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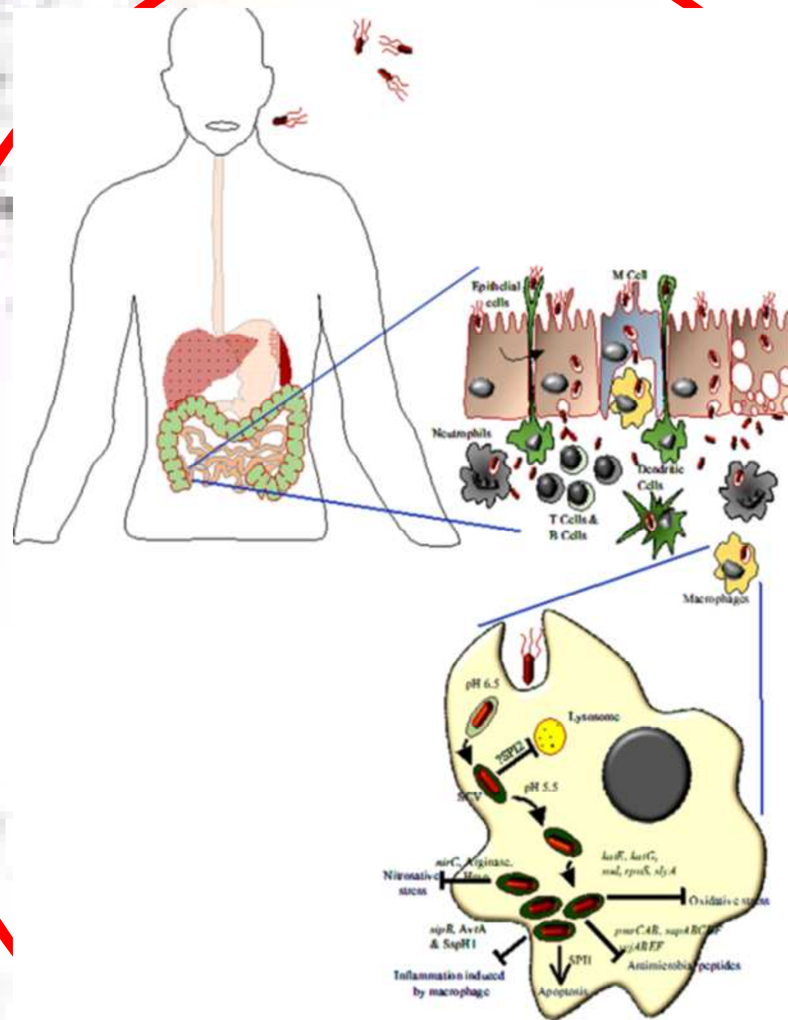
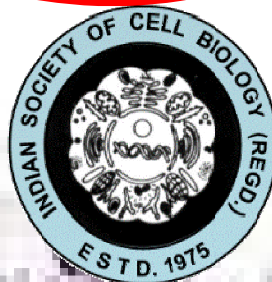
Cell Biology Newsletter





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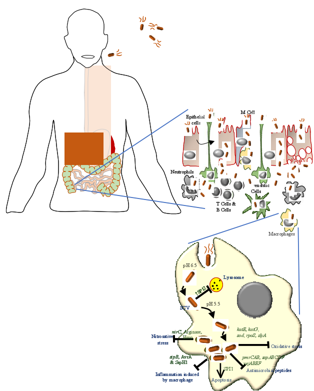

Breaching of gut epithelia and evasion of host immune system by Salmonella *(Adapted from Garai et al., 2012).*

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President message

Dear Members of the Society,

A warm greetings to you all from me and on behalf of all the office bearers. I was pleasently surprised when I was elected as the President of the Society. Having the past experience of presiding over one of the oldest science societies earlier, and having represented the other forums, I readily accepted the mantle.

The challenges facing ISCB are of different nature. Our society is relatively young and needs to grow. The revolution in cell biology we have been witnessing over the last decade is phenomenal. With the advent of newer high resolution imaging and other technologies at a speed faster than we can catch up, the new age cell biology is there to stay. Old questions are being answered with these technologies and new questions can be addressed. Thus the task we have at the moment for ISCB is clear. We need to grow and be more vibrant. We need to enlarge our base and enrol young researchers. In many research institutes and universities, we are witnessing an increase in cell biology research both in quantum and quality. All these new entrants should be encouraged to join our fold. In parallel, all members can make efforts to send more of their students to participate in the annual meeting.

Splendid efforts from the previous office bearers over the years has led to the production of quality News Letters in the past with excellent articles, methodology papers, images etc. It is my turn to request you all like the past presidents, to send high quality images/pictures, reviews related to the field so that our News Letter remains a sought after publication.

Yes. As said above, I look forward to meeting you all in this year's ISCB meeting at Thiruvananthapuram (Dec 6-8, 2015). I also appeal to you all to initiate membership drive and also encourage the youngsters to participate in the conference. Together, let us march ahead.

Sincerely,

V Nagaraja
President

From the Secretary's desk

Dear Honorable members of the Indian Society of Cell Biology

Greetings from the Indian Society of Cell Biology (ISCB) secretariat, Mumbai and a cordial invitation to attend 39th All Indian Cell Biology Conference and annual meeting of Indian Society of Cell Biology to be held at Thiruvananthapuram, Kerala. On behalf of the newly elected office bearers of the society I thank you all for showing confidence in us and congratulate you for electing a dynamic executive committee of the society for the term 2015-2017. As rightly said in the last newsletter by the then secretary, the society is privileged to have Professor V. Nagaraja as its "President" and it is indeed a great experience and pleasure to work under his supervision.

I take this opportunity to put on record the commendable contributions of outgoing office bearers particularly Prof. V. Radha then secretary, for significant additions in the society activity. The most notable one is the release of two issues of the society newsletter per year with its ISSN etc that makes published articles citable in some form. It also opens up opportunity for making ISCB newsletter better visible and accountable so that members can come forward to publish their research articles here and that should serve both news and articles with some academic recognition. Since the society is privileged to have a high profile membership, I am confident this is doable and I take this opportunity to invite discussion on separating publication of ISCB newsletter from ISCB secretariat rather creating a team for this work.

This year I tried bringing some new features in the newsletter for making this source of communication a little more effective and meaningful to readers mainly young members, by not only through bringing good research articles but also through creating corner for 21st century students. Under this new column we invited student's opinion on the research atmospheres they would like to have in their surroundings and what they feel about the need for basic and applied research in India. I found, there are people who talk about these aspects when you sit across the breakfast table and tea/coffee in corridors but rarely come forward to highlight these issues including those who represent 21st century corners and would matter most for the future of Indian science. We received one article and that is given in this issue.

This issue of the ISCB newsletter includes 4 research articles with cover page from the articles that deals mostly interface of prokaryotic and eukaryotic cell biology. This area has witnessed explosive growth globally and the research contributions from India have contributed significantly in cellular and molecular aspects of infectious biology. So much so that microbes are being thought of using for the treatment of cancers, which once upon a time were considered contaminates in animal tissue culture. Then there is an article from a colleague representing 21st Century Students Corners, and given some news for faculties about Department of Atomic Energy (DAE) -BRNS funding through collaborations and opportunity for student's academic growth in India through Homi Bhabha National Institute, a DAE-deemed university.

