CSIR NET Life Science Unit 5

PCD, Ageing and Senescence

Programmed cell death (PCD) is a type of cell death in which a series of molecular steps are involved leading to the death of a cell. This is a specialised mechanism through which the body gets rid of unwanted or abnormal cells. This process causes cell death which even blocks the cancer cell and is known as apoptosis.

The general characteristic of apoptosis is that this process shows morphological change and it is an energy-dependent process. Apoptosis is considered as a vital process which is a combination of turnover of a normal cells, proper functioning and development of the immune system, atrophy of hormones, development of the embryo and chemically induces cell death.

If apoptosis occurs in an inappropriate manner, it leads to several disorders in humans like ischemic disease, neurodegenerative disease, autoimmune disorders and also may have implications in many types of cancers.

For the property to modulate the life/death of a cell, PCD is recognised to have therapeutic potential as well.

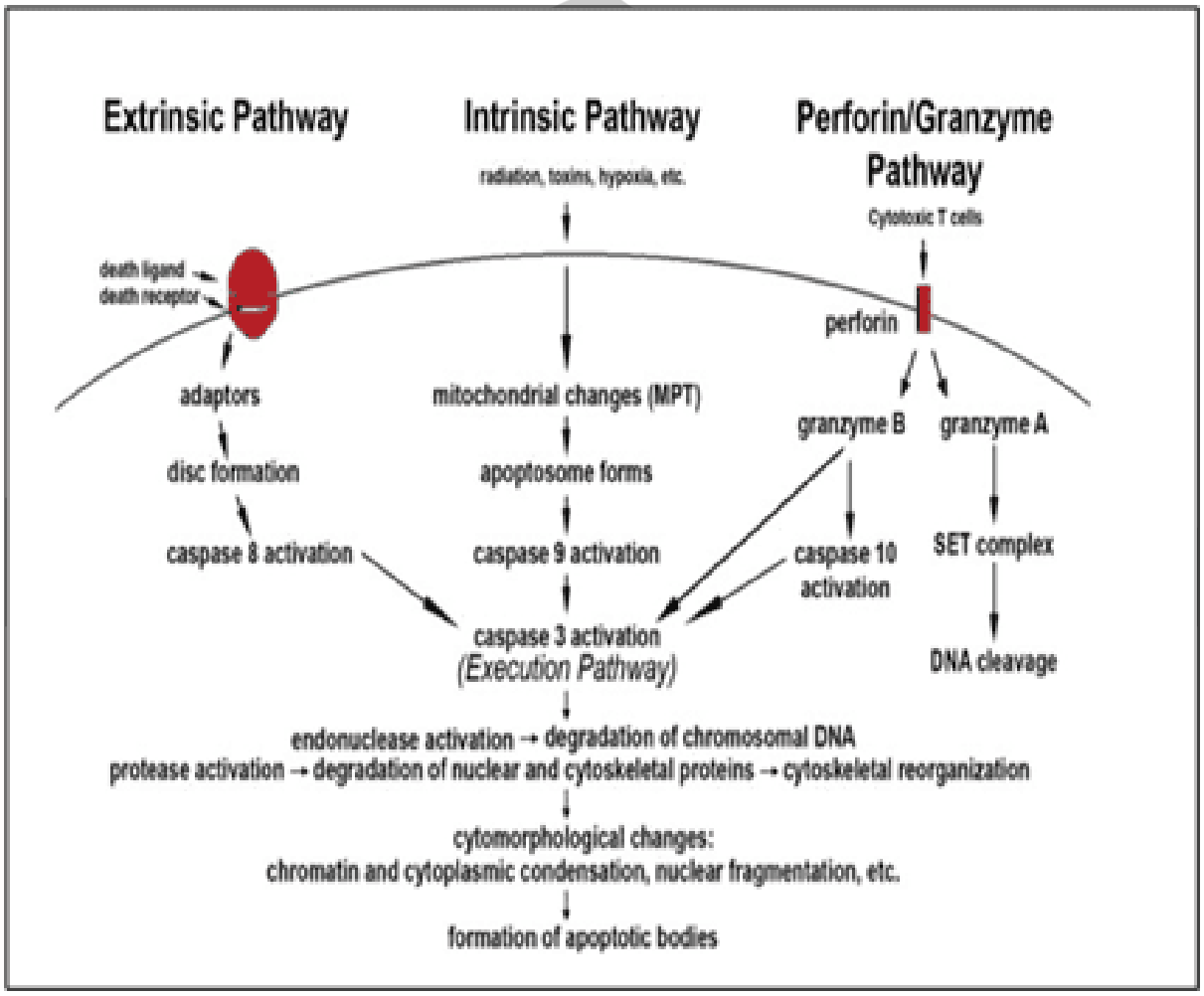
Mechanism of Apoptosis

Apoptosis having has complex and sophisticated mechanism. In this process several energy dependent molecular events are involved in a cascade.

