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REVIEW ARTICLE

Study of various model Organisms and their applications in stem cell biology

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ABSTRACT
Stem cells are specialized cells found in all multi-cellular organisms that have the ability to divide and differentiate into diverse specialized cells and can self-renew to produce more stem cells. Stem cells are the part of the human repair system. The model system approach is powerful tool to study animal development or any other biological process. Model organisms include Escherichia coli bacteria budding and fission yeast, nematodes, maize, Arabidopsis thaliana, fruit flies, and mice. The current review summarizes the different models, types of mechanisms and approaches to study functioning of stem cells and their biological application in stem cell therapy, organ regeneration and regenerative medicine.

***Key Words**: Stem cells. Models, Stem cell therapy, organ regeneration and regenerative medicine.*

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INTRODUCTION

Stem cells are specialized cells found in all multicellular organisms that can divide and differentiate into diverse specialized cells and can self renew to produce more stem cells. Stem cells are the part of the human repair system. Mammals have two broad types of stem cells, first is embryonic stem cells, these are isolated from the inner cell mass of the blast cysts, and second is adult stem cells, these are found in different tissues [1]. Potency is the capacity to differentiate into specialized cell types and capable of giving rise to any mature cell type. Potency of the stem cell identifies the potential to differentiate into different cell types. Totipotent stem cells can differentiate into embryonic and extraembryonic cell types. These cells can give rise to a complete, viable organism. Totipotent stem cells give rise to somatic stem cells and primitive germ- line stem cells. Pluripotent stem cells are the descendants of totipotent cells and can differentiate into all cells, i.e. cells obtained from any of the three germ layers (endoderm, mesoderm, ectoderm). These pluripotent cells are the true stem cells and have self-renewal ability and have the potential to make any differentiated cell in the body of the adult organism. Embryonic stem cells come under this category. Multipotent stem cells can give rise to several cells, only within its closely related family of cells and have limited differentiation ability. Oligopotent stem cells can differentiate only into a few cells, like lymphoid or myeloid stem cells. Unipotent cells can produce only their own cell type but it is distinguished from non-stem cells due to its self-renewable ability. These Unipotent cells include muscle stem cells.[2] iPSCs are targeted as the source of models to study various diseases as they have self renewal and differentiation properties.[3] These iPSCs are identical to human Embryonic stem cells and can become all cell types in the human body. The genes and surface proteins expressed by these cells are like ES cells and can form teratomas which can develop into all three germ layers. [4] Model systems allow us to identify common genes, proteins, and help to know the processes that cause human medical conditions. It also allows us to systematically decode the gene–gene and gene–environment interactions that influence complex multigenic disorders. Human genetic diseases cannot be directly studied in human keeping them as a disease model, therefore to minimize this bridge gap disease model organisms

are designed for studying lethal diseases for interpretation. Model system research has contributed a lot in basic biological knowledge and its application in human medicine. Stem cells are critically important for homeostasis and acute repair of human blood, immune system, epithelia, gut, brain, breast, cornea, lung, and many other tissues of the body. Studies of stem cells in Drosophila, mouse, and other model organisms have greatly enhanced our understanding of the irregulation within stem cell niches generated by nearby supporting stromal cells. Pumilio-like genes depend and appear in the stem cell of Homo sapiens, Drosophila melanogaster, and worm germ line. Epithelial stem cells of both Drosophila and vertebrate require hedgehog signals, while downstream of intestinal stem cells Notch signals play a central role. Studies of gene expression and cellular differentiation during the early stages of mouse embryogenesis are providing new insight into the origin and potentials of embryonic stem cells [5]

CLASSIFICATION OF STEM CELL

Adult stem cell

After the development of embryo adult stem cells are present throughout the body which are undifferentiated then the adult stem cells undergo cell division to repair dying cells and revive damaged tissues and cells. In the living organism the primary role of adult stem cells is to maintain and repair the tissue in which these cells are found. These stem cells are present in tissues such as the brain, blood vessels, blood, skeletal muscles, liver and skin. These cells remain in non dividing state for years until activated by any type of disease or tissue injury [6]

