

An Introduction to Stem Cells

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Stem cells are unspecialized cells having the unique capacity of extensive self-renewal and the ability to give rise to cells of different lineages. They are considered as 'magic bullets' which have the capability to regenerate body tissues that get worn out with age. In fact ageing is considered as a 'stem cell disease' since with age, the stem cell functioning gets compromised and they also reduce in number. This affects the process of tissue homeostasis resulting in tissue/organ failure and ultimately an individual succumbs to death e.g. cardiovascular disease, dysfunction of pancreas leading to diabetes, etc. Throughout life, stem cells play a crucial role to maintain tissue homeostasis and normal organ function and therefore, the excitement at present is whether the age-related compromised stem cell function may be restored by transplanting young stem cells in the aging body tissues. A new research field termed 'regenerative medicine' has thus emerged where doctors, researchers, pharma companies, biotech industries etc. have invested heavily and are very actively carrying out 'clinical trials' with the hope to revolutionize and replace existing drug-based medicine by cell-based therapy.

Stem cells have been categorized as adult stem cells or embryonic stem cells depending on their source of isolation and as pluripotent, multipotent or unipotent based on their plasticity. Besides embryonic stem cells can be made by reprogramming skin fibroblasts by iPS technology and also cancers are associated with cancer stem cells. It has been proposed that various body tissues harbor two sets of stem cells viz. very small embryonic-like stem cells and tissue committed stem cells (or actually the progenitor stem cells).

Details on various aspects of stem cell biology will be discussed and the students will be updated with the recent advances in the field.

Mouse and human embryonic stem cells as well as induced pluripotent stem cells have the potential to differentiate into the three germ layers as well as germ cells. The differentiation into germ cells is achieved either by formation of embryoid bodies or by monolayer culture. The germ cells derived from male mouse embryonic stem cells have resulted in a number of pregnancies, although majority died *in utero* and others died within a few months after birth, due to imprinting defects. Moreover, the efficiency of this differentiation remains low (approximately 0.8 - 5% in humans).

Recently our group has reported the presence of very small embryonic stem cells-like cells (VSELs) in adult human testis and ovarian surface epithelium. These cells are implicated in maintaining gonadal homeostasis throughout life by giving rise to more committed stem cells throughout life. They may be a good source of autologous embryonic-like stem cells and if perturbed are thought to give rise to germ cell tumors. Indeed the female VSELs were found to spontaneously differentiate into oocyte-like structures, embryonic stem cells-like colonies, embryoid body-like structures, parthenote-like structures and also cells with neuronal phenotype. These results challenge the existing paradigm that a female is born with fixed number of eggs. Existence of VSELs in adult ovarian surface epithelium lends support to the importance of stem cell niche (somatic microenvironment) and probably suggests that menopause is due to the compromised somatic niche which is unable to support stem cell differentiation *in situ*.

Further scientific and technological advances in this area could result in derivation of functional gametes from embryonic stem cells or VSELs for treating infertility, to better understand gametogenesis, source of eggs for therapeutic cloning, better insight into menopause, novel contraceptive development and efficient breeding of animals including endangered species.