SDUAHER

SRI DEVARAJ URS ACADEMY OF HIGHER EDUCATION & RESEARCH
TAMAKA, KOLAR – 563103
(A DEEMED TO BE UNIVERSITY)

Fourth National Research Seminar

OPPORTUNITIES & CHALLENGES IN MEDICAL RESEARCH IN INDIA

8-9 March 2013

SCIENTIFIC PROCEEDINGS

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MESSAGE

Sri R.L.Jalappa
President
SDUAHER

I am pleased to note that Sri Devaraj Urs University has successfully organized the 4th National Research Seminar on 8-9 March 2013. It is commendable that the organizers have chosen a very important theme for the Seminar – ***'Opportunities & Challenges for Medical Research in India'***.

Eminent scientists from the country have participated in the seminar and enriched the research culture in our University. The scientific presentations have been brought out in this Souvenir.

-sd-

(Sri R.L.Jalappa)

FOREWORD

Dr.P.F.Kotur, MD, Ph.D
Vice Chancellor
SDUAHER, Kolar

Even though Medical research in India is yet to match the international standards, there has been resurgence of interest in recent years in the same and significant contributions are being made by scientists from some of the premier research institutions of the country. With the strategic enhancement in the number of institutions for medical education and health care service delivery in the country, there is a palpable potential for need based medical research in all these institutions. Complimentary to the scenario is the Government's keen interest in actively promoting research with potential for positive impact on health care delivery systems across the country all aimed at improvising the health status of the community.

Keeping up the tradition of the previous 3 years of organizing a national convention on medical research, this 4th National Research Seminar on the theme of '**Opportunities and Challenges in Medical Research in India**' is being organized by Sri Devaraj Urs Academy of Higher Education and Research, Kolar on 8th – 9th March 2013. It is an appropriate and honest effort made to bring eminent biomedical scientists on a common platform. This effort of sowing the seeds of research in the young minds of the medical students and fraternity is one of the University's foremost goals.

I am happy about the Souvenir being brought out on this occasion, compiling the scientific proceedings of this mega event, which I am sure, shall benefit many young researchers in the time to come.

-sd-
(Dr.P.F.Kotur)

PREFACE

Prof. P.R.Krishnaswamy
Research Advisor for
SDUAHER & Chairman,
4th National Research
Seminar

At our university a significant tradition of academic congregation annually of peers drawn from India and some from overseas has been firmly established. A two-day feast of discourses on advances in medical science, basic biomedical topics, public health and topical community medicine themes have inspired, enthralled and stimulated faculty, students and researchers on the campus. Meticulous planning and conformity to high standards in the choice of topics, eminence of speakers for presentations have received unfailing attention in organizing these events. It is indeed gratifying that the Fourth National Research Seminar held this year has not only kept these bench marks in good tradition, but surpassed those blending elements very foundational for meaningful research in medical teaching institutions, in contemporary terms. Themes on herbal medicines, the burning topic of maternal and neonatal mortality among the rural poor, prevention and interventions thereon, evidence based medicine, challenges in medical research applications – are topics which were addressed and received well. The insightful attention to put these discourses and the eminent speakers together was the hallmark provided by the Honorable Vice-Chancellor Prof P.F.Kotur, who played an inspired part in the memorable event.

In a striking and memorable match to these deliberations, basic biomedical sciences and clinical sciences were recognized both for their topicality and current value, contents of the subject matters, and expertise and eloquence of the speakers. With the keynote address on "Medical Research in an Interdisciplinary Environment" by Prof. P.Balaram, was essentially rendered in most lucid terms his own work on haemoglobins and enzymes like TPI in translational significance. The take home message was *'all basic biological research is of translational value, now or in the future'* and this is the history of medicine. Dr.V.Mohan's discourse on Diabetes epidemic was an epic in its themes and content, a significant portion

being his contribution. 'Disease Biology' in the coming decades by Prof. M.R.S.Rao, 'Brain Plasticity' by Prof. B.S.Rao, 'Disease Pathways in Neurological Disorders' by Dr. Chandran Gnanamuthu and 'Epigenetics in Cancer' by Prof. Kundu all represented the fascinating biomedical research ripe for translational fusion with clinical medicine. In fact, at a near date in the future we would serve the cause of medical science on our campuses well to bring out well edited and formatted monographs of such events. The ongoing work at our University in clinical and laboratory genomics, anecdotal and interdisciplinary in nature was an indicator of the shape of things to come.