Embryonic stem cell

Embryonic stem cells are derived from the inner cell mass of the blastocyst, after 4– 5 days of fertilization. These cells are not totipotent, but these are pluripotent and capable of forming all other cells of the body.[7] The two remarkable properties of these cells are : In vitro culture embryonic stem cells can be grown which is then expanded in number limitlessly in the primary undifferentiated , and throughout long periods of cultivation in vitro they retain the property of pluripotency.[8]

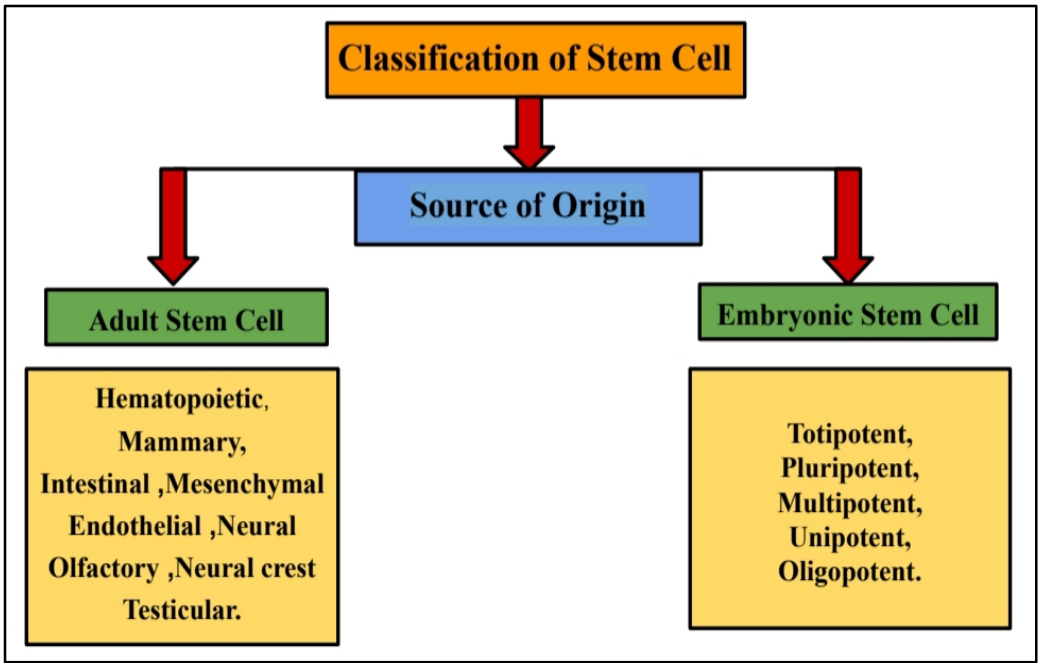

Figure 1. Classification of stem cell based on source of origin

MODEL ORGANISM

The model system approach is a powerful tool to study animal development or any other biological process. Understanding the potential of stem cells is essential for the project of developing stem cell therapies in regenerative medicine. To study the process of manipulation of stem cells model systems, such as dog, mouse, monkey etc are used.[9] Model organisms are essential tools used by researchers all over the world. These organisms have effect of genetic manipulation easier due to its similarity in genes to humans, and are easily maintained in the lab, and have short generation times. Mechanistic studies of cellular processes in a natural physiological setting have been greatly enhanced by the availability of "model" organisms, which are selected in part because their genomes contain a normal and stable

complement of genes and chromosomes. Moreover, these organisms are traceable to a common ancestral parent, with care being taken to minimize the number of generations separating everyone studied from the original parent. Some model organisms which include such lab staples as Escherichia coli bacteria, budding and fission yeast, nematodes, maize, the mouse-ear cress Arabidopsis thaliana, fruit flies Drosophila melanogaster, and mice.[10]

1. Escherichia coli

Escherichia coli, a gram negative and enteric bacterium is a constituent and found in the intestine or gut of all human beings. *E. coli* is non sporulating and has well set up genetic material because of which it has a rapid growth rate and simple needs for its nutrition. *E. coli* is used as a model organism because of various survival condition.[11] E. coli strength, adaptability, absence of difficulty and wide range of use has made it the most vigorously studied organism in the world. *E. coli* has widely distributed species and its diverse form occupies a common niche in which it undergoes an extensive range of environmental and ecological conditions.[12] Advances in microscopy and DNA sequencing have allowed an even more detailed examining of its structures and function by the scientists. *Escherichia coli* serves as the model organism for studying diseases of intestines and septicaemia [13]