Numerous studies have revealed (recognised) the two main pathways that complete the process of apoptosis: ***Extrinsic Pathway*** also known as death receptor pathway and another is ***Intrinsic Pathway*** also known as the mitochondrial pathway. One other pathway also known to involve in apoptosis is the *T-Cell mediated cytotoxicity* and *perforin-granzyme dependence* killing of cell.

- Apoptotic pathway is initiated by caspase3 cleavage that results in DNA fragmentation. Further degradation of cytoskeleton and nucleoprotein occurs after which crosslinking of protein happens and apoptotic bodies are formed. Thereafter, phagocytic cell receptor ligand is expressed and these phagocyte by phagocytotic cells.
- Granzyme A pathway is also activated parallelly. However, this is a caspase *independent* cell death pathway in which single strand DNA is damaged.

- Cells which undergo apoptosis have several biochemical modifications like cleavage of protein, protein cross linking, DNA damage and phagocytic recognition that all reactions together result in a distinctive structural pathology of apoptotic cell(s).
- Caspase is regarded as an inactive proenzyme formed/found in most of the cell types. Once it gets activated, it activates other procaspases also and this allows the protease cascade initiation. Some procaspases possess the activity of aggregation and autoactivation; this type of proteolytic cascade amplify the apoptotic signalling pathway fastening the process of cell death. Different caspases having specific recognition ability to neighbouring amino acids that leading protein cleavage. If once caspase is activated, it is irreversible and the cell goes to its ultimate fate, i.e. death.



<u>Programmed Cell Death in Plants:</u>

Programmed Cell Death Is a Controlled Mechanism that Serves to Eradicate Specific Cells in Either the Developmental Phase or In Response to Specific

Environmental Stimulation. in Plants, the Activation of Programmed Cell Death Take Place During Growth and Developmental Process.

Programme cell death is integral in plant stress response condition, defence, embryogenesis and at the times of tracheary element differentiation.

- Like animals, in plants too it is a genetically controlled method.
- In case of plants, sometimes dying cells acquire certain specific function, for instance, in vascular tissue or in fibre formation this specific type of PCD, is known as *developmental cell death (DCD)*. In cell death episode, DCD is coordinated in vegetative and reproductive organs. The process of DCD is accompanied by membrane blebbing, nuclear condensation and DNA fragmentation.
- At the cellular level, mitochondria plays an important role; alternate oxidase, ROS production, protease and nuclease activities take part in this mechanism.
- In plant apoptosis, cross talk of nitric oxide, ROS activity and catabolic interconversion of products is reviewed, and it was revealed that when thylakoid membrane is dismantled, chloroplast swells and redifferentiates into gerontoplast and after that protein, chlorophyll, lipid and nucleic acid is degraded gradually and photosynthesis is ceased.
- After these subsequent reactions, autophagy occurs.
- Prior to their death, some special cells go for some secondary modifications like lignification, suberification and gelification.
- Some compounds like cinnamic acid, thermospermine prevent premature aging in plants. Hydrogen peroxide and other cytotoxic products in plants are considered as possible mechanism for plant apoptosis.

<u>Importance of Apoptosis</u>

Apoptosis is known as form of cell death which is genetically regulated, and has several roles in human life

1. Apoptosis plays important role in biological processes like embryogenesis, aging, finger development in hands.
2. In apoptosis, damage cells is expelled from the body so it plays an important role in cancer prevention.

3. Also employed in treatment as an anti-inflammatory action like in cardiac diseases.

4. When apoptosis occurs in an inappropriate manner, it become the hub/region of several disease.

5. For its role in disease prevention research is being carried out rigorously to further investigate the role of apoptosis in treatment of several diseases.

