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Dear Members,

It gives us great pleasure in bringing out this edition of Cell Biology Newsletter which serves as a medium of communication between the Indian cell biologists and provides a platform for amalgamation of old and young minds.

Last Cell Biology meeting was held in the beautiful campus of Yashada, Pune and a detailed report of Conference and Symposium on Stem Cells and Pattern Formation is appended herewith which has been meticulously prepared by Dr. S M Ghaskadbi. This edition also contains an interesting article by Dr. Manjula Vinayak on `Queuosine modified tRNAs' which plays an important role in regulation of a number of physiological processes. The abstracts of the award winning presentations are also appended herewith to give a glimpse of the research activities going on in the leading areas of cell biology.

Indian Society of Cell Biology has grown over the years and now has its own website (www.iscb.org.in) which includes the list of all the members, however, many addresses and E-mail IDs are incorrect. We request each one of you to kindly go through the entire list and to please let us know if you can update any of them.

This year the Society will be organizing a three days hand-on workshop of Cell Biology Experiments for School and College Teachers of Varanasi and adjoining areas at Banaras Hindu University from 1st to 3rd October 2009.

The XXXIII All India Cell Biology Conference will be hosted by the University of Hyderabad from 10th to 13th of December 2009. The announcement of the conference is given on the inner back cover of the Newsletter.

Nominations for the Prof J Das Memorial Lecture award for 2009 are invited in the format given in this edition. The prestigious lecture will be delivered in the XXXIII All India Cell Biology Conference at Hyderabad in December 2009.

Proposals for organizing XXXIV All India Cell Biology Conference to be held in December 2010 are invited form the members of the society. The proposals will be placed in the Executive Committee Meeting during XXXIII All India Cell Biology Conference, Hyderabad in December 2009 to finalize the venue.

We look forward to meeting you all during the conference at Hyderabad.

With best regards,

Yours sincerely,

Madhu G Tapadia
(Executive Secretary)

J K Roy
(Secretary)

A report on

XXXII All India Cell Biology Conference and Symposium on Stem Cells and Pattern Formation

Agharkar Research Institute, Pune, 4-6 December 2008

XXXII All India Cell Biology Conference and Symposium on Stem Cells and Pattern Formation was held at MACS-Agharkar Research Institute, Pune 411 004 between December 4-6, 2008. Scientific presentations were arranged in eleven sessions, in addition to a symposium on stem cells and pattern formation and poster session. Nineteen invited eminent scientists and eleven young scientists discussed the latest developments in their chosen fields during oral presentations, while there were eight proffered oral presentations and as many as fifty five posters were also presented during these sessions. Among the student presentations, best five papers were selected for various awards instituted by ISCB and two from the organizers.

Prof. Satyajit Mayor of National Centre for Biological Sciences, India, in his opening presentation, gave a comprehensive overview of the process of endocytosis and the complex molecular-genetic network regulating it in a metazoan cell using a *Drosophila* cell line as a model system. State of the art technologies like high-content, high-throughput RNAi screen and automated image acquisition and analysis were utilized to extract quantitative measures of endocytic uptake at both the single cell and population level. These studies open a new approach to analyze the quantitative phenotypic data from genome-wide perturbation of individual cells as well as population.

Prof. T. C. G. Bosch of University of Kiel, Germany, opened the symposium on stem cells by introducing hydra, a basal cnidarian with unlimited capacity to regenerate and potential immortality, as a good model system to study stem cell biology, cellular senescence, lineage programming, cell fate determination and tissue homeostasis. He also reported the well established and well characterized technologies and strategies to create transgenic hydra lines which can be of immense value in studying role of stem cells in the formation of various specialized tissue types in response to extrinsic signals. These studies have shown that stem cell differentiation in hydra is governed through the coordinated actions of conserved signaling pathways and shares the molecular signatures with stem cells in vertebrates, strongly suggesting a common evolutionary origin of these cell types.

Seminal work of Prof. Makato Asashima and his group from University of Tokyo, Tokyo, Japan, to understand the role of various signaling molecules like activin, retinoic acid and their receptors in switching early undifferentiated embryonic cell mass and embryonic stem cells from vertebrates into diverse, fully functional tissues *in vitro* was one of the highlights of the symposium. Prof. Asashima had to cancel his trip to India at the last moment. He, however, sent power point presentation of his talk which was presented by Dr. S. Ghaskadbi on his request

Pioneer of nuclear reprogramming, Prof. J. B. Gurdon of Gurdon Institute, UK, highlighted various aspects of the reprogramming of vertebrate nuclei without DNA replication or protein synthesis. This process takes advantage of the natural reprogramming activity of eggs which reprogramme sperm nuclei with a 100% efficiency and somatic cell nuclei with 30% efficiency, without transfecting new genes into nuclei. He proposed that understanding and application of mechanisms involved in nuclear reprogramming may revolutionize cell replacement without immunosuppression.

Host-parasite interactions human and *Mycobacterium tuberculosis* was the theme of a very interesting presentation by Prof. S. E. Hasnain, University of Hyderabad, India. He showed that the genome sequence data of the pathogen has led to new understanding in molecular epidemiology, evolutionary dynamics and functional biology of *M. tuberculosis*. Role of quorum sensing in crippling the host immune response, initiated by the pathogen for its own survival, was the focus of the discussion.

