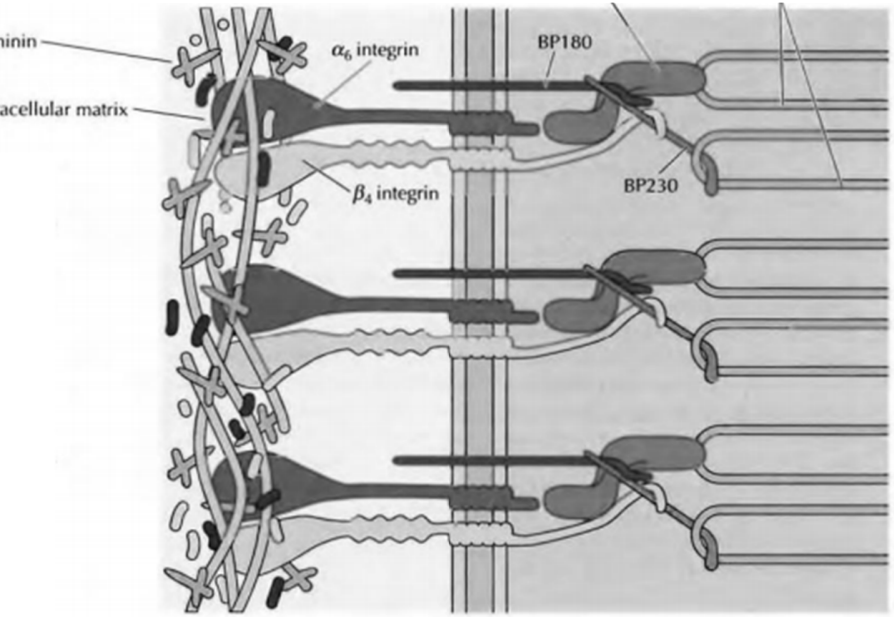
The keratin filaments of epithelial cells are tightly anchored to the plasma membrane at two areas of specialized cell contacts: desmosomes and hemidesmosomes (**Figure 3 and 4**). Attachment of intermediate filaments to desmosomes and hemidesmosomes.
(1)Electron micrograph illustrating keratin filaments attached to the plaques of intracellular protein on both sides of desmosome.
(2)(Figure 3)The desmosomal cadherins (desmoglein and desmocollin) link adjoining cells to intermediate filaments through plakoglobin, plakophilin and desmoplakin.
(3)(Figure4)The integrin α_6 β_4 links the extracellular matrix to intermediate filaments through plectin. BP 180 and BP 230 regulate hemidesmosome assembly and stability.
Intermediate filaments are most needed to strengthen the cytoskeleton of cells in the tissue of multicellular organisms where they are subjected to a variety of mechanical stresses that do not affect cells s in the isolated environment of a culture dish.

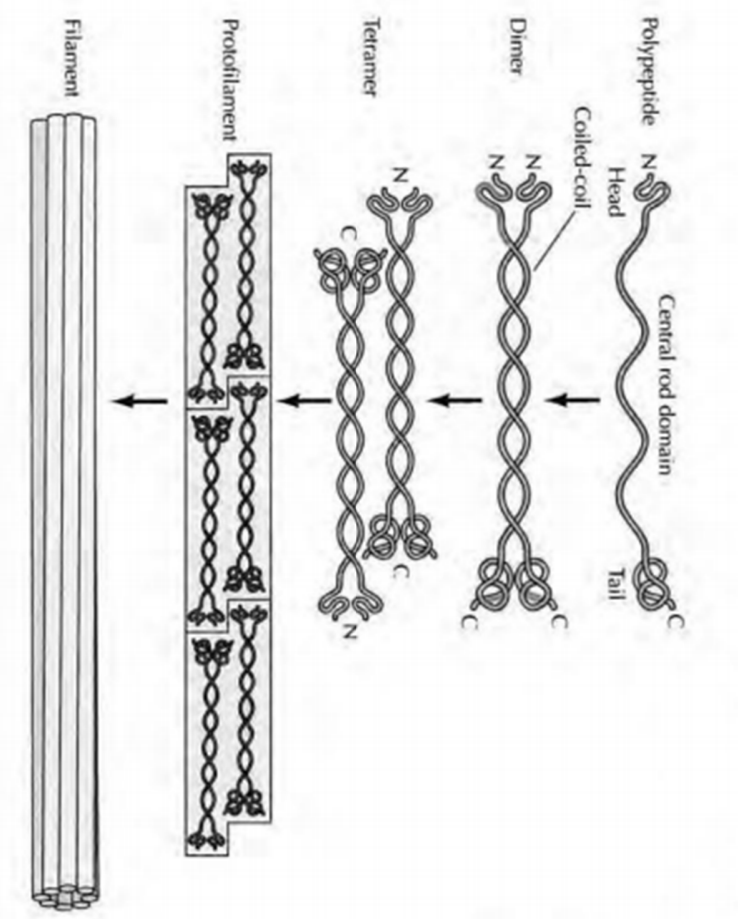
Q.What is EBS?
Epidermolysis bullosa simplex is a disease of human where the patient de3velops skin blisters resulting of the keratin genes, leading to the demonstratin that EBS is caused by keratin gene mutations that interfere with the normal assembly of keratin filaments.

Q.What do you mean by Lous Gehrig's disease? (another name is amyotrophic lateral sclerosis, ALS)
This disease results from progressive loss of motor neurons, which in turn leads to muscle atrophy, paralysis and eventual death. This disease is also characterized by the accumulation and abnormal assembly of neurofilaments. Suggesting that neurofilament abnormalities might contribute to these pathologies.


Plakophilin
Plakoglobin
Desmoglein
Desmocollin
Outside of cell
Desmoplakin
Intermediate filaments


Central rod domain
(α helix, 310–350 amino acids)
N terminus
C terminus
Head
(Variable size and structure)
Tail
(Variable size and structure)


α6 integrin
BP180
β4 integrin
BP230


Polypeptide
Head
Coiled-coil
Central rod domain
Tail
Dimer
Tetramer
Protofilament
Filament