Lastly, once again I request you all to register yourself, submit abstract/attend this year annual meeting of the society and 39th All India Cell Biology Conference jointly organized by IISER-TVM and Rajiv Gandhi Centre for Biotechnology (RCB) in Thiruvananthapuram, Kerala, during December 6-8, 2015. **The Prof. J. Das Memorial Lecture will be delivered during this meeting.**

This issue announces some of the anticipated articles for March 2016 issue of ISCB newsletter. We invite more articles from members for including in subsequent issues. I personally request those members of the society who have the information on various research and academic opportunities in India for post graduate students and post doctoral fellows, to please write a column on this subject for coming issues of ISCB newsletter.

H. S. Misra
(Secretary)

Jagdish Mehta
(Joint Secretary)

Enhancing Factor – a new avatar of secretory phospholipase A2

Rita Mulherkar

Looking back at more than 30 years working as a Scientist at erstwhile Cancer Research Institute, now ACTREC, I recall with pride the work on Enhancing Factor carried under the driving force of Dr. M. G. Deo along with my students and colleagues. It gave us many papers, few reagents, a few accolades and a transgenic mouse at the end of it. The reagents generated during the course of this work such as polyclonal antibodies to EF, EF cDNA as well as the transgenic mouse, have been used by many scientists in India as well as abroad. We were acknowledged for the reagents leading to citations of our papers. Our collaboration with scientists working in the field gave us papers in high impact factor journals including one in Nature Genetics in 1997.

Enhancing Factor (EF) arose out of a simple question – are there alternate sites for synthesis of Epidermal Growth Factor (EGF) other than salivary glands? And serendipity led us to the discovery of Enhancing Factor based on an observation that low molecular weight proteins extracted from mouse intestines enhanced the binding of EGF in a radio-receptor assay, and hence the name. This observation was made initially by Dr. Deo on his visit to Dr. George Todaro's lab at NCI in US, where TGF was being discovered at the time in the mid 80s.

On his return from US and a 50ml Falcon tube filled with lyophilised mouse intestinal extract, we set out to inject rabbits to raise polyclonal antibodies against the crude extract. We were fortunate to raise high titre, specific antibodies against EF. I continued the work on EF and was convinced that this was a project worth pursuing. Some of my senior colleagues advised me not to waste my time on this observation as it was probably an artefact. However, I was convinced of the phenomenon and a few weeks later I was ecstatic when I was able to demonstrate that EF was indeed a protein and required disulphide bonds for its activity. (We – a Ph.D. student Shrikant Mane and I, were treated to dinner at Dr. Deo's house that evening after this small but important discovery!). After this there was

no looking back. All our in vitro data pointed to the fact that EF was an important growth factor modulator although its exact function eluded us.

As we embarked on project-EF, our lab became a factory where hundreds of mice (retired breeders from the Animal House) were sacrificed to extract EF from the intestines. This was carried out routinely by our sincere and enthusiastic technicians – A. V. Jadhav and J. K. Rane. The protein was purified to homogeneity using gel filtration columns and reverse phase HPLC. One day when Dr. V. S. Chauhan, from ICGEB, New Delhi was visiting our Institute, I showed him the SDS-PAGE gel picture of purified EF and asked him if it was clean enough for sequencing. He said it was and he would be happy to sequence it at his institute. In the meantime, two of the students registered under Dr. Deo for the Ph. D programme – Shrikant Mane and Anjali Saraf along with my colleague Dr. Archana Wagle, worked on further characterization of EF and attempted to obtain its amino composition.

At ICGEB, Dr. Chauhan successfully sequenced the first 20 N-terminal amino acids of EF - which I can recite even now! The next step was to find out whether the sequence belonged to any known protein molecule. In the mid 80s we had no computers, nor internet, and hence it was difficult to access any databases such as EMBL. My colleague Dr. Wagle and I took a train to Pune to meet Dr. A. B. Kolaskar at the Zoology Department who was kind enough to blast the sequence on his computer and give a print out on his dot-matrix printer, which was a huge number of pages showing the extent of similarity EF had to different known proteins. Although it was not identical to any known protein, it turned out that EF was a phospholipase A2 (PLA2) which had not been identified in mouse so far.

Next we carried out experiments to check whether EF had PLA2 activity and reported for the first time that EF was the mouse secretory PLA2. Using the high titre polyclonal antibodies raised in my lab in rabbits, we along with my colleague Mrs. Shefali Desai demonstrated by immune-histochemical staining that the main source of EF in the mouse intestines was the Paneth Cells located in the intestinal crypts (Fig 1). The antibodies used at a dilution of 1:25,000 for immune-histochemistry and at 1:5000 for Western blotting were highly specific. We also found that the expression of the EF protein was present in the outer root sheath in new born mouse hair follicles. The immune-staining of the intestinal

sections was so clean and specific to Paneth cells, that we had numerous requests from abroad for our high titre antibodies from scientists working on Paneth cells. We were acknowledged for the antibodies by numerous workers in their publications.

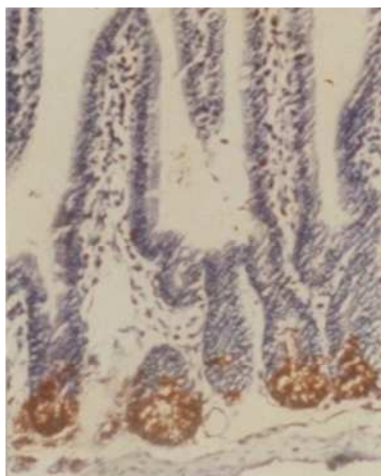

Fig. 1: Mouse intestinal section stained with H&E and anti-EF. Paneth cells at the base of the villi show positive staining which is brown in color here.

In the mid 80's, molecular biology techniques were still not as common as they are today although DNA / RNA extraction was becoming quite common. Cloning and RT-PCR were newer techniques – unlike today where every lab does RT-PCR. We set out to amplify EF cDNA by RT-PCR. Since we had the N-terminal sequence for EF we designed degenerate primers based on the first 6 amino acids in the sequence and along with oligo $(dT)_{17}$ primers, we amplified the EF cDNA from RNA extracted from mouse intestines – without having access to RNA extraction kit or cDNA synthesis kit or PCR kit! We were ecstatic to see a nice clean band ~700bp in size amplified in the reaction. My Ph.D. students Renuka Rao, Varsha Patki, Abhay Redkar and Charusheela Deshpande all contributed to the genetic studies on EF. Using ^{35}S-dATP, Renuka and I sequenced the amplified cDNA – the first sequence of mouse secretory PLA2 to be submitted to EMBL nucleotide sequence database with an accession number X74266. From the cDNA sequence we derived the amino acid sequence. Another Ph.D. student – Shilpa Kadam, cloned the EF gene in an expression vector, made recombinant EF and also carried out mutational analysis to demonstrate that the EF activity was distinct from the PLA2 activity.

In order to understand the function of EF, we were contemplating expressing EF in the mouse skin. We obtained the expression vector with the Human Keratin 14 (K14) promoter from Dr. Elaine Fuchs. Shilpa successfully cloned the EF cDNA in the expression vector under human K14 promoter, which was her parting gift to us.