2. Maize (*Zea mays)*

Zea mays or maize or corn is the most important crop eating plant with the highest economic value in the whole world. Maize agronomic importance has made it model organisms for research purposes and various experiments. Genome evolution, developmental physiology, epigenetics, pest resistance, heterosis, quantitative inheritance, and comparative genomics could be studied by using maize plant as a one the model, however rice (*Oryza sativa*), sorghum (S*orghum bicolor*), wheat (*Triticum spp*.), and barley (*Hordeum vulgare*) etc are used for research purposes but Maize(*Zea mays*) is used majorly for genetic research. A wide collection of mutant stocks, large chromosomes, large nucleotide diversity, and genetic colinearity of maize have been spotted as a centerpiece for genetic, cytogenetic, and genomic research. [14]In 1900's maize distribution , collection and describing was started for research..The pros of using maize for genetic research was its number of key features. Endosperm texture is affected by dozens of genes.Aleurone ,the outermost layer colour is also affected which shows a eye catching information about the genotype. Chromosome of *Zea mays* paved a number of research and discoveries which includes genetic recombination to physical exchange of chromosomal segments. Abundant amount of pollen grain of maize plant is easily gathered and new mutant plants are created by mutagenized with chemical which allows researchers to montier lethal mutant plants easily. [15]

3. *Thale cress* (Arabidopsis thaliana)

Recently Arabidopsis plant is also considered as a model organism for many studies and research in plant science.Arabidopsis is an angiosperm, dicotyledonous plant which serves as a convenient model for plant biology but also in fundamental biology research , structure and function to all eukaryotes.Many techniques and research materials are developed by Arabidopsis research group which makes it s model organism.These incorporate basic methodology for concoction and insertional mutagenesis, effective techniques for performing crosses and presenting DNA through plant change, broad assortments of freaks with differing phenotypes, and an assortment of chromosome maps of freak qualities and atomic markers.

4. Arabidopsis thaliana

Arabidopsis thaliana has recently become the organism of choice for a wide range of studies in plant sciences. Arabidopsis serve as a convenient model not only for plant biology but also for addressing fundamental questions of biological structure and function common to all eukaryotes. The Arabidopsis research community has developed most of the methods and resource materials expected of a model genetic organism. These include simple procedures for chemical and insertional mutagenesis, efficient methods for performing crosses and introducing DNA through plant transformation, extensive collections of mutants with diverse phenotypes, and a variety of chromosome maps of mutant genes and molecular markers .The capacity to spare hereditary stocks as seeds has limited the exertion required to keep up these freaks over significant stretches of time. Notwithstanding mutagenesis and mapping endeavors, hereditary investigation of Arabidopsis has extended as of late to incorporate specific subjects of wide premium, for example, epigenetics, quality hushing, quadruplicate examination, centromere mapping, and opposite hereditary qualities. Research with Arabidopsis has offered atomic subtleties on a portion of the qualities required inside a utilitarian genomics setting. Quadruplicate investigation got conceivable in Arabidopsis with the disengagement of the group of four freak in which four dust grains got from a solitary meiotic occasion stay appended when discharged from the anther however by and by take an interest in treatment. [16]

5. Drosophila melanogaster

The fruit fly, Drosophila is brought to practice the discipline starting from pridomial genetics to the evolution of tissues and organs. *Drosophila melanogaster* genome is 60% compatible with that of humans, is unnecessary, and about 75% of the genes amenable for human diseases are compatible in flies. These characteristics along with concise generation time low assistance cost with effective genetic tools get the permission for admissible fruit flies to research the sophisticated pathways relevant in biomedical research, including cancer. Drosophila have a simple fertilization process with a short life period. These two highlights put too much for the success of drosophila. melanogaster in form of model organism. [17] biocidal variation was to play a crucial role in drosophila genetics and the shortcoming of crossing over in male flies does that mean the mixture of genes on a chromosome is maintained in the male line and would not break down due to crossing over. This proved a remarkable benefit to drosophila genetics.[18] through the innovation of complex genetic tools and the sobriety of drosophila made to study deep into the stem cell biology that would not be thinkable in a vertebrate model system. [19]

6. Mice (*Mus musculus*)

Mice (*Mus musculus*), same as the general mouse in the house. They are widely used as an experiment model due to human like features. They also belong to the mammalian kingdom. In relation to cell structure or anatomy there is a slight difference between humans and mice, as mammals and humans are similar creatures. Since they have identical features with humans than any of the above examples, so they are ideal prototypes for making conclusions about humans. Mice are selected as prototype mammal life forms due to their small size and easy to keep. They have a full series of genomes. Most compatible with an identical mutation is a human orthologue, and mostly a similar phenotype may be manifested. This made scientists more competent to know more about specific genetic diseases that took place in human beings.

