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Editorial

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Come October and all in the Biomedical field await the announcement of the Nobel laureates in our fields. The 2016 Nobel Prize in Physiology or Medicine was awarded to Professor Yoshinori Ohsumi, for his discoveries of mechanisms underlying autophagy. The Nobel Prizes are announced for the most important discoveries for the benefit of mankind, at Karolinska Institutet, Stockholm. Dr. Ohsumi, Ph. D., from University of Tokyo, Batch of 1974, did a three year post-doctoral at Rockefeller University, New York, USA, and later established his research team at the Tokyo Institute of Technology. Dr. Ohsumi discovered and elucidated mechanisms underlying autophagy, a fundamental process for degrading and recycling cellular components. In the 1990's, Yoshinori Ohsumi, envisaged a series of innovative experiments using baker's yeast to identify genes essential for autophagy, and unravelled the mechanisms for autophagy initially in yeast and confirmed the process in mammalian cells.

Ohsumi's discoveries led to a paradigm shift with respect to the concept of recycling the content of mammalian cells. His discoveries revealed the fundamental path to understand the role of autophagy in several physiological processes, particularly in response to stress due to starvation, response to infection and other stresses. Mutations in genes associated with autophagy often leads to diseases including infections, neurological diseases and cancer. The Nobel laureate built his dogma on degradation as a critical function in living cells, with the lysosome organelle containing enzymes for digestion of cellular contents for degradation of cellular constituents. The autophagosome vesicles, engulfing cellular contents such as damaged proteins and organelles, fusing the contents/organelle with the lysosome, and degradation of the contents into smaller constituents, providing the cell with nutrients and

building blocks for renewal.

Yoshinori Ohsumi focused on protein degradation in yeast mutants in a vacuole similar to lysosome in mammalian cells, and identified 15 critical genes comprising a cascade of proteins in complex cellular pathways in autophagy. He demonstrated that the proteins regulated distinct stages of autophagosome initiation and formation. Autophagy provides fuel for energy and building blocks for renewal of cellular components during stress, and can eliminate intracellular bacteria and viruses. Autophagy contributes to embryo development and cell differentiation. Besides, autophagy eliminates damaged proteins and organelles, and provides a critical balance for the errors, wear and tear in the ageing process. Deregulation in autophagy has been associated with Parkinson's disease, type 2 diabetes, genetic diseases, age related problems in the elderly, and cancer. Dr. Ohsumi thus provided target molecules to develop drugs to target autophagy in various diseases, through his extensive research.

Another current issue in India is cervical cancer in Indian women, and hence we would like to briefly summarize the current International meeting on 'Cervical Cancer Prevention & Control in India and Beyond – A comprehensive Approach Towards Elimination', held on 16-18th October 2015, New Delhi, organised by Global Health Strategies with several international/national partners including American Cancer Society, and WOMEN DELIVER. The issue is so intense that several Non-Government Organisations working to alleviate Cervical Cancer were felicitated by the organisers 'In appreciation of their Inspiring and Enduring Commitment to Fight Against Cervical Cancer' by Hon'ble Minister of State, Ministry of Health and Family Welfare, Government of India.

The central theme of the meeting, repeatedly reinforced at the inaugural session by Dr. N. K. Ganguly, Former Director, ICMR, New Delhi, Chris Elstoft, Deputy High Commissioner, Australian High Commission, New Delhi, Dr. C. N. Purandare, President, International Federation of Gynecology and Obstetrics (FIGO), Dr. Soumay Swaminathan, Secretary, Department of Health Research, Ministry of Health and family Welfare, Government of India and Director General – ICMR was: 'Cervical Cancer is Preventable, and it is imperative to change the course of the

disease and 'Women Need Not Die of the Disease. Preventing cervical cancer is the right thing to do, the only thing to do'. The main features to be considered in order to achieve the goal needs to focus on 'Cervical Cancer Screening in Women and Uptake of Human Papilloma Virus (HPV) Vaccine in Girls'. The statistics of Cervical Cancer in India are appalling with an estimated 123,000 new cases diagnosed annually, and 67,000 deaths due to the disease, contributing 25% of the global cervical cancer incidence and death by a single country – India. We need to be aware that every eight minute an Indian woman is dying of cervical cancer in India. HPV vaccines with proven 70% prevention of cervical cancer is available and accessible to 5% women in rural India, the most vulnerable women.