Fig. 2: Homozygous K-14-EF transgenic mouse (F2) with normal sibling **Hairless homozygous mouse on left next to a wild type sibling.**

In 1992, I had gone to Dr. Steven Hinrichs lab in Nebraska to learn the transgenic technology of microinjection of DNA into single cell mouse embryos. With Shilpa's EF construct cloned under the K14 promoter and my next student, Bhakti Kirtane, we set out to make transgenic mice. This was quite a frustrating experience initially as I did hundreds of microinjections into single cell embryos, transferred them into surrogate mothers and, Bhakti and my technician Nirmala screened hundreds of new born pups with no luck. However, one day we got lucky and we got two new born pups' DNA samples which were positive for the transgene in the PCR reaction. Out of the two pups one showed a phenotype where as in the other mouse the gene was silent. Today we have a colony of transgenic mice expressing EF in the squamous epithelial cells and show aberrant hair follicles and

hair growth. When two transgenic mice were crossed, the homozygous mice were found to be hairless (Fig.2). These are being used by scientists at ACTREC who are interested in stem cells in hair follicles.

Thus starting from a simple observation followed by hard work and perseverance we managed to purify a molecule, sequence it and finally express it ectopically in mouse skin. Although we were slightly disappointed that EF was not a 'new' molecule, we were the first to report its presence in the mouse intestinal Paneth cells and report its complete amino acid sequence. We gave a known molecule – secretory phospholipase A2, a new function that of a growth factor modulator.

Author is an ex-Outstanding Scientist in TMC-ACTREC, Navi Mumbai. A veteran member and was the President of Indian Society of Cell Biology during 2009-2011.

Life of pathogens inside vacuole: An insight through Salmonella

Preeti Garai and Dipshikha Chakravortty*

Infectious diseases caused by pathogenic microbes pose a serious threat to human health and therefore form an essential topic of research in microbiology today. It is difficult to comprehend that pathogenic organisms of microscopic dimensions can bring down the entire immune system of a much larger host animal. To develop effective therapeutics against these pathogens, it is important to understand the adaptive strategies followed by them to survive inside or outside host. A suitable pathogen to serve this purpose is the enteric pathogen Salmonella due to its short generation time and feasibility of genome modification by recombinant DNA technology.

Vacuolar pathogens

The ability to reside inside the host cell is the best tactic used by intracellular pathogens, which enables them to easily bypass the humoral immunity of the host. They further escape from the intracellular immunity, such as lysosome and inflammasome, mostly by forming a protective vacuole-bound niche derived from the host itself. Some of the most dreadful diseases caused by these vacuolar pathogens include tuberculosis by Mycobacterium and typhoid fever by Salmonella. Intracellular pathogens can either survive in a self-constructed niche in the form of a vacuole, a more preferred choice, or they may choose to live in the cytoplasm of the host cell. Few intracellular pathogens follow an alternate less preferred strategy to survive inside host cells as they do not form a niche but develop strategies to survive inside the cytoplasm such as Shigella and Listeria (1). Other best studied vacuolar pathogens hijack the endophagocytic pathway of the host at various stages bearing the surface markers of that specific stage.

Salmonella resides in an intracellular vacuole termed as Salmonella containing vacuole (SCV) that arrests the host endosomal pathway at the late endosome stage. Although, it acquires the late endosome markers, such as vATPases and LAMP1, it eventually loses some of them like mannose-6-phosphate receptor which differentiates it from the late

endosome (2). Mycobacterium infection involves formation of Mycobacteria pathogen vacuole (MPV) that does not mature after the early endosome stage while being associated with the corresponding markers like EEA1 and Rab5 (2). This arrest at early endosome stage prevents the fusion of the MPV with the phagolysosome and hence the clearance of the pathogen. Another example, Brucella containing vacuole (BCV), displays early endosome related markers like EEA1, Rab5, etc. and eventually takes an unconventional route of becoming endoplasmic reticulum (ER) derived autophagosome maturing into ER (2). In case of Legionella infection, Legionella containing vacuole (LCV) bears autophagosome associated markers like Atg7 and Atg8 and further matures into rough ER like organelle (2). Chlamydia form Chlamydia trachomatis inclusion (INC) which moves to the microtubule organizing center (MTOC) like Salmonella. Notably, the vacuolar structure INC is segregated from the typical endomembrane pathway unlike other pathogens (2). Toxoplasma forms a host plasma membrane derived parasitophorous vacuole (PV), which is completely independent of vesicular trafficking of the host cell. The membrane of PV gets incorporated with LDL cholesterol with the help of postlysosomal vesicles (2).

All vacuolar pathogens encounter similar challenges inside the vacuole including resistance to host defense, limitation of nutrients, proliferation while remaining inside the vacuole and maintenance of host cell integrity for pathogen's own requirement. As a result, these pathogens possess similar mechanisms of survival inside the vacuole. Thus, it is convenient to study one model vacuolar pathogen to understand their pathogenesis.

Salmonella as a Model Intracellular Pathogen

Salmonella represents a group of Gram-negative facultative anaerobic intracellular pathogenic bacteria which costs millions of lives across the world every year. The genus Salmonella is categorized into two species S. bongori and S. enterica, based on the high (96–99%) sequence similarity of their genomes. There is only one subspecies under S. bongori namely subspecies V, whereas S. enterica comprises the remaining seven subspecies I, II, IIIa, IIIb, IV, VI and VII. Subspecies I is specific to warm blooded animals like mammals and others can infect only coldblooded animals including reptiles. There exist more than 2,500 serovars of Salmonella. The serovar *Salmonella enterica* serovar Typhi (S.

Typhi) infects only humans and higher primates. Whereas *S. typhimurium* has a wide range of host including rodents, cattle and birds (3).

Salmonella enters the host by ingestion of contaminated food. The passage through the feco oral route of the host subjects Salmonella to various stress conditions. Salmonella not only sustains these stress conditions but also establishes itself by expressing several virulence associated genes. For example, acidic pH in stomach induces expression of STM1485 that helps in better intracellular replication of Salmonella (4). After reaching the intestine, Salmonella breaches the epithelial lining with the help of type three secretion system 1 (T3SS1) and is carried by macrophages to the systemic sites like liver and spleen (3). Salmonella constantly resists the immune responses generated by host by multiple strategies. For instance, to protect the bacterium from antimicrobial peptides, Salmonella synthesizes proteins assigned to transport these peptides for degradation, like yejABEF and sapABCDF operons (5, 6). The smartness of Salmonella in deviating host defense is reflected in the strategy of retaining one bacterium per SCV to reduce the count of lysosome per SCV (7). Oxidative and nitrosative stresses are two most prominent immune strategies of host that can also be combated by Salmonella. For example, the detrimental effect of nitric oxide generation from arginine by host is counteracted by arginase of Salmonella which competes with iNOS for arginine (8). Also arginine is transported inside SCV via host (mCAT1 and mCAT2B) and endogenous (ArgT) arginine transporters (9).

Since, it is easier to perform genetic engineering in Salmonella as compared to other pathogenic bacteria, it can be exploited to generate information for the comparatively fastidious pathogens. The process of vacuole formation in case of intravacuolar pathogens is similar to SCV formation up to certain stage, for instance, Mycobacterium, Brucella, Legionella and Chlamydia exploit endosomal pathway and avoid fusion with lysosome by various strategies, one of them being the accumulation of cholesterol in vacuolar membrane, as seen in Salmonella (2). To quote example of extrapolation of information obtained from work on Salmonella to other pathogens, the characterization of arylamine N-acetyltransferases (NATs) in Mycobacterium in inactivating the antitubercular drug isoniazid was done based on the knowledge of NATs in Salmonella (10).