While studying evolution of cellobiose utilization in *E. coli*, Dr. S. Mahadevan and his group from Indian Institute of Science, Bangalore found that wild type strains of the bacterium, usually unable to metabolize cellobiose, can be mutated do so under experimental conditions and this happens by the genetic modification of the regulation of the responsible operon under selective pressure. Work on *Neurospora crassa* by Dr. D. P. Kasbekar and his team from Centre for Cellular and Molecular Biology, India, is a revival of interest after a hiatus of 30 years, in mutation *fmf-1*. This mutation is proposed to be involved in sexual differentiation and expression of genes involved in mating pheromone signaling. In protistan parasite *Entamoeba histolytica*, during stress, ribosomal biogenesis is regulated not by shutting down rRNA transcription, but by accumulating large amounts of pre- rRNA, ready to be processed when normal growth resumes as shown by the study led by Dr. Sudha Bhattacharya of Jawaharlal Nehru University, India.

Cell-cell interactions and generation of cell diversity in *Drosophila* embryos were discussed by Dr. D. Strutt and Dr. H. Strutt of University of Sheffield, UK and Dr. G. M. Technau of University of Mainz, Germany. The former two talks mainly dealt with the way the cells coordinate their polarity with their neighbours and correct patterning through a family of proteins called core planar polarity proteins. These proteins are shown to participate in contact-mediated cell-cell interactions. Using a combination of genetic and cell biological techniques, this group has shown how the core polarity proteins are assembled and distributed in their subcellular locations. Dr. Technau showed how cell diversity is generated in the growing CNS of *Drosophila* embryos and its segmental patterning. Development and characterization of *Drosophila* model to study human motor neuron disease called amyotrophic lateral sclerosis, which brings about progressive neurodegeneration, is reported by Dr. A. Ratnaparkhi, currently of Agharkar Research Institute, India and her colleagues from University of California Los Angeles, USA. Using the information generated from animal experimentation, Dr. A. Chattopadhyay's team from Centre for Cellular and Molecular Biology, India generated a cellular model for human congenital disorder called Smith-Lemli-Optiz Syndrome (SLOS), caused by abnormal cholesterol biosynthesis. They showed that metabolic replenishment of cholesterol ameliorates the symptoms. These studies could prove useful in developing future strategies for treatment of the disease.

Dr. J. Dhawan also of Centre for Cellular and Molecular Biology, India, showed the involvement of multiple mechanisms in promoting the function of resting stem cells. Using mononucleated stem cells of skeletal myocytes called satellite cells, her group studies how dormant stem cells maintain their genome in a mutation-free state, maintain their identity as muscle progenitors and remain available for repairing the damaged myofibers by returning to active proliferative state. Another aspect of skeletal muscle regeneration and myoblast differentiation was explored in the work of Dr. H. D. Schorder of Odense University, Denmark. His group has showed the involvement of DLK1 gene product in modulating muscle regeneration and differentiation and its possible therapeutic implication in muscular dystrophy. Dr. S. Goswami from Jawaharlal Nehru University, India presented his work on a novel gene called SG2NA with a possible role in regulation

of cell differentiation. It is a good candidate gene for the role of a master regulator since it has multiple isoforms arising from alternative splicing and differential polyadenylation and different cellular localization.

Latest work of Dr. P. B. Seshagiri, Indian Institute of Science, India, shows that mammalian embryos need proper co-ordination between growth factors, cytokines and proteases as well as cellular components like trophectodermal projections in dissolving zona pellucida prior to implantation. . Embryo- derived cysteine proteases and cathepsins play crucial role in this process. Methylation is one the mechanism in gene regulation, chromatin organization and imprinting in mammals. However, how and when does the developmental methylation of specific genes come to play is not known. Work of Prof. R. Raman of Banaras Hindu University, India, shows that *de novo* methylation commences much later than implantation in mammalian embryos and completes in stepwise manner neonatally and tissue-specifically. It envisages a role to chromatin organization in determining the time of methylation in embryonic genes. Dr. A. Basu of University of Burdwan, India and his colleagues from University of New Mexico School of Medicine, USA showed that plasminogen activator inhibitor stimulates angiogenesis in oxygen induced mice retinopathy. This is proposed to be a new therapeutic target in preventing or treating pathological angiogenesis. Using proteomics approach, a novel protein (zinc finger protein like -1, ZFPL-1) involved in maintaining the *cis* Golgi complex integrity was identified by Dr. Y. Ghanekar, presently of Agharkar Research Institute, India and colleagues from University of Manchester, UK.

Three groups from Advanced Centre for Treatment, Research and Education in Cancer, India, working on various aspects of carcinogenesis and possible treatments were represented in the present conference. Dr. S. N. Dalal showed that loss or reduction of a desmosomal plaque protein called plakophilin3 leads to a decrease in cell-cell adhesion which stimulates neoplastic progression and metastasis. Dr. S. Zingde demonstrated that an array of 12 autoantibodies, directed towards oral cancer associated antigens, can prove to be good tool to identify cancer of the gingivo-buccal complex. Gene therapy using adenovirus mediated prodrug activation is made more efficient and effective using histone deacetylase inhibitors as reported by Dr. R. Muherkar. This is achieved by enhanced receptors for engineered adenovirus and increased transgene expression, leading to increased cell death of a squamous cell carcinoma cells. These studies are likely to lead to phase 1 gene therapy clinical trials for human patients.