The mandate and consensus with the cumulative expertise and experience of the delegates was – 'HPV vaccine should be given to girls in the age group of 10–12 years, with emphasis on School Based Campaigns'. The challenges with the health officials, doctors and various groups for implementation of screening strategies and HPV vaccination will be – Public Education, Understanding and Practice, Acceptance, Coverage and Financial/Manpower resource. An investment in 'Health Care for Women' needs to follow the government efforts in 'Maternal and Child Care' campaign with a comprehensive approach with reduction in maternal/child mortality to 50% of the figures to 44,000 deaths. A comprehensive approach will make a difference in reducing cervical cancer incidence and deaths. Ms. Barkha Dutt, Consulting Editor, NDTV, moderating the session 'Elimination of Cervical Cancer in India: A Utopian Dream or a Possible Reality?' with excellent national/international participants including Reshma Pai - President FOGSI (Elect) 2017, Madhu Chopra, Managing Director – Studio Aesthetique, Neerja Batle – Professor Department of Obstetrics and Gynecology, All India Institute of Medical Sciences, New Delhi, Christine Kaseba-Sata - Former First Lady, Republic of Zambia, Genevieve Sambhi – Former Miss Malayasia and a cervical cancer survivor, to name a few. Barkha Dutt reiterated that 65 countries have already accepted HPV vaccination program, adopted as a national program.

It is essential to remove any stigma associated with cervical cancer, and assure safety of the vaccine with no

serious side-effects in HPV naïve girls, is the critical information for all the stakeholders. The sessions on Scene Setting, Bringing Screening Services to Women, Global experiences in introducing Vaccines, Availability, Accessibility and Affordability of Treatment, set the tone for the India to battle cervical cancer. Dr. Dhananjaya Saranath highlighted the contribution of Cancer Patients Aid Association indicating a holistic approach and 'Total Management of Cancer', the vision and mission of CPAA. The focus of CPAA included – Cancer Awareness and Screening, Diagnosis, Patient Care, Research on Psycho-Social-Behavioral aspects of Cancer Patients and HPV molecular diagnostic tests, Affordable Cancer Insurance in conjunction with New India Assurance as partners, and rehabilitation for cancer survivors through 'CPAA Rehabilitation Centre' providing a modicum of economic/financial independence.

The take home message from the meeting deliberations were extremely optimistic emphasizing necessity of planned cervical cancer awareness with screening, treatment and follow-up. The meeting ended with the delegates committed to 'Cervical Cancer Screening and HPV Vaccination' in order to bring to reality 'Elimination (to zero) of Cervical Cancer'. The presence of manufacturers of quadrivalent HPV vaccine, assured their commitment to cervical cancer elimination, emphasizing priority to 'Women Health in India'. The role of media, National Radio/Television/Print and Digital Media support will ensure success of 'Women Health – Free of Cervical Cancer'.

Dr. Sankaranarayan, International Agency for Research in Cancer, Lyon, France, in his closing remarks appreciated the highly educative learning experience for all, the deliberations imparting a wealth of information. He summed up the comprehensive approach to prevention of cervical cancer in India, with the major recommendations and the road map as follows:

- Implementation of screening for women 30 – 65 years of age
- HPV Vaccination for all adolescent girls
- Mechanism of referral, treatment, management and palliative care
- Promotion of Research and Development towards new indigenous vaccines, and technologies to address cervical cancer diagnosis, prevention and

control
- Removal of associated stigma
- Awareness of Rights of women with respect to reproduction, sex and health
- Collaboration and Partnerships
- Sustainable financing
- Strengthening of health systems and generation of adequate trained workforce
- Engage with media and sensitization of medical professionals, scientists
- No female to be left behind'

The overreaching holistic impact of the meeting on women health was clear to all.

The current Biomedical Research Journal issue discusses an interesting theme of **Clusterin in cancer: A tumor suppressor gene or an oncogene?** by Dr. Tanuja Teni and Rajashree Kadam, Advanced Centre for Treatment, Research and Education in Cancer (ACTREC), Tata Memorial Centre, Kharghar, Navi Mumbai. Clusterin (CLU), a molecular chaperone critical in cancer, lying at the cross road of life and death, as it functions as both an oncogene and a tumor suppressor gene in specific contexts, and hence a multifunctional gene. The contradictory functions of clusterin are reflected in promoting cell survival, activating autophagy and apoptosis, and on the other hand promoting tumor progression and inducing resistance to cancer treatment in vivo. This protein is ubiquitously expressed in diverse tissues and conserved across species, and is required to respond to exogenous or endogenous stress signals. Custirsen (OGX-011), a second generation antisense oligonucleotide sensitizes cancer cells to chemotherapy and radiotherapy, and in combination with HDAC-Inhibitor (Valproate) regresses tumor growth. Dr. Teni and Kadam, lucidly review the contrasting roles of CLU in cancer and associated regulatory mechanisms, highlighting Clusterin variants and functions.