Cell culture model for Salmonella pathogenesis

As different target cells provide different environmental conditions for growth of Salmonella, they meet different fates. Infecting model cell-lines with Salmonella has revealed useful information about the mode of infection by intracellular pathogens. The cell lines HeLa, Intestine-407, HT-29 etc. serve are useful for studying Salmonella infection of monolayer of epithelial cells. Caco-2 and MDCK cell-lines on the other hand can be polarized to mimic the brush border of the gut providing a more physiological relevant model system (3). A murine macrophage like cell line RAW 264.7 is the most useful model cell line to study intracellular survival of Salmonella within macrophages. Other cell lines like murine macrophages J774-A.1 can also be used. Dendritic cells (DCs) phagocytose Salmonella and present antigens to the specific $CD4^+$ T and $CD8^+$ T cells. Although they do not provide a hospitable environment for the survival of the pathogen, they act as steady carrier of Salmonella for its passive dissemination to systemic sites (3). Primary cells isolated from bone marrow for animal models or healthy humans are used as model for dendritic cells in vitro. The human monocyte cell line THP-1 can provide for the in vitro model for monocytes.

Animal models for Salmonella pathogenesis

Use of animal models to study Salmonella pathogenesis helps to extrapolate the results to humans. There are suitable models for both kinds of salmonellosis occurring in humans i.e. enteritis and typhoid. The susceptible mouse strains Balb/c and C57BL/6, lacking Nramp1 protein, are used most commonly for *S. Typhimurium* infections, as the manifestation of disease in these mice closely resembles typhoid fever in human (11). Pretreatment with streptomycin renders mouse a suitable model to study gastroenteritis (12). Unfortunately there is no ideal animal model available for S. Typhi infection. There is provision of artificial systems like iron treated mice that compensates for the inability of S. Typhi to grow in iron deficient condition in mouse model (13). However, these are not preferred over the natural mouse model for *S. Typhimurium* infection. Introduction of humanized mice namely humanized immune system (HIS) mouse model, with the incorporation of human immune cells into the reticuloendothelial system of mouse, seems to be a promising animal model for S. Typhi infection (14). The nematode *Caenorhabditis elegans* is also used

to study the innate immune response during Salmonella infection (15). The availability of these animal model systems for various serovars has made it possible to understand pathogenesis of Salmonella better.

Conclusion

The diversity in the modes of evasion of Salmonella from host immune system gives an overall view of major strategies followed by most of the intravacuolar pathogens. Difference in the pathogenesis of different serovars, Typhi and Typhimurium, demonstrate the complicated lifestyle of a pathogen that can be tuned according to the type of host. Adaptation of such variable lifestyles is attributable to acquisition of numerous virulence associated genes over millions of years. The orchestrated action of these virulence proteins result in two major modes of Salmonella infection, local gastroenteritis or systemic typhoid. The latter imparts minimal damage to host providing optimal conditions for survival of pathogen. Recent contradictions of many established facts, such as spatiotemporal overlapping expression of SPI1 and SPI2, survival within hostile environment of neutrophils and dendritic cell mediated dissemination, describe the challenges lying in the future of Salmonella related studies. Apart from being a successful pathogen, Salmonella has served to be a useful system for various therapeutic and biotechnological applications such as tumor reduction and vaccine delivery. This further paves the path for extensive research to dissect the unknown aspects of Salmonella infection.

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Drosophila Hematopoiesis: New perspectives

Ghosh S, Singh A, Mandal S, Mandal L*

Blood cell development in Drosophila has been shown to have similarities to that of vertebrates despite some 550 million years of divergence (Evans et al., 2003). Hemocytes arise from distinct developmental waves during their development and share important signaling components necessary for their formation and differentiation. Their characterization can help elucidate basic mechanisms of blood cell development in vertebrates.

In the last few years Drosophila, thus has emerged as a very popular model to study hematopoiesis. Studies from several laboratories have illuminated the process of blood cell formation in Drosophila both during larval and embryonic stages (Crozatier et al, 2004; Evans et al., 2003; Hartenstein, 2006; Mondol et al, 2011). While the active site of hematopoiesis was reported in embryo and larvae, it was the belief of the field that no new blood cells are formed in adult fly. Studies demonstrated that the hemocyte population in the adult fly was primarily of embryonic and larval origin (Holz et al., 2003; Honti et al., 2014; Lemaitre and Hoffmann, 2007). We, however, chose to differ with the above notion. Our argument was, since Drosophila is much more exploratory in its adult life, the chances of its encounter with diverse and complex pathogens is much higher than larval phase. Thus, solely depending on the inherited stock of hemocytes might not ensure a successful combat with diverse immune challenges. We thus embarked on to an investigation directed in detailed characterization of blood cells in adult fly.

The new surge of blood cell development in Drosophila Adult:

Our study pinpoints the presence of four blood cell clusters in the fly abdominal segments. Although the aggregated hemocytes seem to be closely associated with the fly heart tube, these clusters are actually dorsal to it. The hemocytes within the cluster are intercalated in an extensive grid of extracellular matrix protein like Laminin A and Pericardin.

Interestingly, these proteins are engaged in an adhesive interaction with the hemocytes, as the loss of them affects the nesting of the blood cells. Strikingly, vertebrate bone marrow is also enriched with Laminin A (Gu et al., 2003, Siler U et al., 200) and Collagen IV like (Nilsson et al., 1998) (Drosophila Pericardin) proteins wherein these ECM components are proposed to play a pivotal role in adhesion of hemocytes.

Our lineage tracing studies clearly demonstrates that these clusters are made up of a medley of different lineages. Both the lineages of embryonic and larval hemocytes were well represented in these clusters. In addition, the cluster also houses heterogeneous progenitor cells, some of which seems to have originated from the tertiary and quaternary lobes of the larval hematopoietic organ, the lymph gland. These progenitors are capable of de novo generation of plasmatocytes and also can give rise to crystal cells, the occurrence of which was previous unknown in adult flies (Binggeli et al., 2014). Thus, these hemocyte clusters are not just a stockpile of blood cells but harbours progenitors that can differentiated on site into distinct lineages. These sites of active hematopoiesis thus prompted us in naming them as "adult hematopoietic hubs" (Fig. 1).

The resident hemocytes in the hematopoietic hub are primed for immune challenges:

The plasmatocytes within this hub shows dynamicity in their number with age. Using a marker for differentiated plasmatocytes (hml-GFP), we found that there is a gradual increase in their number till day fifth post eclosion, thereafter, with aging; a steady fall in the plasmatocyte number is observed. Our further investigation revealed that the initial increment in number of plasmatocytes till fifth day post eclosion is due to the formation of new plasmatocytes from the resident precursors as well as homing of circulating hemocytes in young adults. Alternatively, the gradual loss in resident plasmatocytes in the hub post eight day of eclosion indicates that the aging adult is using the hemocytes from the hub to combat infections.