Clonal propagation of plants through seeds involves formation of seeds while avoiding normal process of meiosis and fertilization of the egg cell and is called apomixis and results in fixation of genetic character. Transfer of apomixis to food crops can lead to large increase in yield and accelerate plant breeding. Dr. I. Siddiqi of Centre for Cellular and Molecular Biology, India, discussed progress towards the identification pathways and genes involved in the normal sexual reproduction and their alterations to bring about apomixis.

12th Prof. S. P. Ray-Chaudhury 75th Birthday Endowment Lecture of this year was delivered by Prof. S. K. Sopory of International Centre for Genetic Engineering and Biotechnology, India on molecular signatures linked to stress tolerance in plants. He overviewed the effects of abiotic stress leading to the enhanced expression of a number of genes and resulting in the modulation of various physiological and metabolic factors. Applying latest technologies in molecular biology and biotechnology, his group has shown that, in addition to the known regulation via transcription factors, epigenetic changes like histone modifications are also affected under stress conditions. Over-

expression of different genes, involved in different cellular and biochemical functions, confers stress tolerance. These studies show that manipulation of two of the enzymes of glyoxalase pathway can lead to the development of transgenic plants that are tolerant to both salinity and drought stress.

Dr. S.P. Modak, formerly of Pune and Karnataka Universities, India, presented an algorithm to construct multi-parametric molecular evolutionary trees in three dimensions. It involved performing multiple sequence alignment of nucleotide/ amino acid sequences and estimating evolutionary distances between all pairs for each trait in the 3 D space among all species.

Dr. L. S. Shashidhara of IISER- Pune, India presented his views on teaching cell biology in IISER mode of post school education. He proposed several improvements in the way biology is taught to students at various levels of education and strengthening the basic concepts. This would lead to development of interest and curiosity about scientific observations as well as aptitude for enquiry among students.

A total of 55 posters were presented on the diverse areas of Cell Biology during the poster sessions. All posters were on display on the first two days and sufficient time slots were allotted to the posters. A large number of posters were from student members of the society. Most of the posters, especially the students' posters, were of high quality. Since these sessions gave an opportunity to all the interested participants to search the posters of their interest and to discuss the work at length, good interactions between the presenting author and the participants were seen. As large number posters were presented, the highlights of each of them is not being presented here.

AWARDS TO STUDENT MEMBERS

On the whole the deliberations through platform and poster were stimulating and highly educating. From eleven oral presentations by student members, the paper entitled "DNA damage induced p53 downregulates *Cdc20* by direct binding to its promoter causing chromatin remodeling" by Ms Taraswi Banerjee, Indian Institute of Chemical Biology, Kolkata, was selected for Prof A S Mukherjee Memorial Award; while the paper entitled "Androgen-induced sex reversal and androgen receptor (*AR*) mediated gonadal differentiation in the lizard, *Calotes versicolor*" by Mr Arindam Chakraborty, Banaras Hindu University, Varanasi, received Prof S R V Rao Award and the paper entitled "Hierarchical organization of Hedgehog and its functional significance" by Ms Neha Vyas, National Centre for Biological Sciences, Bangalore, received the Conference Award.

Out of forty two posters presented by student members, the poster entitled "A novel non-coding RNA in developing gonads of Crocodylus palustris: a candidate gene having role in temperature dependent sex determination" by Mr Amit Anand, Centre for Cellular & Molecular Biology, Hyderabad, was adjudged Prof S R V Rao Award; the poster entitled "Signal transduction pathways involved in lamin reorganization in muscle cells" by Ms Ritika Gurung, Centre for Cellular & Molecular Biology, Hyderabad, was given Prof B R Seshachar Memorial Award; the poster entitled "Chicken SG2NA has multiple isoforms with differential expression during early embryonic development" by Ms Singarapu Nandini, Jawaharlal Nehru University, New Delhi, received Dr Mansi Ram Memorial Award, while the paper entitled "Involvement of Wnt4 and Cyp19A1 during ovarian differentiation in Indian garden lizard, *Calotes versicolor*" by Ms Vidisha Tripathi, Banaras Hindu University, Varanasi, received the Conference Award.

Report prepared by
Dr S M Ghaskadbi
Agharkar Research Institute, Pune

Review Article

Biological Impact of Queuosine Modification of tRNA

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The most characteristic feature of tRNAs is presence of hypermodified nucleosides in the anticodon loop and stem (positions 27-40) which contribute to decoding properties of tRNA molecules during translation [1,2]. The hypermodified nucleosides, found in the wobble position of tRNAs, play a direct role to maintain translational efficiency and fidelity by modulation of codon-anticodon interaction and helps to maintain correct reading frame during translation. They may not be essential for viability but play an important role in fine tuning of tRNA activity [3]. One of such hypermodified base is queuine which is a base analogue of guanine. Queuosine was first discovered in the first position of anticodon loop of *Escherichia coli* $tRNA^{Tyr}$. Later it was found that queuosine is also present in the same position in *E. coli* $tRNA^{His}$, $tRNA^{Asn}$, and $tRNA^{Asp}$ [4]. These tRNAs are known as Q-family of tRNAs. The N-7 position of purine ring is substituted with a C-7 in queuosine, which is the site of attachment for aminomethyl ether to a dihydroxycyclopentenediol ring. The basic queuosine molecule is defined as 7-(3,4-trans-4,5-cis-dihydroxy-1-cyclopentene-3-yl-aminomethyl)-7-deazaguanosine [5].