7. Caenorhabditis elegans

Caenorhabditis elegans are the tiny worn comes from the nematode family.Multi–cellular life form to have their genome absolutely in a series first come from their family. They are in the form of little and transparent organisms, who have 959 cells in a special position. While studying and through research scientists got beneficial information about these cells which is very useful for innovation, and these organisms can be utilised in trying to acknowledge the ageing and cancer. They can live for an infinite time period when kept in the freezer. They have their genome totally in a series with small lifetime, make them low cost prototype organism. [20]

APPLICATION OF STEM CELL

The aim of any stem cell therapy is to restore the injured tissue which cannot heal by itself. Stem cell therapy contains more than merely transplanting cells in the body and operating them to develop new healthy tissues. It might also be believable to assimilate stem cells already in the body to work overtime and generate new tissue. Through their assurance of stem cell therapy, they have provided a wide future for the therapeutic world. [6]utilization of stem cell therapy holds considerable assurance for the remedy of many war zone's injuries and their complex problems.Some of the damages which can be cured through exercise Some of the damages which can be cured through exercise of stem cell development include skin, sensory organs, nervous system tissues, the musculoskeletal system, circulatory / pulmonary tissues and genitals / testicles and of severe radiation disorder and the growth of novel biosensors. The new experimental evolution in these fields proposed the solution to lower the serious outcomes ofthe wounds and vulnerability hurt in warfare. Stem cells (embryonic stem cells and adult stem cells) serve as the main tool for tissue engineering, stem cells have been demonstrated to be useful in defending reaction to infections, as well as enhancing the potentiality to treat persistent ailments such as osteomyelitis and osteoarthritis. The defensive blast lungs with pulmonary fibrosis and another lungs injury can be cured by MSCs and ESCs.[21]

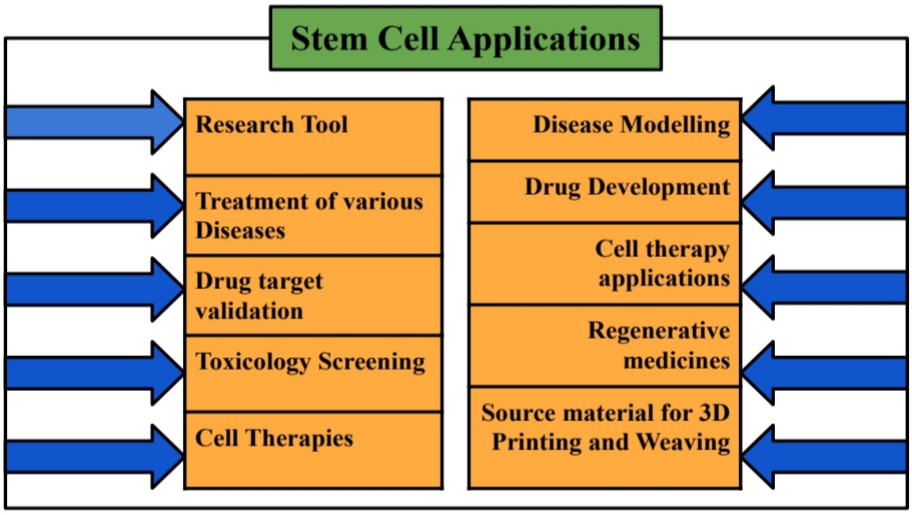

Figure 2. Various Applications of Stem Cells

REGENERATIVE MEDICINES

The six classes of undifferentiated cells, that is, undeveloped immature microorganisms (ESCs), tissue explicit forebear foundational microorganisms (TSPSCs), mesenchymal undifferentiated cells (MSCs), umbilical rope undifferentiated cells (UCSCs), bone marrow undifferentiated cells (BMSCs), and prompted pluripotent undifferentiated cells (iPSCs), have numerous guarantees in regenerative medication and illness therapeutics.