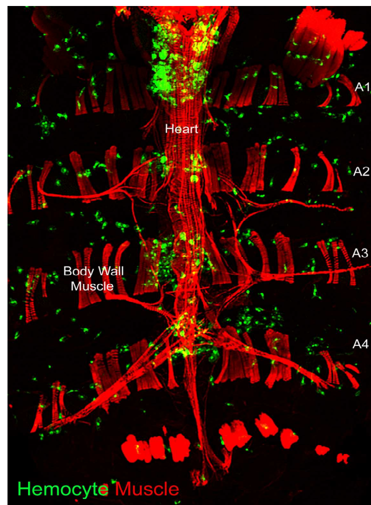

Fig. 1. Hematopoietic Hub-in-Adult fly. Hemocyte (green) are embedded in extracellular matrix (ECM) (red).

If that is so, the plasmatocytes within the hub should have the ability to mount response to an immune challenge. Indeed when challenged with RFP labeled bacteria (E. coli) the plasmatocyte in the hub are able to phagocytose the bacteria, confirming the fact that they are primed and ready to encounter immune challenges. Strikingly, soon after infection, within a span of 24 hours, the hematopoietic hub has only few hemocytes present. This speedy release of bulk hemocyte population from the hub within such a short duration emphasizes the involvement of the hub in aiding the adult fly to deal with infections.

Studies conclude that unlike larval hemocytes, Drosophila adult hemocytes are locked in senescence (Honti et al., 2014). However, these otherwise quiescent hemocytes are coaxed to proliferate in a bacterial infection indicating that an immune signal might have evoked this response. Interestingly, this mirrors a similar situation in vertebrate wherein an immune response prompts enhanced hematopoiesis in the bone marrow and in peripheral tissues. It would be intriguing to decipher the molecular signals involved in the regulation of hematopoiesis during an immune response.

Hematopoietic hubs constitute a Simpler version of Bone Marrow

The circulating hemocytes generated during embryonic and larval stages home to the hematopoietic hub. This bears a resemblance with seeding of the mammalian bone

marrow(Mikkola and Orkin, 2006), extending the conservation of hematopoietic events across the two taxa. The onset of definitive hematopoiesis occurs in the larval hematopoietic organ, the lymph gland. Some of the precursors that undergo expansion within the lymph gland actually homes into the hematopoietic hub in adult fly. These precursors are not homogeneous. Some of them can directly differentiate into plasmatocyte fate. While few bipotent precursors exist, which initially turn on Notch and those that subsequently maintain Notch signaling adopts crystal cell fate. Interestingly in those where Notch signaling has been down regulated adopts plasmatocyte fate. Thus, we conclude that precursors are of two kinds a) biased for plasmatocyte lineage and b) balanced bipotent precursors that can give birth to both plasmatocytes and crystal cells.

Strikingly, this mirrors a resemblance to the different types of HSCs present in the vertebrate the bone marrow. Based on their capability to give rise to either myeloid or lymphoid precursors they are classified into three types: a) myeloid biased, b) lymphoid biased and c) balanced HSCs that are bipotent in nature and thus can give rise to both myeloid and lymphoid lineages (Muller-Sieburg et al., 2004; Muller-Sieburg et al., 2002).

We speculate that since Drosophila hemocytes are only of myeloid lineage, the precursors in the hematopoietic hub of adults are of therefore of two kinds.

The conservation of hematopoietic events mentioned above along with the fact that the cells of the hub are embedded in a functional network of ECM proteins that include Laminin A and Pericardin, projects this hematopoietic hub as a simple version of the vertebrate bone marrow. We believe that this simpler yet genetically amenable model will help us in addressing problems related to normal and aberrant hematopoiesis, hematopoietic stem cells, wound healing and aging.

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Note: This article is the summary of work already published. Readers are suggested to read the following paper for further details.

Ghosh S, Singh A, Mandal S & Mandal L (2015) Active Hematopoietic Hubs in Drosophila Adults Generate Hemocytes and Contribute to Immune Response. Develop Cell 33:478-88.

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Toll like Receptors for cancer therapy: Prospect and problems

Aradhana Singh and Anupam Basu*

Toll like receptors (TLRs) are evolutionary conserved germ line encoded pattern recognition receptors (PRRs) (Zhao et al., 2014, Awasthi et al., 2014). TLRs expresses mainly in immune cells but it also expresses in non immune cells like urogenital, intestinal, respiratory tract, endothelial, fibroblast and other cells Over-expression of TLRs has been reported in many cancers (So and Ouchi, 2010) that may be pro-tumorigenic or antitumorigenic (Huang et al., 2008, Basith et al., 2012). TLRs recognizes pathogen associated molecular pattern (PAMPs) expressed by pathogens to trigger most appropriate host immune response to abolish the infection. Apart from exogenously derived PAMPs, endogenously derived damage-associated molecular patterns (DAMPs) from dead or stressed cells are also ligands of TLRs (Melisi et al., 2014). Up till now, at least 10 members of TLRs family have been recognized in humans (Frosali et al., 2015). Positions of TLRs in the cells are variable. TLR1, 2, 4, 5 and 6 are expressed on the surface of the cells that whereas TLR3, 7, 8 and 9 were generally in endosomal/lysosomal membranes as they recognize nucleic acid structures (Szatmary , 2012). But recently it has been reported that TLR 3 may induce cell proliferation through cell surface (Bondhopadhyay et al., 2015). On the basis of their potential value of antitumor activity, TLRs are good choice for combination therapy for cancer. A variety of TLR agonists are presently under clinical trials for their antitumor capability either as monotherapy or as adjuvants to vaccination or other therapeutic modalities (Kaczanowska et al., 2013, Lu, 2014)

TLR 2 agonist polysaccharide krestin (PSK) shows antitumorigenic activity when administrated orally in transgenic mice by activating CD8 (+) T-cell and NK cells (Yusuf ,2014). In colon cancer, CpG islands of TLR 2 promoter are hypermethylated (Baylin et al., 2008), It has been reported that advance stage of cervical cancer expresses TLR2 (Ghosh et al. 2015). Chemically synthesized dsRNAs poly A-U or poly I-C is the main agonist of TLR3. Preclinical study shows induced type 1 interferon production by blood mononuclear cells by these two ligands. In human prostate and breast cancer cells, TLR3 shows pro-apoptotic

effect. Apoptosis is a effective mechanism of tumor cell removal, therefore TLR3 ligand can be a exceptionally useful tool for cancer therapy (So and Ouchi, 2010).TLR3 stimulation is associated with anti-tumorigenic effects in most of the cancers like breast, colon, cervical, head and neck, melanoma, myeloma and prostate cancer but hepatocellular carcinoma shows pro-tumorigenic effects also. In lung cancer, there is both pro-tumorigenic as well as anti-tumorigenic activity of TLR3 is reported (Kaczanowska et al., 2013). TLR3 has been over-expressed in many cancers including breast cancer (Yusuf, 2014). It has been shown that cell surface stimulation of TLR3 liagnd Poly (I:C) can promote proliferation and metastasis of breast cancer cells (Bondhopadhyay et al., 2014). Phase II/III clinical trial has been undertaken using TLR 3 agonist Poly-I-C along with Flt3L low-grade in lymphoma patients under, NIH, USA (Trail ID: NCT01976585, 2013).