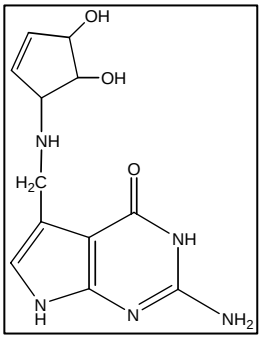

Fig.1: Structure of queuine

The original transcript of Q-family tRNA contains guanine in the first position of anticodon which is post-transcriptionally modified with queuine during maturation. Queuine is irreversibly inserted into the precursor tRNA by base exchange reaction catalyzed by modifying enzyme tRNA-guanine transglycosylase. Queuine is ubiquitously present throughout the living system from prokaryotes to eukaryotes including plants with exception of archaebacteria, mycoplasma and yeast. Prokaryotes can synthesize queuine *de novo* by a complex biosynthetic pathway however; eukaryotes are unable to synthesize either the precursor or queuine itself. They utilize salvage system and acquire queuine as a nutrient factor from their diet or from intestinal microflora.

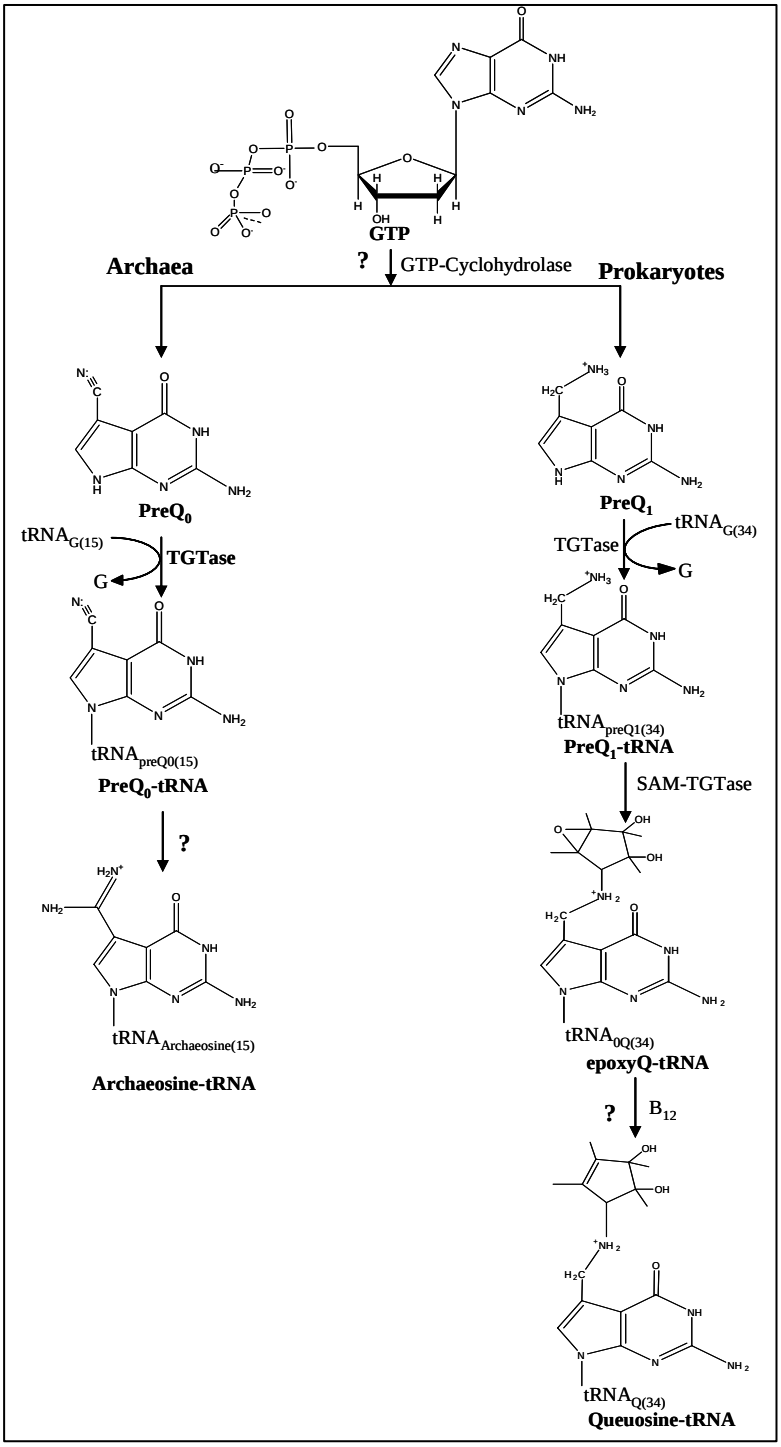

Fig. 2: Biosynthesis of queuosine in prokaryotes

The tRNAs of Q-family are completely modified to Q-tRNAs in terminally differentiated somatic cells. However, Q modification of tRNA is often incomplete in undifferentiated rapidly growing cells, embryonic tissues and regenerating hepatocytes [6]. Similarly queuine deficiency in tRNAs is observed in human placenta [7]. Alteration in the level of queuine in tRNA has been observed during differentiation and development of *Dictyostelium discoideum* , *Drosophila melanogaster* and during development and aging of rats [8,9]. Variations in the modification level of tRNAs occur in eukaryotes from organ to organ.