The crowning glory to the two day seminar was conferred by none other than the country's doyen and leader in medical research, Dr. V.M.Katoch, the Director General of Indian Council of Medical Research. An outstanding researcher in his own right and a realistic and pragmatic leader who has provided clarity and direction to the country's medical research, with problems in public health receiving the most attention and resources, Dr. Katoch's pronouncements on what areas need thrust and how networking with other agencies can maximize outcomes and emphasis on commitment at all levels made a deep impression on the participants. One could surmise from his comprehensive, lucid and clear pronouncements of policy, critique and positive suggestions for active research, that we could count on his leadership to surely make rapid strides in medical research. Dr. Katoch indeed put an indelible stamp of his intellectual purity and commitment to public health through relevant medical research. The fourth National Research Seminar will be remembered by some of us at the meeting for his inspiring presence.

We may justifiably hope that the annual National Research Seminar we continue to hold in Kolar will go far innovatively, will continue to be cerebrally stimulating and productively spurring us to newer levels of creativity in research and services.

-sd-
(Prof. P.R.Krishnaswamy)

CONTENTS

Fourth National Research Seminar, SDUAHER, 8-9, Mar 2013
Scientific Program Schedule
***Venue*: University Auditorium, SDUAHER, Kolar**
DAY 1: 8th March 2013 (FRIDAY)

10.00-10.30 am	**Inauguration of 4th National Research Seminar By Sri RL Jalappa, President of SDUHER Dr.P.F.Kotur, Vice Chancellor of SDUAHER, Chief Guest-Prof.P.Balram, Director of IISc, Bangalore**		
Time	***Speaker***	***Title***	***Chairpersons***
10.30-11.30am	**Padmashri Prof. P. Balaram,** Director, IISc, Bangalore	Key-Note Address on 'Medical Research in an Interdisciplinary Environment'	
11.45-12.30 pm	**Padmashri Prof. M.R. Satyanarayana Rao,** President, Jawaharlal Nehru Centre for Advanced Science Research, Bangalore	"Disease Biology in the coming Decade(s)"	**Dr.Shivaprasad S Goudar** Research Coordinator, JNMC, Belgaum **Dr.Harendra Kumar** Prof & HoD, Dept. of Pathology, SDUMC, Kolar
12.30-1.15 pm	**Padmashri Dr.V. Mohan,** Dr.Mohan's Diabetes Specialties Centre, Chennai	"Diabetes Epidemic in India – Why and What can be Done?"	**Dr.Nilgar** Prof of OBG, JNMC, Belgaum **Dr.Lakshmaiah** Med Suptd., RLJ Hospital
2.00-2.45 pm	**Dr.B.S.Shankarnarayana Rao** Add Professor Dept. of Neurophysiology NIMHANS, Bangalore	'Novel Research approaches to unravel the Brain Plasticity & Repair mechanisms: New Challenges in treating Neurological & Psychiatric Disorders'	**Dr.Subarna Roy** RMRC (ICMR), Belgaum **Dr. Kathyanee Kutty** Prof & Head of Physiology SDUMC, Kolar
2.50-3.35pm	**Dr. Chandran Gnanamuthu** Formerly Prof & Head of Neurology at CMC, Vellore. Neurologist-SDUMC, Kolar	'Disease Pathways in Neurological Disorders'	**Dr.Sanjiv D Kholkute** Director, Nat Inst of Research (ICMR), Mumbai **Dr.P.R.Krishnaswamy** Research Advisor, SDUAHER
3.40-4.25pm	**Dr. Stephen Brett** Head for Research, Directorate of Anaesthetics & Critical care. Imperial College Health Care, NHS Trust, London, UK	"Matching Study Design to the Research Question"	**Dr.Shivaprasad S Goudar** Research Coordinator, JNMC, Belgaum
6.00-7.30 pm	**Cultural Programme**		

DAY 2: 9th March 2013 (SATURDAY)