Ageing and Senescence

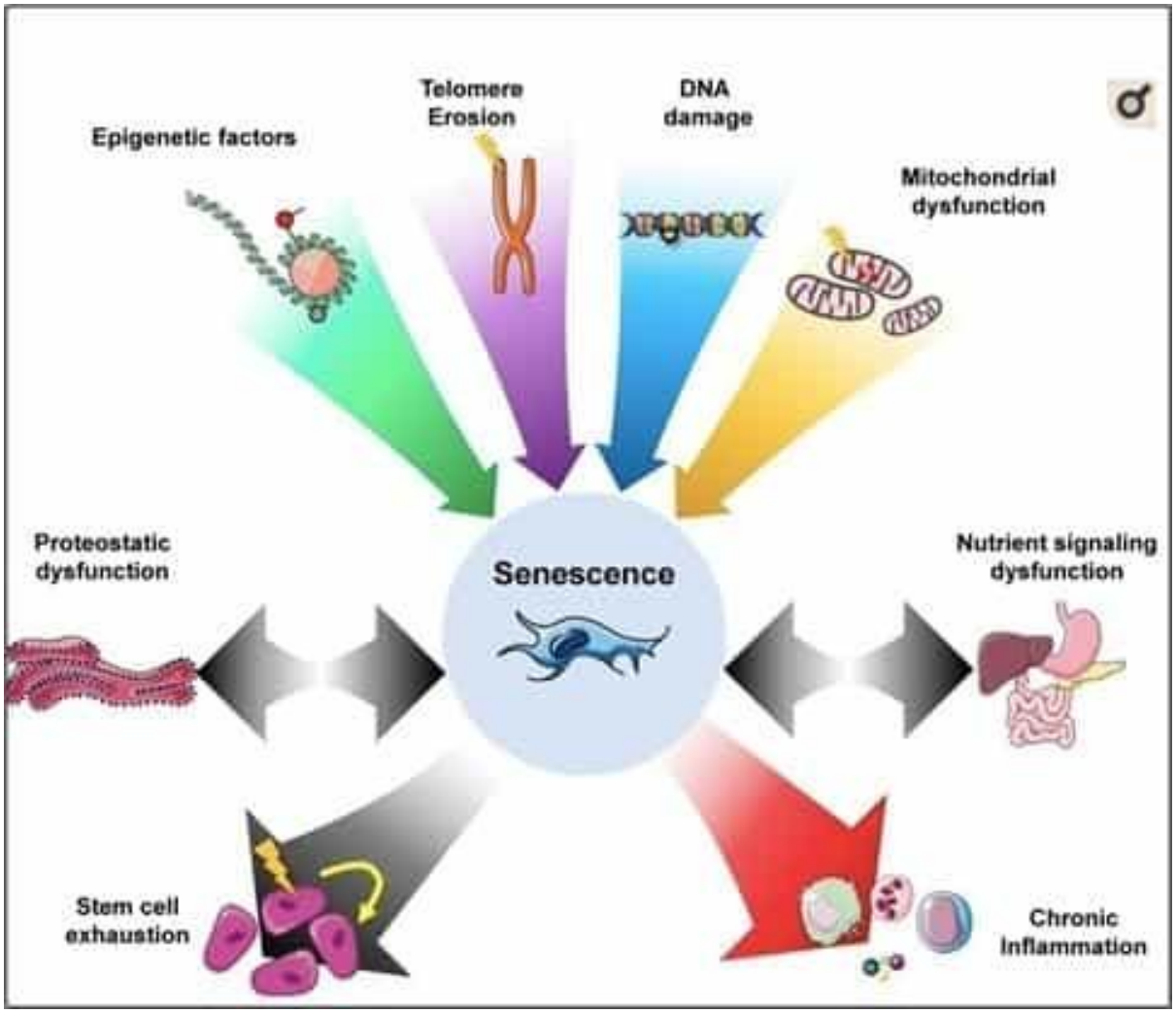


Fig. Senescence as key indicator of aging

Ageing is a gradual and functional decline of cells. In mammals, ageing occurs in multiple organs heterogeneously that causes progressive deformation of tissue and finally that tissue becomes dysfunctional. Ageing is a risk factor for several diseases such as dementia, osteoporosis cardiovascular disease, pulmonary fibrosis and glaucoma. Factors involved in ageing divided into three categories.