Physiological role of Q-tRNA

The precise physiological role of queuine/Q-tRNA could not be established till date. The role of queuine may be to protect organisms against stress [10] as queuine free diet fed to germ free mice does not show any pathological symptoms in stress less environment [11]. A correlation between queuine abundance and stress tolerance has been reported by Gaur *et al.* [12].

Queuine plays an important role in tyrosine biosynthesis in mammals [11]. In absence of queuine, tyrosine becomes an essential amino acid for normal development of mouse.

Queuine promotes the activity of the antioxidant enzymes like catalase, superoxide dismutase, glutathione reductase, glutathione S transferase etc. suggesting that queuine ne may be regarded as antioxidant compound to protect antioxidant defense system [13].

Regulation of anaerobic metabolism

Free base queuine or Q-tRNAs play an essential role in adaptive regulation of glycolytic metabolism depending upon anaerobic or aerobic conditions. Specific changes in LDH level and isozyme pattern by queuine are observed in *Dictyostelium discoidium* [14] and in cancerous mouse [15,16] to down regulate anaerobic metabolism. Queuine protects HeLa cells from hypoxic stress and improves metabolic adaptation [17].

Modulation of cancer promotion

Queuine inhibits cell proliferation of a number of cell lines including Colo-DM320 cells, PC-12 cells, U87 cells, Hep G2 cells, ascites tumor cells, transformed NIH-3T3 cells and EGF supported proliferation of HeLa cells, however, proliferation is stimulated in case of HeLa S3 cells, A-431 and HL-60 cells [18]. Queuine induces cell differentiation in cancerous cells .

Lack of queuine in the first position of anticodon is found in tRNAs of Q family from various tumor cells. The degree of hypomodification is related to the severity of malignancy in human lymphoma, leukemia, lung cancer, ovarian carcinoma and brain tumor. A correlation between the level of queuosine modification of tRNA in cancerous tissues of human and grade of malignancy has been reported by several laboratories [19, 20]. The level of Q-lacking tRNA is substantially greater in high grade of malignant lymphomas and immunoblastic lymphomas than low grade malignancies. The amount of queuosine deficient tRNA is strongly correlated to the histopathological grade of malignancy. Queuosine deficiency of tRNA increases in metastastic ovarian malignant tumors compared to primary ovarian malignancies. The level of queuine deficiency in tRNA is found significantly higher in astrocytomas (malignant brain tumor) than in meningiomas (benign brain tumors). Transfer RNA isolated from liver of cancerous mouse is hypomodified with respect to queuosine as compared to normal mouse liver

[21]. Queuine administration leads to Q-tRNA modification along with decrease in proliferation capacity of tissues. There is a positive correlation between the level of queuosine modification of tRNA and survival of the patients [20].

Queuosine hypomodification of tRNA in cancer might be due to one or a number of different causative factors such as decrease in incorporation of modified base queuine due to inactivation of the enzyme or loss of queuine uptake regulated by protein kinase C by aberrant kinase or phosphatase activity or loss of ability to salvage queuine from tRNA turnover process. It may be possible that queuine is not salvaged completely and excreted with urine due to high turnover rate of tRNA [22] or due to inactivation of TGTase. The presence of methylated purines in cancer cells inhibits TGTase activity and queuosine modification of tRNAs.

Queuine/Q-tRNA and cell signaling

The most important extracellular signaling molecules regulating cell proliferation are growth factors which provide increased survival response to cancer cells. Queuine down regulates mitotic signaling initiated by epidermal growth factor receptor *in vitro* by tyrosine phosphorylation of specific membrane associated proteins [23]. Addition of queuine to queuine starved cells affects protein synthesis and protein phosphorylation [24,25]. Queuine dependent down regulation of *c-myc* and *c-fos* expressions are observed in HeLa cells as well as in cancerous mouse liver. Queuine is possibly involved in regulation of apoptosis by decreasing *bcl-2* gene expression [18].

Conclusion

Free base queuine or queuosine modified tRNAs play an important role in regulation of a number of physiological processes. They decrease oxidative stress, inhibit anaerobic metabolism, down regulate proto oncogenes, which collectively lead to protection against tumor progression. Thus queuine/ Q-tRNA may be regarded as an anticarcinogenic agent. Our understanding about their precise action at molecular level is still incomplete. Further research is needed to explore the wholistic action of Q-tRNA in cellular machinery.