ESCs, sourced from ICM of gastrula, have enormous guarantees in regenerative medication. These cells can separate into in excess of 200 sorts of cells speaking to three germ layers. With characterized culture conditions, ESCs can be changed into hepatocytes, retinal ganglion cells, chondrocytes, pancreatic ancestor cells, cone cells, cardiomyocytes, pacemaker cells, eggs, and sperms which can be utilized in recovery of tissue and treatment of infection in tissue explicit way. TSPSCs in regenerative medication: tissue explicit stem and better cells can possibly separate into different cells of the tissue. Naturally inward ear foundational microorganisms can be changed into sound-related hair cells, skin forebears into vascular smooth muscle cells, mesoangioblasts into tibialis foremost muscles, and dental mash undeveloped cells into serotonin cells. The 3D-culture of TSPSCs in complex biomaterial offers ascend to tissue organoids, for example, pancreatic organoid from pancreatic begetter, intestinal tissue organoids from intestinal forebear cells, and fallopian tube organoids from fallopian tube epithelial cells.

Mesenchymal foundational microorganisms are otherwise called stromal cells. Upon transplantation and transdifferentiation these real MSCs recover into ligament, bones, and muscle tissue. Heart scar framed after cardiovascular failure and liver cirrhosis can be treated from MSCs. ECM covering gives the specialty condition to MSCs to recover into hair follicle, invigorating hair development

Transplantation of UCSCs to Krabbe's sickness patients recovers myelin tissue and recoups neuroblastoma patients through reestablishing tissue homeostasis. The UCSCs organoids are promptly accessible tissue hotspots for treatment of neurodegenerative malady. Peritoneal fibrosis brought about by long haul dialysis, ligament tissue degeneration, and flawed hyaline ligament can be recovered by UCSCs. Intravenous infusion of UCSCs empowers treatment of diabetes, spinal myelitis, foundational lupus erythematosus, Hodgkin's lymphoma, and inherent neuropathies. Rope blood undifferentiated organisms banking profits dependable wellspring of foundational microorganisms for customized treatment and regenerative medication.

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USE IN RESEARCH

1. **Embryonic stem cells** of human helped the scientists to explore how early human cells become committed to the major descents of the body; how these descents lay down the foundation of tissues and organs of the body; and how myriad functional cell type ,which control normal function in adult are formed by the differentiation of the cell within these foundation. The knowledge gained by these researches impact many fields. The research on these human ES cells helps to enhance the understanding of causes of birth defects and hence leads to its possible preventions and cure. Inspection of several human diseases is severely inhibited due to lack of in vitro models. Some of the pathogenic viruses like human immunodeficiency virus and hepatitis C virus grow only in chimpanzee or human cells. ES cells provide cell and tissue types that will greatly enhance the inspection of these and other viral diseases.
2. **Gene Therapy**. In this therapy, genes that provide a missing or necessary protein, or cause a clinically applicable biochemical process, are introduced into an organ for a therapeutic effect. It is critical for the gene-based therapies, especially which use DNA sequences, that the desired gene that is introduced into an organ stem cell should achieve long term expression and therapeutic effect. However, techniques for delivering the therapeutic DNA have been greatly improved since the first gene therapy protocol, there are as yet no genuine successes. Delivery problems, loss of expression or insufficient expression are important limiting factors in successful application of gene therapy and these limitations can overcome by transferring genes into stem cells [23]

CONCLUSION

The introduction of stem cells in research areas plays a vital role in understanding the mechanism of differentiation and basic cause of diseases. These stem cells are used in treatment of different diseases like skin injuries, spinal cord therapy, parkinson's diseases, cancer, wound healing, etc. Use of model organisms in research fields upgraded the knowledge of fundamental processes and hence accelerated the development of different biological fields. Some of the model organisms are Drosophila melanogaster, mouse, C. elegans, E. coli. Stem cell research is not limited only upto developmental stages. There is a very wide range of applications of stem cells in regenerative medicine, stem cell therapy, organ regeneration, gene therapy and many more.

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