According to the existing condition of tumor microenvironment through various phases of cancer advancement or metastasis, TLR4 can exert pro or anti cancer effects (Awasthi et al., 2014). TLR 4 has been reported to be over expressed in various tumors (Mai et al., 2013). Challenging with TLR4 agonist LPS to hepatocellular carcinoma increase the cell proliferation (Wang et al., 2013). Upon silencing of TLR4 by siRNA decrease the invasive ability of cancer (Earl et al., 2009), On the contrary, it has been reported that there is increasing of metastasis in murine model breast cancer, upon silencing of TLR4 (Ahmed et al., 2013). Phase I clinical trial under NIH, USA with TLR 4 agonist glucopyranosyl lipid A stable-emulsion (GLA- SE) along with radiation therapy shows improved results of the patients suffering from sarcoma (Trial ID: NCT02180698, 2014). In another study, administration of GLA-SE with MART-1 antigen (melanoma antigen recognized by T-cells 1) enhances immune response (Trial ID: NCT02320305, 2014). In the multicenter phase I/II clinical trial with intratumoral injection of G100 (potent TLR4 agonist) to the patients of Merkel Cell carcinoma and sarcomas, shows positive response (Trial ID: NCT02501473, 2015).

TLR5 was reported to be over expressed in breast as well as human gastric cancer cells. Upon stimulation with TLR5 agonist, flagellin, there is a blockade in breast cancer cell

proliferation via down regulation of cyclin B1, cyclin D1, and cyclin E2 in mouse model. Flagellin challenged human gastric cancer cells were proliferative by overproduction of IL-8. In tissue culture of head and neck cancer cells and in xenograft model of human colon cancer, flagellin stimulation, suppresses tumor growth (Kaczanowska et al., 2013). Phase I clinical trial has been performed using Entolimod (TLR-5 agonist) on locally advanced or metastatic solid tumor that cannot be removed by surgery (Trial ID NCT01527136, 2011).

Imidazoquinoline compounds are the core agonists of TLR 7/8. Synthetic imidazoquinoline compounds were used during clinical trials (So and Ouchi, 2010). TLR7 and TLR8 have been reported to be over expressed in lung cancer. Ligand challenge increases the chemoresistance of this cell line followed by treatment with combination of cycloheximide, cisplatine, carboplatine, doxorubicin, and Navelbine (Cherfils-Vicini, 2010). Clinical trial under NIH, USA using agonist Imiquimod on recurrent or metastatic breast cancer has been done (Trial ID: NCT00899574, 2009). In a, single center controlled study using Imiquimod had been completed to analyze the Immune escape mechanisms of HPV-associated lesions and to evaluate the efficiency and mechanisms of vulvar intraepithelial neoplasias 2/3 (VIN) and anogenital Warts (Trail ID: NCT00941811, 2009). In melanoma yet another TLR 7 agonist Resiquimode (R848) has been studied as vaccine in combination with gp100 (g209-2M), and MAGE-3 (Trial ID: NCT00960752, 2009). TLR8 agonist VTX-2337 along with monoclonal antibody, cetuximab shows positive result in locally advanced, recurrent, or metastatic squamous cell cancer of the head and neck (SCCHN) (Trial ID: NCT01334177, 2011). TLR 8 agonist VTX-2337 together with pegylated liposomal doxorubicin hydrochloride or paclitaxel was studied at phase I trial and it is predicted that they may kill more tumor cells than they do alone. (Trial ID: NCT01294293, 2011).

A wide range of in-vitro cell lines as well as human cancer samples, including breast cancer, gastric cancer, hepatocellular carcinoma, cervical squamous cell carcinoma, glioma, prostate cancer, colorectal cancer and neuroblastoma over expresses TLR9 (Melisi et al., 2014, Ghosh et al. 2015). TLR9 shows evidences of both pro-tumoric and anti-tumoric effects (Melisi et al., 2014). In human glioma cell, stimulation of TLR9, suppresses the

proliferative activity via cell cycle arrest (Li et al., 2012). But in another report, it has been shown that TLR 9 increases the invasive capacity of glioma (Wang et al., 2010). In human breast and gastric cancer, TLR 9 induces cell growth via over production of MMPs. While in lung cancer same effect observed via overproduction of IL-8, IL-1 and IL-6 (Kaczanowska et al., 2013). Phase I/II clinical trial of TLR 9 agonist SD-101 in combination with radiation therapy and monoclonal antibody, ipilimumab showed positive result in B-cell lymphoma. (Trial ID: NCT02254772, 2014). Clinical trial using other TLR agonists CpG7909 in combination with URLC-10-177 and TTK-567 on advanced or recurrent esophageal cancer had been undertaken (Trial ID: NCT00669292, 2008). Another clinical trail with TLR9 agonist IMO-2055 combined with FOLFIRI cetuximab on patients with colorectal cancer had also been undertaken (Trial ID: NCT00719199, 2008).

In spite of very promising use of TLRs for adjuvant therapy or combination therapy, there are few limitations. Most of the TLRs have dual role for cancer progression. For this reasons some of the clinical trials have been withdrawn. Recently from our laboratory, it has been shown that when breast cancer cells were challenged with the TLR-3 ligand Poly (I:C), through cell surface there was cell proliferation On the other hand cytoplasmic delivery of poly (I:C) causes growth retardation (Bondhopadhyay et al., 2014). This may be due to alternative mode of TLR signaling or variations of the expression of TLRs in the tumor micro-environments. Thus understanding the TLR signaling pathway in different tumor and its micro- environments are crucial for the success of the TLR mediated drug formulation.

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Clinical Trail No, NCT02320305 Peptide Vaccine With Glucopyranosyl Lipid A - Stable Oil-in-Water Emulsion (GLA-SE) for Patients With Resected Melanoma.

ClinicalTrials.gov Identifier: NCT02501473 Phase 1/2 Study of Intratumoral G100 Therapy in Patients with Follicular Non-Hodgkin's Lymphoma.

ClinicalTrials.gov Identifier: NCT00899574 Phase II Evaluation of Imiquimod, a Topical Toll-like Receptor 7 (TLR7) Agonist in Breast Cancer Patients with Chest Wall Recurrence or Skin Metastases.

ClinicalTrials.gov Identifier: NCT00960752. Activation of pDCs at the Tumor and Vaccine Site with a Toll Like Receptor (TLR) Agonist.

ClinicalTrials.gov Identifier:NCT00941811. An Explorative, Single Center and Controlled Study to Analyze the Immune Escape Mechanisms of HPV-associated Lesions and to Evaluate the Efficiency and Mechanisms of Imiquimod Treatment of Vulvar Intraepithelial Neoplasias 2/3 (VIN) and Anogenital Warts.

ClinicalTrials.gov Identifier: NCT01294293. A Phase I Study of VTX-2337 in Combination With Pegylated Liposomal Doxorubicin (PLD; NSC# 712227) or in Combination With Weekly Pactilaxel (NSC #673089) in Patients With Recurrent or Persistent Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer.

ClinicalTrials.gov Identifier: NCT00669292. Phase I/II Study of URLC10-177 and TTK-567, Novel Tumor Specific Epitope Peptides Restricted to HLA-A*2402 Derived From Tumor Associated Antigens, Combined With CpG7909, a TLR9 Agonist, in Patients With Advanced or Recurrent Esophageal Cancer.

ClinicalTrials.gov Identifier: NCT00719199. Open-label Phase 1b Study of FOLFIRI Plus Cetuximab Plus IMO-2055 in Patients With Colorectal Cancer Who Have Progressed Following Chemotherapy for Advanced or Metastatic Disease.