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Abstracts of Award Winning Presentations by Student Members at the *XXXII* All India Cell Biology Conference, Pune

Prof A S Mukherjee Memorial Award for Best Platform presentation

DNA damage induced p53 down regulates *Cdc20* by direct binding to its promoter causing chromatin remodeling

Taraswi Banarjee, Somsubhra Nath and Susanta Roychoudhary
Indian Institute of Chemical Biology, Kolkata

Improper chromosome alignment during metaphase triggers the Spindle Assembly Checkpoint (SAC) which arrests further cell division. SAC operates just preceding mitotic exit, marking it to the last resort for a cell to revert any chromosomal damage or duplication error. Anaphase promoting complex (APC) to initiate Metaphase–Anaphase transition. *CDC20* has been found to be overexpressed in many tumors and has been proposed to be a potential cancer therapeutic target. In this study we show ectopically expressed or DNA damage induced endogenous p53 binding site on the *Cdc20* promoter. Site directed mutation of this p53 binding site followed by luciferase assay revealed the failure of transcriptional repression of the *Cdc20* promoter by p53 under DNA damaged condition. ChIP and EMSA studies proved that p53 uses this site to directly bind the *Cdc20* promoter. This binding is exclusive to the DNA damaged condition and is not seen under normal cellular condition. ChIP studies have also revealed that upon DNA damage, p53 along with HDAC1 and the corepressor mSin3A are recruited to the *Cdc20* promoter thereby causing chromatin remodeling by increased histone methylation and deacetylation. We have also done mutational analysis of the *Cdc20* promoter to prove that under physiological conditions this p53 mediated repression is independent of the p21 pathway. Implication of the p53 mediated repression of *Cdc20* will be discussed in the context of chromosomal abnormality in tumor cells.

Prof S R V Rao Award for Best Platform presentation

Androgen-induced sex reversal and androgen receptor (AR) mediated gonadal differentiation in the lizard, *Calotes versicolor*

Arindam Chakravorty and Rajiva Raman
Banaras Hindu University, Varanasi

In almost all the non-sex chromosomal, TSD reptiles where hormone-induced sex-reversal is reported, reversal is invariably towards the female sex regardless of estradiolor testosterone treatment. In Indian garden lizard, *Calotes versicolor,* all male hormone-treated embryos emerge as males. Treatment with estradiol shows no response. We have cloned androgen receptor (*CvAR)* gene from *C. versicolor,* and studied its expression in genital ridge (GR) following dihydrotestosterone (DHT) administration (day 8 &12) (bipotential gonad). Comparative expression analysis of two male specific genes *CvSox9*, *CvDmrt1* and a female specific marker *CvWnt4* in both treated and controls revealed that in untreated embryos expressions of C*vAR, CvSox9* and *CvDmrt1* was quantitatively dimorphic (present/high in some, absent/low in others). *CvWnt4* expression was exclusive of the other three genes, indicating ovarian fate of the embryo. In the DHT-treated (30µg/egg) embryos *CvAR* was expressed in almost each GR with a distinct down-regulation of *CvWnt4* while *CvSox9* and *CvDmrt1* showed no difference from the control

patterns. These results confirmed that in testis differentiation *CvSox9* and *CvDmrt1* act upstream of *CvAR.* However, subsequent development/differentiation is largely hormone-regulated and probably *AR* mediated. When treated and control MGC transcriptomes were subjected to differential display PCR, a non-SMC chromosome condensation protein was found to be up-regulated in treated embryos. Our results suggest a temporal hierarchy (*CvDmrt1/CvSox9→CvAR*) in the pathway of testis determination. However, subsequent gonadal differentiation is predominantly hormonal not only in *C. versicolor* but reptiles in general, regardless of their mode of sex determination.

Conference Award for Best Platform presentation

Hierarchical organization of Hedgehog and its functional significance

Neha Vyas, Debanjan Goswami, Pranav Sharma, H A Ranganath, K VijayRaghavan, L S Shashidhara, R Sowdhamini and Satyajit Mayor
National Centre for Biological Sciences, Bangalore

Hedgehog (Hh) is one of the morphogen involved in patterning of developing tissues. It is post translationally modified by palmitate and cholesterol at its N-terminus and C-terminus respectively. Paracrine signaling is one of the requirement of this dually lipidated, membrane anchored morphogen for patterning of the developing tissues. Our study has revealed that cell surface Hh molecules are organized at different length scales, ranging from nanometer to visible scale. While the lipid modifications provide the tamplate for its nanoscale organization, Hh also requires cues from the protein domain for a distinct cell surface organization. Further this distinct nanoscale organization is required for its ability to interact with cell surface HSPGs and subsequently for long range singaling.

Prof S R V Rao Award for Best Poster presentation

A novel non-coding RNA in developing gonads of *Crocodylus palustris:* a candidate gene having role in temperature dependent sex determination

Amit Anand, R Phanindranath, Lalji Singh, Ramesh K Aggarwal
Centre for Cellular & Molecular Biology, Hyderabad

In recent past some mRNA like non-coding RNAs have been shown to play important role in gene expression regulation e.g. *HSR-1, Hotair, Xist* that are involved in heat shock response, Hox genes regulation, X-chromosome inactivation, respectively. We report here one novel mRNA like ncRNA having a possible role in temperature dpendent sex determination (TSD), wherein the incubation temperature determines the sex of the developing embryo.

