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Unit-II
Stem Cells in Neurodegenerative Diseases

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STEM CELLS IN NEURODEGENERATIVE DISEASES

INTRODUCTION:

- Neurodegenerative disease is a kind of chronic, progressive nervous system disease characterized by neuron degeneration or apoptosis.
- Current treatments cannot prevent the development of the disease. Possible alternative treatments include cell therapy, especially with the use of mesenchymal stem cells (MSCs).
- Neurodegenerative diseases are common neurological diseases that are characterized by the large loss of specific neurons; these diseases include Parkinson's disease (PD), Alzheimer's disease (AD), and amyotrophic lateral sclerosis (ALS).
- A key pathological feature of these diseases is the accumulation of misfolded proteins in the brain, leading to neurological dysfunction and disease

STEM CELL CLASSIFICATION:

- Stem cells are highly unspecialized cells that are the basis for every tissue and organ. Stem cells are characterized by the ability to self-renew and the ability to differentiate.

- These include
  - embryonic stem (ES) cells,
  - progenitor cells,
  - mesenchymal stem cells (MSCs),
  - neural stem cells (NSCs) and
  - induced pluripotent stem (iPS) cells.

- The progressive loss of structure, function, and number of neurons, including death of neurons, underlies all neurodegenerative diseases.

NEUROLOGICAL DISEASES

- **Trauma**-SCI
- **Vascular**-Stroke
- **Degenerative**- Parkinson's disease, Huntington's chorea, Amyotrophic lateral sclerosis, AD etc.
- **Chronic inflammatory and immune mediated-** multiple sclerosis
- **Genetic diseases in children-** neuronal ceroid lipofuscinosis, mucopolysaccharidoses, Leucodystrophies and muscular dystrophies.

PARKINSON'S DISEASE:

- Dopamine is a key neurotransmitter that is used to send signals from one neuron to another and is involved in motor control.
- Patients with Parkinson’s disease (PD) suffer symptoms from dopamine deficits produced by the disease targeting the destruction of dopamine-producing neurons in the substantia nigra.
- As the disease progresses, patients may present symptoms such as muscle tremors, muscle rigidity, deficits in movement, problems with thinking, and aggregates of a protein called alpha-synuclein in their brains.

- Currently, the primary treatment modality is supplementing dopamine (Levadopa) to compensate for the deficit in the brain that is produced by the disease destroying dopaminergic neurons.
- Scientists are working with ESCs and iPSCs and inducing their differentiation into mature dopaminergic cells that can survive and function after transplantation.
- Thus far, these stem cell transplantation treatments for PD have demonstrated some success in animal models using mouse, rat and monkey brains.

Huntington's Disease:

- Potential treatments for HD, which is a fatal, inherited neurodegenerative disorder, caused by progressive loss of GABAergic medium spiny neurons (MSNs) in the striatum of the forebrain.
- NSCs for HD treatments have been developed from various sources, such as the brain itself, the SCs, and the somatic cells of HD patients.
- Induced NSCs, derived from somatic cells as a new stem cell source for transplantation, are less likely to form tumors.
- Given that the stem cell transplantation strategy for treatment of HD, as a genetic disease, is to replace the dysfunctional or lost neurons, the correction of mutant genes containing the expanded CAG repeats would be promising.

Amyotrophic Lateral Sclerosis

- ALS is a progressive, incurable neurodegenerative disease that targets motor neurons. Several factors contribute to the difficulty in finding effective therapies for ALS.
- There was no way to test if a drug would even work on motor neurons, the cells affected in ALS, because they couldn't be obtained in large numbers.
- Cell-based therapies have generated widespread interest as a potential therapeutic approach but no conclusive results have yet been reported either from pre-clinical or clinical studies.
- In a leap forward for the field, Harvard scientists derived human induced pluripotent stem cells — mature cells that are manipulated back to a stem cell state — from the skin and blood of ALS patients.

Alzheimer's Disease:

- Scientists have discovered a novel way to convert human skin cells into brain cells, an advancement that offers hope for regenerative medicine and personalized drug discovery and development.
- Researchers have come up with a recipe for making functional neurons directly from human skin cells, including those taken from patients with AD.
- The converted neurons are beginning to yield insights into what goes wrong in an Alzheimer's brain and how diseased neurons would respond to treatment.
- In earlier approaches to generate neurons from skin cells, those adult cells first had to be returned to an embryonic stem cell state.
- Those cells are hard to come by - less than one percent of cells are typically reprogrammed successfully.
- when the cells were placed into the brains of developing mice, the converted cells were able to connect up to the existing circuitry.

CONCLUSION :

- Today, stem cell therapy offers promising hope for almost all forms of neurodegenerative diseases including PD, Huntington's disease (HD), Alzheimer's and amyotrophic lateral sclerosis (ALS).
- The fundamental mechanism underlying all forms of neurodegenerative diseases is progressive loss of structure, function or number of neurons, including death of neurons.
- At a molecular level, there are many parallels among the different forms of neurodegenerative diseases.
- Unfortunately, the current available treatment options neither pharmacological nor neurosurgical are efficient in arresting the progression of the neurodegenerative processes.

THANK YOU