Time	*Speaker*	*Title*	*Chairpersons*
9.30-10.15am	**Dr.Sanjiva. D. Kholkute,** Director, National Inst. for Research in Reproductive Health (ICMR), Mumbai	'Herbal Medicine: Challenges and Research Needs'.	**Dr.AVM Kutty** Registrar, SDUAHER **Dr.B.G.Ranganath** Prof & Head of Community Medicine, SDUMC, Kolar
10.20-11.05 am	**Dr. Subarna Roy,** Regional Medical Research Centre, Belgaum	"Publications in Medical Research and Present Challenges ".	**Dr.S.R.Prasad** Prof of Microbiology & Director of PG Studies, SDUMC, Kolar
11.20-12.05pm	**Dr.Shivaprasad. S. Goudar,** Director, Dept. of Medical Education Research co-ordinator, Women's & Children Health Unit, JNMC, Belgaum	"Community Based Interventions for Preventing Maternal and Neonatal Mortality in Resource Poor Settings: Experiences of Jawaharlal Nehru Medical College, Belgaum"	**Dr.M.Narayanaswamy** Prof & Head of OBG, SDUMC, Kolar **Dr.C.Muninarayana** Prof in Community Medicine, SDUMC, Kolar
12.10-1.00 pm	**Dr. P.F. Kotur** Vice-Chancellor SDUAHER, Kolar	"Evidence Based Medicine"	**Dr.Shivaprasad S Goudar** Director, Dept of Medical Education & Research Coordinator-Women & Children's Health Unit, JNMC, Belgaum
1.45-2.25 pm	**Prof.P. Kondiah,** Dept. of Molecular Reproduction, Development & Genetics, IISc, Bangalore	"Gene expression studies and their utility in the management of Cancer patients"	**Dr.P.R.Krishnaswamy** Research Advisor SDUAHER, Kolar
2.25-3.05 pm	**Dr. P.R. Krishnaswamy** Scientific Advisor SDUAHER, Kolar	"The Kolar Experience in Laboratory Driven Medical Research – Some Anecdotes"	**Dr.Subarna Roy** Regional Medical Research Centre, Belgaum **Dr.J.Krishnappa** Asso Prof in Paediatrics, SDUMC, Kolar
3.05-3.30pm	**Prof. Tapas. K. Kundu,** Jawaharlal Nehru Centre for Advanced Science Research, Bangalore	"Epigenetics and Cancer: Targeted for New Generation Therapeutics".	**Prof. P.Kondaiah** Dept of MRDG, IISc, Bangalore **Dr.Azeem Mohiyuddin** Prof & Head of ENT, SDUMC, Kolar
3.30-4.15 pm	**Dr.V.M. Katoch,** Secretary- Dept. of Health Research, Director General-ICMR, N-Delhi	**Valedictory Address** **"Changing Scenario of Opportunities for Medical Research in Medical Colleges"**	

Opportunities of Medical Research in Medical Colleges

Dr.V.M.Katoch,
Secretary, Department of Health Research,
Director - General, ICMR,
MOHFW, Government of India
New-Delhi

There is a need to produce a doctor of modern medicine who is well versed with the necessary skills for the current health care practice in the country. Hence there is need for greater thrust on health research by scientific breakthroughs, well defined research system and strong processes and regulatory systems. Also there is a strong need to carry out research on public health problems of the locality. To succeed as a medical innovator one has to solve the problems by doing research.

The current situation of research in India has many pitfalls. To name a few are lack of adequate infrastructure/ manpower, inadequate funding / priority, inadequate regulatory structures and inadequate coordination and translational mechanisms

Health of people in the country is worsened by epidemiological and demographic transition which has led to following newer problems. There is

a. New and re-emerging diseases
b. Decline in mortality and fertility rates and ageing of the population
c. Widening of health inequities between rich and poor
d. Increasing burden of chronic diseases

The scope of research is vast in our country. It can be addressed by use of modern biology and by increasing the capability at all institutions especially in medical colleges.

Some thrust areas in research are

1. Drug resistance and study on misuse of drugs
2. Genetic diseases
3. Accidents and trauma

4. Neonatal mortality
5. Acute diarrheal diseases and Acute respiratory infections
6. Pyrexia of Unknown Origin
7. Cancer and Kidney diseases
8. Gender issues
9. Mental health
10. Unsafe water leading to communicable diseases and non-communicable diseases
11. Over nutrition and under nutrition
12. Availability of drugs at affordable prices
13. Appropriate and affordable regimens or procedures

ICMR research grants are available to researchers and institutes like Sri Devaraj Urs Medical College in Kolar is well poised towards it. Though new discoveries in various areas of health are needed it is important to understand the thrust areas for research to obtain grants from ICMR. ICMR not only provides grants but also works towards promotion and guidance on research. ICMR has put in place appropriate acts, guidelines, regulatory authorities and structures to evaluate and recommend technologies, programmes, studies, etc. Enactment of an ethics Bill and the establishment of the National Bioethics Authority, creation of national health research forum and establishment of mechanisms for benchmarking, mapping, accreditation of health research institutions, etc, are some of the mechanisms in place to facilitate research in the country.

ICMR has worked in the past four years towards the betterment of research in India by

a. Developing human resources skilled in conducting research in medical colleges and offering special ICMR program for financial support
b. Improving the technology for surveillance and diagnosis
    i. Establishing a network of laboratories at apex, regional, state and district levels (one medical college as a centre for 2 -3 districts)
    ii. Surveillance network for non communicable diseases

There are success and failures of innovation and implementation in the country. There is the success story of excellence in designing treatment methods namely DOTS for tuberculosis and MDT for leprosy. Strong political commitment and helpful bureaucrats facilitate the success stories and the transformation of health scenario in the country. Innovations in clinical applications are not worth mentioning. The recent innovations in the country are not inspiring.