The ncRNA like transcript was identified in a global screen for genes differentially expressed during early TSP (temperature sensitive period) in the bipotential gonads of *Crocodylus palustris*. Subsequently, full 3kb long cDNA was obtained by RACE, which was found to be an mRNA like ncRNA showing no similarity to any database sequence except for a 160 bp region homology to a solute carrier gene (*SCF35F5*). The possibility of the ncRNA being product of the intronic region of *SG35F5* locus was ruled out by genome walking. The detailed expression analysis of ncRNA showed that: 1) its both strands are transcribed; 2) one strand expresses 35-40 folds more than other one only at male promoting temperature (MTP), and 3) the ncRNA at MPT specifically localizes in

the developing vasicularcords and not even in the interstitium. Further, ncRNA overexpression induces many genes involved in the male sex determination/differentiation *viz., Dmrt1, Amh, Sox9 etc.* in the GAM-derived primery cell lines. Thus, the study provides the first evidenceof an mRNA like ncRNA having a possible role in male-sex determination in a TSD species.

Prof B R Seshachar Memorial Award for Best Poster presentation

Signal transduction pathways involved in lamin reorganization in muscles cells

Ritika Gurung and Veena K Parnaik
Centre for Cellular & Molecular Biology, Hyderabad

Lamins form a filamentous network at the nuclear periphery and are also localized in the interior of the nucleus. Lamins impart structural integrity to the nucleus and interact with the nuclear membrane proteins as well as gene regulatory factors. The A-type lamins display cell type specific expression while the B-type lamins are expressed in all somatic cells. As most mutations in the human lamin A gene cause muscle-specific diseases, there is considerable interest in identifying a role for lamin A in muscle cells. Earlier studies from the group showed that intranuclear lamin speckles were reorganized into diffuse network at the onset of muscle differentiation in a process that required cyclin D3 and the retinoblastoma protein (pRb). To understand the role of cyclin D3 in this process, we analyzed its binding to cell cycle markers and observed that cdk4-cyclin D3-PCNA-lamin A form a complex in myoblast nuclei. These cell cycle markers and pRb phosphoforms also showed matrix association, consistent with a role for the nucleoskeletal structure in muscle gene regulation. To examine the effects of cyclin D3 on gene expression, we are carrying out a comparative analysis of myoblasts and cyclin D3-expressing myoblasts. We have used an adenoviral gene delivery system to overexpress cyclin D3 in myoblasts. Our studies suggest a role for the p38 MAP kinase pathway in cyclin D3-mediated lamin reorganization.

Dr Mansi Ram Memorial Award for Best Poster presentation

Chicken SG2NA has multiple isoforms with differential expression during early embryonic development

Singarapu Nandini, Vidya Patwardhan, Surendra Ghaskadbi, Shyamal Goswami
Jawaharlal Nehru University, New Delhi

SG2NA (S-G2 phase nuclear antigen) was originally identified as a tumor antigen with its expression enhanced in the S and G2 phases of cell cycle. It is a member of the striatin family characterized by four protein-protein interaction domains, a caveolin-binding motif, a coiled-coil structure, a calmodulin-binding domain and a WD repeat domain, suggesting that it is a signaling or scaffold protein. Although, members of striatin family (Striatin, Zinedin and SG2NA) have been shown to interact with Phocein and protein phosphatase 2A (PP2A), thereby attributing their role in vasicular trafficking and cell signaling,their role in metazoan biology is largely unknown. We recently have reported that in mouse, SG2NA has multiple splice variants with differential expression in various tissues. Here we report that chicken SG2NA also has at least four splice variants with potential roles in tissue differentiation and development. Northern and RT-PCR analysis showed that at least one variant is brain specific. Also Northern analysis suggests that the transcript profile of SG2NA is developmentally regulated in tissues like heart, liver and

skeletal muscle. Further, each isoform of SG2NA transcript might undergo differential polyadenylation with progress of embryonic development. *In situ* analysis of the expression profile of two of the variants in early chick embryos shows asymmetrical and differential expression in the heart field. Taken together, splicing variation of SG2NA might have some critical roles in differentiation and maturation in metazoan cells.

Conference Award for Best Poster presentation

Involvement of Wnt4 and Cyp19A1 during ovarian differentiation in Indian garden lizard, *Calotes versicolor*

Vidisha Tripathi and Rajiva Raman
Banaras Hindu University, Varanasi

Calotes versicolor is a reptile that lacks distinguishable sex chromosomes as well as environment dependent sex determination. A few evolutionarily conserved sex determination pathway genes have already been identified and characterized in this species, indicating a genic control of gonad differentiation. Among those *CvSox9* and *CvDmrt1* have been shown to be critical for the initial development/differentiation of male gonad and later the differentiation is largely dependent on sex steroids. However, a critical factor responsible for the determination of ovarian fate is still to be established. In the present study we have cloned the *Wnt4* and *Cyp19A1* gene from this species and analyzed their expression in genital ridges in both normal and aromatase inhibitor treated embryos. Our observations suggest a temporal difference of expression between *Wnt4* and other male determining markers [viz. *CvSox9*], *Wnt4* being expressed at later stages of development when the expression of majority of male determinants is either declined or switched off. In subsequent development *Wnt4* and *Cyp19A1* becomes dimorphic such that individual embryos express either *CvWnt4* or *Aromatase* or *CvSox9* and *CvDmrt1*. These results provide evidence in support of *CvWnt4* and *CvAromatase* as female pathway genes. The temporally distinct expression of these genes appears a novel mechanism of sex determination whose significance needs to be explored. Our results advocate the involvement of *Wnt4/Aromatase* in directing female gonadogenesis at a stage of development in those embryos where male development failed to initiate.

