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Editorial

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It is mandatory to understand human cell biology in order to benefit mankind for better health and quality of life. There is immense amount of information on all aspects of cells with the advances in biotechnology and information technology, free availability and sharing of scientific and clinical data, and hence translation and application of the information. In the current issue of the Biomedical Research Journal, our authors have reviewed mitochondrial genetics and mitochondrial DNA (mtDNA) mutations in diseases, structures and chaperones of proteasome, and Selenium biology, toxicology and radioprotection. The next series of articles look at genomic variants as risk factors contributing to susceptibility in breast cancer and benign prostatic hyperplasia transformation to prostate cancer. The technology paper highlights BacMam mediated gene transfer in neural cell types.

The field of mitochondrial genetics and association with sporadic and inherited diseases has broadened considerably in the last decade, with current focus on mtDNA variations and effects in a varied spectrum of complex human diseases. The defects in mtDNA often cause disruption in cellular energy, manifests in a large number of human diseases. Dr. Jaya Vyas and Dr. Namrata Londhe, Genetics Department, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India, have reviewed the 'Role of Mitochondrial Genetics in Complex Diseases', with the aim to guide the reader through certain key concepts of mitochondrial genetics and aberrations in classical mitochondrial diseases and additional complex diseases. The authors elaborate on the mitochondrial genome and maternal inheritance patterns. The role and implications of mtDNA mutations in complex diseases including aging, and a glimpse of mitochondrial role in endocrine, neurological, cardiac, cancer pathologies are discussed, with a

comprehensive bibliography. Dr. Jaya Vyas also elaborates on the NGS technology and associated inherent challenges in diagnosis of mitochondrial diseases.

The review on another organelle – Proteasome with a focus on the chaperones, is reviewed in the article 'Assembly and Beyond – The Structure and Functions of Chaperones of the Proteasome', by Dr. Prasanna Venkatraman, Advanced Centre for Training, Research and Education in Cancer, Kharghar, Navi Mumbai. The Proteasome is a protein degradation "machine" within the cell that digests proteins tagged with ubiquitin, into short polypeptides and amino acids. A human cell contains about 30,000 proteasomes. These barrel-formed structures can break down practically all proteins to 7–9-amino-acid-long peptides. The authors succinctly explains two models of assembly of Proteasome subunits, and roles of four chaperones – PSMD9, PSMD10, PAAF1 and S5B in the assembly of Proteasome. The review is a must read for an understanding of the role of chaperone in the formation of the 26S proteasome, and envisages various novel roles for the chaperones.

A need of compounds for protection of individuals from high-dose acute radiation exposure in space and radiotherapy in cancer, with less toxicity, enhanced protection and longer acting is a need in medicine. The review 'Selenium: Chemical Biology, Toxicology and Radioprotection' by K. Indira Priyadarsini, Beena G. Singh and Amit Kunwar, Radiation and Photochemistry Division, Bhabha Atomic Research Centre, Mumbai, emphasises on the radioprotective potential of selenium in both the inorganic salt, sodium selenite, and organic Se compound with various amino acids to form selenomethionine and selenocysteine. Other studies on radioprotection and protection against chemical carcinogens by different forms of Se are reviewed. The selenium compounds are evaluated as drugs or adjuvants for viral diseases and cancer.

Genomic variants, represented as single nucleotide polymorphisms are gaining importance as critical risk factors in several cancers. It is common knowledge that exposure to high risk factors such as tobacco smoking does not lead to lung cancer or oral cancer in exposed individuals, although tobacco

contributes greater than 80% attributable for the cancers. Also the response to same treatment for identical cancer (histopathological/grade/stage) in age/sex matched individuals is not similar. While some patients may recover with good prognosis and overall survival, others may not respond to treatment and indicate bad prognosis. The differences including risk to develop cancer may reside in the genome of individual, which is unique as estimated by the presence of 10 million SNPs per genome. Presence of synonymous or non-synonymous SNPs in specific genes in the intronic or exonic regions, has been correlated with increase/decrease risk to cancer, as also response to treatment and prognosis. SNPs are low penetrance alleles and hence single SNP contributes only a small amount to a person's overall risk of developing breast cancer. However, a panel of SNPs may reflect appropriate risk of breast cancer. Two research articles in the current issue, present data on SNPs in specific genes in breast cancer and benign prostate hyperplasia. The article 'Polymorphism of Hormone Synthesis and Metabolizing Genes and Breast Cancer Risk: A Multigenic Case-control Study' by Dr. Sunita Saxena, Dr. Ashwani Mishra and Dr. Anurupa Chakraborty, National Institute of Pathology, New Delhi, investigated SNPs in CYP17, Androgen Receptor (AR) and Vitamin D Receptor (VDR) SNPs and association with increasing risk of breast cancer, and developed a multigenic model of breast cancer susceptibility to identify women with a panel of the SNPs indicating high risk of breast cancer. The authors reinforced that the polygenic SNPs contribute important risk factors to estimating risk to breast cancer. Benign prostatic hyperplasia (BPH) is a common disease prevalent in elderly men, however the genetic variants in BPH are not extensively examined in Indian men. BPH and prostate cancer (PCa) share certain common pathological characteristics, hence susceptibility loci for PCa contribute to BPH risk and BPH aggressiveness in men. Dr. Sarita Gupta and colleagues from Department of Biochemistry, The Maharaja Sayajirao University of Baroda, Vadodara, investigated SNPs in steroid hormone genes Androgen Receptor (AR), Prostate Specific Antigen (PSA/KLK) and Estrogen Receptor-β (ER-β) genes for risk of BPH transformation to prostate cancer. Both the studies emphasize that

genetic risk factors add valuable information to what we already know can affect a woman's risk of developing breast cancer, and risk of men to progress from BPH to PCa. Thus, SNPs of genes associated with cancers are valuable risk factors and can be used as a potential tool for improving cancer diagnosis and treatment planning.

Baculovirus gene transfer into mammalian cells, referred to as BacMam, is the use of baculovirus to deliver genes to mammalian cells. Baculoviruses are insect cell viruses modified to express proteins in mammalian cells. The unmodified baculovirus is able to enter mammalian cells, however the genes are not expressed unless an appropriate promoter is incorporated upstream of the gene of interest. Further baculovirus and mammalian promoter modified baculovirus (BacMam) are non-infectious as these do not replicate in humans. The BacMam gene delivery technology is a transient expression system, which facilitates expression of single or multiple genes up to 48 kb, has high transduction efficiencies and minimal cytopathic effects. Dr. Uma Lakshmipathy and her colleagues – Rene Qunitanilla, Navjot Kaur, Barbara Calabrese, and Mahendra Rao elaborate on 'BacMam Mediated Gene Transfer in Neural Cell Types' with efficient transduction efficiencies and gene expression in neural stem cells. The authors generated neurospheres, neural rosettes and neural stem cells from human embryonic stem cells, and transduced the cells with BacMam 2.0 GFP. The technology has potential applications for functional screening assays in drug discovery for neurodegenerative diseases, and for delivery of genes into neural cell types, and understanding functions of the genes in the cells.