Public health architecture of India was thought of by a Britisher, Joseph Bhore just before Independence. The country implemented it well with great amount of success but cannot have the pride of creating it. Public health emphasis is still on importing ideas from well established western institutions and medical schools. Affordable tools of intervention including hygiene by Indian investigators are hardly cited.

Translational Research at ICMR

ICMR has created a system of translational research. Twenty six translational research cells have been established at ICMR's institutes and centres. A translational research cell has also been established at ICMR headquarters which coordinates the programmes of ICMR's institutes/centres under translational research and assist in carrying forward their technologies for implementation. Around 102 technologies and programmes of ICMR's developed in these institutes and centres have been identified between 2008-10.

Other agencies which funding for health research

DST - Department of Science and Technology is the umbrella science agency in the country which funds biomedical basic and applied research in a significant manner. Areas o include funding includes those pertaining to infectious and non communicable diseases. DST funded research has influenced almost all facets of medical sciences. Many leads from this research including newer areas such as nanotechnology have been available.

DBT- Department of Biotechnology has made a major impact on development of biotechnology related products. Several diagnostics, vaccines and other health care products have been developed with financial support from DBT. Programmes of DBT such as SBIRI have made a significant change on the Indian research front.

CSIR - Council of Scientific and Industrial Research laboratories have developed several drugs / vaccines for the prevention and treatment of tuberculosis, malaria, leishmaniasis, diabetes mellitus, thrombosis and others. Products from CSIR are available for fertility control. Several devices / appliances from CSIR are also ready. Open Source Drug Discovery (OSDD) programme of CSIR is creating waves.

DRDO – Defence Research Development Organization has developed several methods for diagnosis of infectious diseases, bioremediation, vector control as well as alternate more nutritious foods. Good affordable equipment such as respirators has been developed by DRDO laboratories.

ICAR – Indian Council of Agricultural Research is focusing on production of adequate amount of right kind of food and also partnering with ICMR on control of zoonotic diseases.

Departments of Atomic Energy, Department of Space, Department of Information technology and other user Ministries like Women and Child Development, Environment and Forests, Rural Development, etc, are providing / are willing to provide their collaborative support in the field of health research.

Major Roadblock of research in India

Mindset of community

Mindset of user community specially the middle class is a major driver of industrial and social growth. Major section of our medical fraternity is suffering from colonial inferiority complex. Public has subconscious fixation for the word "foreign". As a result our indigenous "Indian" medical products, especially micro devices and other appliances start with a big disadvantage against similar "imported" varieties. The Government and enlightened people within the civil society will have work hard to catalyze attitudinal changes among the scientific community and the general community.

Evaluation and Regulatory Process as Roadblock

Translation requires all support from peer groups for evaluation and field testing and finally regulatory approvals. Due to various reasons this process has been very slow. There are very few laboratories (in government and private sectors) that could quickly provide either samples

or carry out independent evaluation. Regulatory structure has not been keep pace with the changing needs.

Commitment of Stakeholders

To create a vibrant network conducive for translation research strong commitment from innovators, promoters and regulators in government as well as private set ups is required. Industry and several players (regulators as well as promoters) will have to be active and work in a mission mode. There will have to be some market assurance to industry and farmers to produce what the people need. Market forces will drive the process once it reaches the market

Positive commitment

There are some examples of success in research and development due to political commitment

DBT and ICMR have facilitated the establishment of dedicated institutes and set-ups for translation research and a grand vision for translation in this country. The political commitment and administrative action shown by the Government tasted success in the management and control of H1N1 pandemic. The market demand has promoted creation of facilities like clinical research organizations (CROs). This phenomenon is not observed in all the relevant sectors which are important. One reason could be poor interest of market forces at that moment of time.

Intersectoral cooperation and coordination

It is an essential and complementary interest. Joint projects funded by each partner need joint selection process and joint monitoring. At the level of Director General and the Secretary of ICMR, MOHFW, the identification of common areas for coordination and cooperation are;

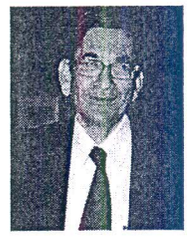
- Molecular diagnostics: DBT, DST, DRDO, ICMR
- Therapeutics: CSIR, ICMR, DBT
- Zoonosis, food safety and nutrition: ICMR, ICAR
- Vaccines: DBT, ICMR

- Knowledge management and HSR: MOHFW; ICMR, DIT, etc.
- Medical equipments: DRDO, CSIR, DST, ICMR, MOHFW
- MOHF, Department of Women and Child, Social Welfare, Education, Space, DOEF, etc. to be involved in translation and implementation research.