Indian Society of Cell Biology

Dear Members,

The Indian Society of Cell Biology has instituted Prof J Das Memorial Lecture" as a mark of its respect to Professor J Das and in recognition of his immense contributions to Cell Biology. Nominations are invited from all Life and Ordinary members of at least three years standing for Prof J Das Memorial Lecture to be delivered at XXXIII All India Cell Biology Conference to be held at University of Hyderabad, Hyderabad, from 10th to 13th of December 2009.

The person to be nominated need not be a member of the Society when nominated but may be requested to become a member in due course of time. The person to be nominated will ordinarily be an Indian citizen at the time of nomination/selection and should be an eminent scientist who would have made outstanding original contributions to Cell Biology or contributed substantially to growth of the subject in India. A list of previous speakers are given below :

Prof P Balram (IISc, Bangalore)

Prof M R S Rao (JNCASR, Bangalore)

Prof P P Majumder (ISI, Kolkata)

Prof V Nagaraja (IISc, Bangalore)

Please send the nomination in the enclosed proforma so as to reach us by 15th September 2009. The bio-data of the nominee may be sent by E-mail to jkroy@bhu.ac.in.

With best regards,

Yours sincerely,

J K Roy
Secretary, ISCB
Department of Zoology
Banaras Hindu University
Varanasi 221 005

NOMINATION FORM FOR PROF J DAS MEMORIAL LECTURE

Name & Address of the member making the nomination:

Nomination

I wish to nominate.....
(address.....)
for PROF J DAS MEMORIAL LECTURE. I have obtained consent of the nominee for the purpose. The biodata etc of the nominee are enclosed herewith.

Date Signature of the nominating member

NOTICE FOR GENERAL BODY MEETING OF THE SOCIETY

The Annual General Body meeting of the Indian Society of Cell Biology will be held

on 12th December 2009

at 6.30 pm

in the DST Auditoroum, University of Hyderabad, Hyderabad

All members are requested to attend the meeting.

The agenda for the meeting will be :

1. **Welcome by the President**
2. **Confirmation of the minutes of last General Body Meeting held at Pune in 2008**
3. **Presentation of annual report by the Secretary**
4. **Presentation of financial status of the Society by the Treasurer**
5. **Announcement of venue of next meeting**
6. **Any other matter with the permission of the chair**

FROM TREASURER'S DESK

All ordinary and student members of the society are requested to renew their membership, if it has not already been done. Demand drafts may be drawn in favour of "Indian Society of Cell Biology" payable at `Varanasi' and may be sent to Dr A Mukherjee, Treasurer ISCB, Department of Molecular & Human Genetics, Banaras Hindu University, Varanasi 221 005

XXXIII All India Cell Biology Conference
&
International Workshop on Cell Cycle Regulation

10-13 December, 2009

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Prof. A. S. Raghavendra, Dean School of Life Sciences, Univ. of Hyd.

Prof. S. Dayananda, Head, Dept. OF Animal Sciences, Univ. of Hyd.

SPEAKERS

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Dr. Utpal Nath, IISc, Bangalore

Prof. Sudhir Kumar Sopory, ICGEB, New Delhi

Dr. Utpal Tatu, IISc, Bangalore

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US$. 100/- Overseas Participants

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Rs. 2000/- Indian participants

US$ 75 overseas participants

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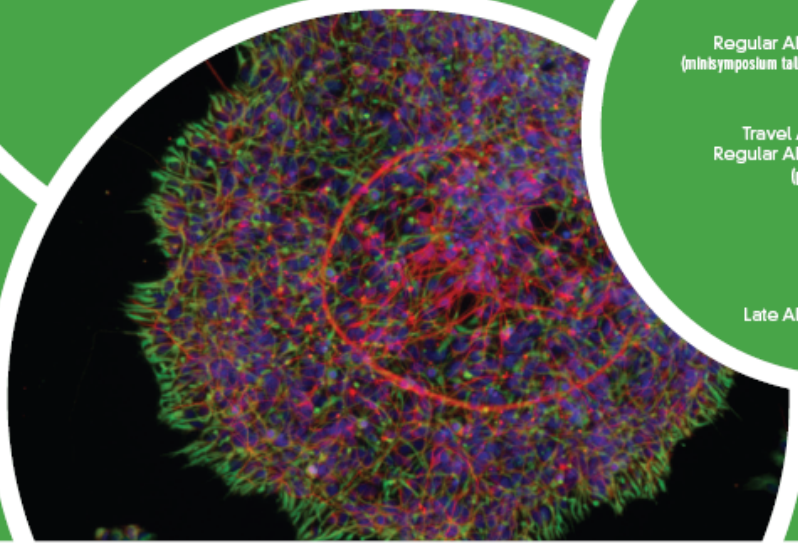

IMPORTANT DEADLINES

JULY 30
Regular Abstract Submission
(minisymposium talk or poster consideration)

SEPTEMBER 1
Travel Award Application
Regular Abstract Submission
(poster consideration only)

OCTOBER 1
Early Registration

OCTOBER 15
Late Abstract Submission