ClinicalTrials.gov Identifier: NCT01527136. Entolimod in Treating Patients with Locally Advanced or Metastatic Solid Tumors That Cannot Be Removed By Surgery.

ClinicalTrials.gov Identifier : NCT01728480 Entolimod in Treating Patients With Stage III-IV Squamous Cell Head and Neck Cancer Receiving Cisplatin and Radiation Therapy.

ClinicalTrials.gov Identifier: NCT01204684. Dendritic Cell Vaccine for Patients With Brain Tumors

ClinicalTrials.gov Identifier: NCT01334177. TLR8 Agonist VTX-2337 and Cetuximab in Treating Patients with Locally Advanced, Recurrent, or Metastatic Squamous Cell Cancer of Head and Neck.

ClinicalTrials.gov Identifier: NCT02254772. TLR9 Agonist SD-101, Ipilimumab, and Radiation Therapy in Treating Patients With Low-Grade Recurrent B-cell Lymphoma.

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21st Century Corner

Science and India

What is Science?

In my opinion it is the systematic arrangement of observation, thoughts, ideas, study and experimentation and the objective of which is to identify the hidden questions behind the physical Universe and understanding the principle behind it. The universe we see today has been brought to the present shape by some of the great people we got in the world because of their constant thinking, keen observation and the desire to ask themselves the question why? What if Einstein wouldn't had seen and thought of why apple can't go up and only falls down or what if Columbus wouldn't have thought of exploring the earth, we wouldn't have got the idea that earth is round. These are some very simple examples which suggest that thinking, observation and curiosity to know are the fundamentals of Science and if you are observing your surrounding and curious to know why the things are the way it appears to be, you can answer many questions in life.

What is Pseudo-science?

As the name suggests, pseudo means 'fake'. While real Science is identifying the evidence, designing the meaningful experiments, testing of hypotheses, establish theories, and then draw reliable conclusions and make a statement, pseudo-Science is nothing but collecting lots of cited publication, set up a hypothesis, repeat some of the experiments in a modified way, collect hearsay, and on top of that pore over ancient religious or mythological works. Sometimes it is even like, have a result, built a hypothesis and prove it. I feel hard to even believe how many Scientists, in India, are working as an independent investigator who has some real questions to answer. I think very few.

India is itself the place of origin of a number of remarkable discoveries. Contribution of India to Mathematics by understanding zero and one, the Pythagoras theorem and what not tells the involvement of India in Science through ages. The Indus Valley civilization has evidence of the origin of Science in India. Some of the extra-ordinary technologies used by

the people of these civilizations are the proof of origin of technologies since ancient times. But even today, with 1.3 billion population and a steady growth rate, we still have far to go to even come into competition with the even the other developed Nations. So, the question arises why even with such a stark beginning India is still lagging behind the rest of the world in the quality of Science they do and are often underscored in their scientific temperament. Indians are now representing the world as a CEOs' of most of the leading technology and research based companies in US and other countries. They are representing almost all the sectors in the world including Science. Then why the people with the same brains can't produce the same quality work or can't take the level of Science to bring in India as well among the topmost leading country in Science? Out of 1.3 billion people in India, why not even 1300 people are able to represent India in India. For example, DRDO which is one of the most reputed organizations in the country for defense, was at the urge of being getting closed because of the inability to give expected advancement. Where are we lacking? Are we not doing real science in India??

According to one of the leading newspaper report, survey suggests "India spends less than 1% of its gross domestic product (GDP) on R&D. China spends 2%, the US 2.8%, Japan 3.4% and Korea 4%. India's share of global R&D stands at a dismal 2.7% when compared with 30% for the US. Even China now accounts for almost 15% of such spending, having doubled in total between 2008 and 2012'. Some questions I keep getting answers being a researcher: Why the researchers in India are not given so much importance? Why we can't have 100 institutes like IITs and IISC so that maximum people are able to get similar level of exposure and are excited to do real Science? Why our country can't bring research to a leading level that people get fascinated in doing it and not just do it for the sake of getting money or some publications? Why 90% students keep Ph.D. as their last option in their career goal and the rest 10% also who keeps, 9 % would like to go abroad because they think that the level of Science and research will not be comparable to the other powerful Nations like US? Why we are so much restricted in terms of technologies and facilities available in our research Institutes. Why after putting some 10 long years in studies and getting doctorate degree, the highest degree in any field, Indian Researchers have to struggle to get job and settle. Why we don't have enough good research institutes which

require scientists and offer those reputable jobs and those who have these jobs, they think of representing India at an international level instead of taking it just merely a job of publishing article? And many more!

For some I think we have the answer. We have to dream of India where we build a scientific temperament in the children right from the beginning which fascinates them for doing real Science and not just Pseudo-Science. We have to dream of India where almost 90% of the Indians prefer opting for Research and want's to be a next Dr. Abdul Kalam. We have to dream of a nation where the children are brought up in an environment so that People are fascinated by Science and get the best opportunities to represent India, in India. Though the significant steps are being taken up by the Government in this regard, but a lot more has to be done. We have to bring the research institutes of India to such a level that everybody have the desire to be a part of it, be it terms of money or technologies. We have to bring back the brains of India back to India so that they can create miracle here itself. And this is not at all impossible!!

Dr. Natasha Jaiswal
Indian Institute of Science,
INDIA.

All India Cell Biology Conference announcements

The annual meeting of the Indian Society of Cell Biology year 2015, and 39th All India Cell Biology Conference is being jointly organized by IISER-TVM and Rajiv Gandhi Centre for Biotechnology, during Dec. 6-8, 2015, at Thiruvananthapuram, Kerala.

Details can be found out on conference webpage www. http://conference.iisertvm.ac.in/cbc, which is also displayed on society webpage www.iscb.org.in

All are requested to register and attend the conference.

New proposals are invited for hosting next annual meeting and 40th AICB conference in year 2016. Please send your request for discussion in next EC meeting to be held in Thiruvananthpuram, Kerala.

Department of Atomic Energy –Board of Radiation and Nuclear Sciences (DAE-BRNS) funding for Research Projects in India

Department of Atomic Energy has been promoting collaborative research by granting Research Projects (RP) to different academic and R&D institutions in India, through its Board of Research in Nuclear Sciences' (BRNS). During the recent years, a lot of changes have taken place in the functioning of BRNS. Current mandate is to bring about synergy between scientists working on different aspects of the same problem. BRNS would be promoting complementary research on topics which either relevant to the DAE programs, innovative or scientifically attractive at par with world class research. One of many initiatives adopted by the BRNS in this direction is to provide contact details of some of the DAE scientists, called the Principal Coordinator (PC), who would be actively participating in formulation, coordination and execution of research projects involving one or more number of researchers (Principal Investigators: PI) from Non-DAE units.

Investigators across India are invited to interact with the prospective PC, formulate full project as per the guidelines given in the Project Proposal Application (PPA) form and submit collaborative research proposals, if their expertise and interest match with the titles displayed on BRNS website www.daebrns.gov.in. As the BRNS activities are fully web based and its contents are regularly updated, the notifications and updates on the site must be checked at its webpage http://daebrns.gov.in , and apply for BRNS funding.