1. Primary- in this type cause of age-associated damage is included
2. Antagonistic- response towards damage is includes
3. Integrative- this type includes consequences of response and culprit of aging phenotypes.

Senescence is a type of cellular response that limits the proliferation of aged or damaged cell(s) during the normal development of the cell. Senescence has major physiological implications as it is also needed to maintain homeostasis in tissues. It induces stable growth arrest that is accompanied by various phenotypic alterations which included remoulding of chromatin, metabolic reprogramming, and an increase in autophagy.

After establishing the causative role of senescence, during ageing it is easy to identify how senescence contributes to different age-related pathologies. The below figure describes some senescence markers used in the pathology of age-related diseases.

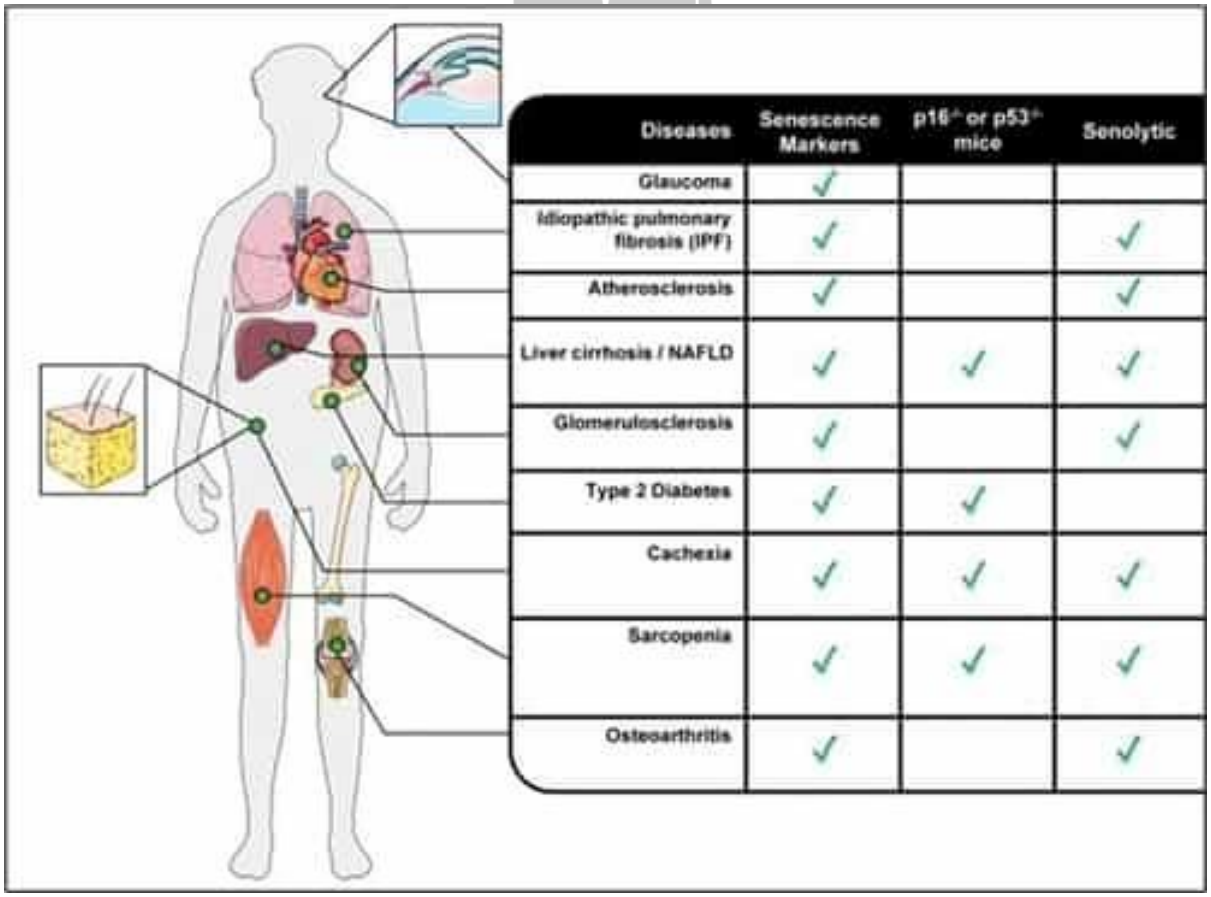


Fig. Markers of senescence (biomarkers) in age related diseases