The article on **Chemoprotectants in cancer chemotherapy: an update,** by Abhishek Basu, Arin Bhattacharjee, and Sudin Bhattacharya, Department of Cancer Chemoprevention, Chittaranjan National Cancer Institute, 37, S. P. Mukherjee Road, Kolkata, adds another dimension to cancer chemotherapy emphasizing use of chemoprotective agents to alleviate the toxic side effects of chemotherapeutic agents in cancer treatment. Chemotherapy is associated with significant toxicity and various

adverse impacting the outcome of treatment. The review highlights various US-FDA and several European regulatory agency approved chemoprotectants including amifostine, aprepitant, dexrazoxane, filgrastim, sargramostim, mesna, oprelvekin, palifermin, recombinant human erythropoietin, as well as indicate additional agents in cancer patient management. The authors point to the lacuna in the field in identification of novel, effective chemoprotectants.

In the same vein, we have Drs. Limbkar Kedar, Vaijayanti Kale and Lalita Limaye, from Stem Cell Laboratory, National Centre for Cell Science, NCCS complex, University of Pune Campus, Ganeshkhind, Pune, Maharashtra, give us a succinct article on recovery post irradiation on **Oral feeding with Arachidonic acid (AA) and Docosahexanoi acid (DHA) help in better recovery of haematopoiesis in sub-lethally irradiated mice.**

The authors experimentally depict the effect of polyunsaturated fatty acids (PUFAs) by oral administration of PUFAs-AA/DHA on haematopoiesis of sub-lethally irradiated mice in comparison to non-irradiated mice. The bone marrow cells of the mice were harvested and depletion was noted in the total nucleated cell (TNC) count, side population (SP) and $lin^{-}Sca\text{-}1^{+}c\text{-}kit^{+}$(LSK) phenotype, and hemogram data of the PBCs. DHA or AA in the irradiated mice showed significantly higher number of BM-MNCs and increased percentage of SP and LSK cells, indicating better recovery and suggesting that DHA or AA may serve as useful dietary supplements in patients exposed to irradiation.

Mathematical modeling of viral epidemics: a review, by Pratip Shil, National Institute of Virology, Pashan, Pune, is an absolute must for all. Mathematical models to describe transmission and propagation of diseases have gained momentum particularly in the recent past with tremendous applications towards understanding the epidemiology of various diseases including viral diseases including Influenza, SARS, measles, bacterial disease such as tuberculosis, and drug resistant Staphylococcus. The advances in computational biology has enabled virtual simulations and mathematical modelling, particularly to understand the transmission routes and the epidemics/pandemics and facilitate informed decisive interventions and

vaccinations. Dr. Shil lucidly explains the various mathematical models and their applications in the study of virus driven epidemics.

Malaria which should have been a low incidence disease today, is still a sword of damocles in India and several countries, and hence the overview of **Recent advances in the treatment of malaria**, by Drs. Santosh R. Nandan, Evans Coutinho and their colleagues from Organics Pvt. Ltd. and Bombay College of Pharmacy, Mumbai, is timely. Malaria is a major cause of mortality and morbidity, and a well-developed treatment regimen including the artemisinins as well as safety preventive measures, have reduced the global burden of malaria in several countries. However, drug resistance is a developing problem in almost all infections including malaria. The authors focuses on clinical drug candidates with activity against several stages of the malarial parasite life cycle.

The final article on **Biomagnetic interaction of functionalized iron oxide nanoparticles with bovine serum albumin** by Dr. Sudeshna Chandra, Sunandan Divatia School of Science, NMIMS (Deemed-to-be) University, and Mr. Mayank Gupta, Department of Metallurgical Engineering and Materials Science, Indian Institute of Technology Bombay, Powai, Mumbai, highlight functionalized iron oxide (magnetic) nanoparticles as promising candidates for detection and sensing of target molecule. The study reports use of different macromolecules viz. glycol chitosan (GC), poly ethylene glycol methyl ether (PEGME) and poly sodium stereo-4 sulphate (PSSNa) to functionalize and cap magnetic nanoparticles. The magnetic nanoparticles were characterized and the structural and surface properties evaluated. Bovine serum albumin (BSA) was immobilized on the functionalized MNPs and using AC susceptibility studies the physical properties were measured.

The current issue of Biomedical Research Journal takes you from the doable today as seen by our 2016 Nobel Laureate Professor Yoshinori Ohsumi, to elimination of cervical cancer in India, the chemoprotectants and PFAs for better cancer patient management on chemotherapy and radiotherapy, to epidemiology and transmission studies by mathematical modelling, outlook into possible better therapy in malaria to the final contemporary topic of functionalized iron oxide nanoparticles.