Homi Bhabha National Institute (HBNI)

(Research and academic opportunities for students in India in Department of Atomic Energy)

Homi Bhabha National Institute (HBNI) was accredited as a deemed to be university by the Ministry of Human Resource Development (MHRD) vide notification dated June 3, 2005, to encourage pursuit of excellence in sciences (including engineering sciences) and mathematics in a manner that has major significance for the progress of indigenous nuclear technological capabilities. HBNI is working towards its mandate and brings together the academic programs of ten premier institutions of the Department of Atomic Energy (DAE) located in different parts of India. Ten institutions are Bhabha Atomic Research Centre, Indira Gandhi Centre for Atomic Research, Raja Ramanna Centre for Advanced Technology, Variable Energy Cyclotron Centre, Saha Institute of Nuclear Physics, Institute for Plasma Research, Tata Memorial Centre, Harish-Chandra Research Institute, Institute of Mathematical Sciences, and Institute of Physics. These Institutes, called as the constituent institutes (CIs) of HBNI have been engaged in research for several decades and their coming together makes HBNI is a research university par excellence.

HBNI educates students at the doctoral and masters level, and its academic programmes cover chemical sciences, engineering sciences, **health sciences**, **life sciences**, physical sciences, and mathematics. Like other reputed institutes and universities, HBNI activities are supervised and managed by a Council of Management, an Academic Council and various Boards of Studies. Faculty at HBNI has excellent research credentials and many members of faculty are recipient of prestigious academic awards. HBNI admits Ph.D. students in all disciplines of sciences including **Health** and **Life Sciences** to work in BARC, TMC and its other CIs. HBNI grants DAE research fellowship to eligible students selected through a highly competitive written test / GATE scores followed by a very interactive yet rigorous interview. For further details please visit university webpage www.hbni.ac.in.

MOHIT K. SAIGAL &CO
CHARTERED ACCOUNTANTS

B-37/122, SAIGAL HOUSE
MAHMOORGANJ, VARANASI
UTTAR PRADESH-221010
PH.0542-2360015, M.No.7275660055

INDIAN SOCIETY OF CELL BIOLOGY

BALANCE SHEET AS ON 31 MARCH,2015

LIABILITIES	AMOUNT	AMOUNT	ASSETS	AMOUNT	AMOUNT
CAPITAL FUND ACCOUNT:			INVESTMENTS		
Opening Balance	2,170,383.05		As per Schedule '1'		2,509,962.17
Add: Excess of Income over Expenditure	243,241.00	2,413,624.05	CURRENT ASSETS & LOANS & ADVANCES :		139,873.00
			As per Schedule '2'		
L[illegible]E MEMBERSHIP FEES:			CASH & BANK BALANCES:		
Opening Balance	610,463.00		Cash	23,690.10	
			SBI, Varanasi	454,524.78	
Add: during the year	104,100.00	714,563.00	State Bank Of Hydrabad	137.00	
					478,351.88
Audit Fees Payable					
TOTAL		3,128,187.05	TOTAL		3,128,187.05

For INDIAN SOCIETY OF CELL BIOLOGY

Executive Secretary
INDIAN SOCIETY OF CELL BIOLOGY

P[illegible]CE : VARANASI
DATE : 23.09.2015

As Per Record Produce Before us

Mohit K. Saigal
(PARTNER)
M.NO. 016988

MOHIT K. SAIGAL & CO
CHARTERED ACCOUNTANTS

B-37/122, SAIGAL HOUSE
MAHMOORGANJ, VARANASI
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INDIAN SOCIETY OF CELL BIOLOGY
Receipts & Payment A/c for the period 01.04.2014 to 31.03.2015

RECEIPTS		AMOUNT	PAYMENT		AMOUNT
To **Opening Balances:**			By Investment in FDR (HDFC)		300,000.00
Cash in Hand	64.10		By Shyam		20,000.00
SBI, Varanasi	300,839.78		By Printing & Stationery		3,137.00
State Bank Of Hydrabad	48,839.00	349,742.88	By APCOB Travell Grant		10,000.00
			By XXXVIII AICBC meeting Grant		25,000.00
			By Honorarium		6,000.00
			By Grants for Hands on Workshop, Luck.		20,000.00
To **Membership Fees :**			By Postage Exps.		117.00
Student & Ordinary.	27,310.00		By Mementos		15,875.00
Life Membership Fees	104,100 00	131,410.00	By Travell Support Exps.		28,263.00
			By XXXIX AICBC meeting Grant		25,000.00
			By Hands on Workshop, Lucknow		20,000.00
			By Misc, Exps.		2,677.00
To Interest on SB A/c		9,668.00	By Bank Charges		750.00
To Interest From HDFC		264,350.00			
To HDFC FDR Matured		200.000.00			
			By **Closing Balances:**		
			Cash	23,690.10	
			SBI, Varanasi	454,524.78	
			State Bank Of Hydrabad	137.00	478,351.88
Total		955,170.88	Total		955,170.88

For INDIAN SOCIETY OF CELL BIOLOGY

Executive Secretary
INDIAN SOCIETY OF CELL BIOLOGY

PLACE : VARANASI
DATE : 23.09.2015

As Per Record Produce Before us

(Chartered Accountants)
(CHARTERED ACCOUNTANTS)

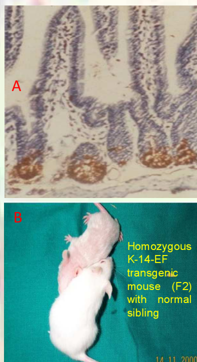
Mohit K. Saigal
(PARTNER)
M.NO. 016988

Anticipated articles for next issue of Newsletter

1. Bacterial model system for studying molecular basis of radiation resistance in mammalian cells
2. *In vitro* model for cytokinesis in eukaryotes
3. Cell cycle regulation and territorial movement of functional chromosomes in response to DNA damage in eukaryotes.
4. Topoisomerases, their functional diversity and promising targets of antibacterial and anticancer drugs.
5. Peptides mimicking helical structure of double stranded DNA and their appearances in directed basic research.
6. Nanoscience and nanotechnology, and non-coding small RNA research in India and expectations (views).
7. Green and Clean energy for environmental safety

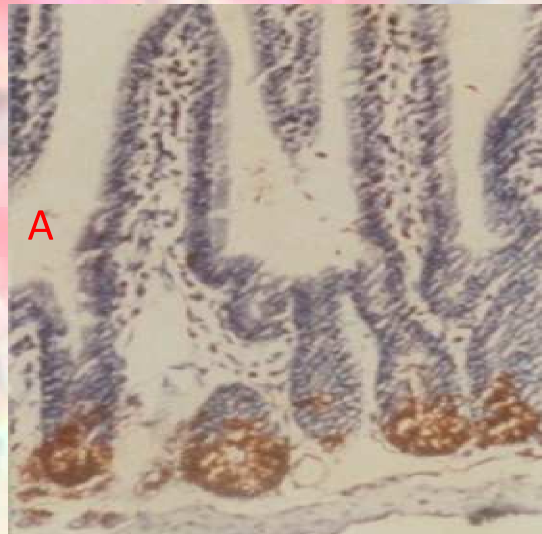
> ***Whatever you are doing, put your whole mind on it. If you are shooting, your mind should be on the targets.*** **Swami Vivekananda**

Back cover illustration



A. ***Mouse intestinal section stained with H&E and anti-EF. Paneth cells at the base of the villi show positive staining which is brown in color here.***
B. ***Hairless homozygous mouse on left next to a wild type sibling.***

CellBiologyNewsletter



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