There is an immediate need to establish own pathways for research and importantly to build up groups to promote research in Health and Medicine.

"Biological science is incomplete without linking to clinical practice and epidemiology"

Medical Research in an Interdisciplinary Environment



Prof. P. Balram,
Director,
Indian Institute of Science,
Bangalore

The field of engineering has long been associated with the medical sciences. Wilhelm Conrad Röntgen, a German physicist on 8th of November in 1895, produced and detected electromagnetic radiation in a wavelength range today known as X-rays or Röntgen rays. This achievement earned him the first Nobel Prize in Physics in 1901. Subsequently this technology was applied to the radiological study of bones. Since then with the advent of this novel technology the evolution of medical science and research has been closely intertwined.

The term proteomics coined by Marc Wilkins in 1994 refers to the study of the 'proteome' which is the entire protein complement expressed by a cell. The production of proteins at the cellular level is dependent on the nutritional status and also affected by the presence of diseases. Therefore the understanding of proteomics will lead to the better understanding of disease processes and enable the evolution of a cure.

The discovery of sickle cell anaemia by Linus Pauling using the Longsworth scanning diagrams of carbomonoxyhaemoglobin following electrophoresis (Tiselius) was the first proof of human disease caused by an abnormal protein. Also, sickle cell anaemia became the first disease to be understood at the molecular level. Using electrophoresis it was demonstrated that individuals with sickle cell disease had a modified form of haemoglobin in their red blood cells and individuals with sickle cell trait had both the normal and abnormal forms of haemoglobin. This was also the first demonstration that Mendelian inheritance determined the specific physical properties of proteins and not simply their presence or absence. This came to be considered as the dawn of molecular genetics. Thus it was established that alterations in protein structure (Haemoglobin) lead to profound changes in biological function leading to the development of disease. Ingram established that the β globin chain of sickle cell haemoglobin differed from the normal chain at a single amino acid. Later Pauling found that

this alteration comprised of the substitution of amino acid valine instead of glutamate in the sixth position on the β globin chain.

Science is often driven by new technology rather than by new concepts - Freeman Dyson. This insightful quote is a demonstration of how the invention of 'mass spectrometer' has revolutionalised the field of molecular biology. Mass spectrometry (MS) is the science of displaying the spectra of the masses of the molecules present in a given sample. It is used for determining the elemental composition of a sample. Mass spectrometry works in the following manner: A sample (which may be solid, liquid or gas) is ionized. The ions are separated according to their mass-to-charge ratio. The signal is processed into the spectra of the masses of the particles of that sample. The elements or molecules are identified by correlating known masses with the identified masses.This instrument can thus reveal the chemical constituents of any given substance and has been used extensively in the field of medicine. From the analysis of human serum albumin to the analysis of extraterrestrial organic matter in the Murchison meteorite, has been carried out using this instrument. Some of the utilization of the mass spectrometer is to study the changes caused by oxidative stress, infection and metabolic diseases on human serum albumin to better understand disease processes.

The future prospects include, Mass spectrometric characterization of haemoglobin tetramers for the identification of heterogeneity of subunit (Quaternary) structure and quantitation of heterogeneous haemoglobin tetramers.

The discovery of Triosephosphate isomerase (TPI) is path breaking. This enzyme catalyzes the reversible inter-conversion of the triose phosphate isomers dihydroxyacetone phosphate and D-glyceraldehyde 3-phosphate. TPI is considered not only to be an enzyme but a component of the protective pathway that limits the potentially deleterious accumulation of DHAP, a toxigenic compound. TPI plays an important role in glycolysis and is essential for efficient energy production. In humans, deficiencies in TPI are associated with a progressive severe neurological disorder and are also characterized by chronic haemolytic anemia. While there are various mutations that cause this disease, most include the mutation of glutamic acid at position 104 to aspartic acid. Thus if the genomics of this enzyme and the potential

mutations in humans are better understood the diseases produced can be treated or even cured at the cellular level.

The various fields of genetic engineering, molecular biology, proteomics, transcriptomics, metabalomics, computational sciences and medicine should collaborate with one another and only in the nexus of such integration, will medical research flourish and pave the way into a brighter and healthier future.

Disease Biology in the Coming Decade(s)

Dr. M.R. Sathyanarayana Rao,

Jawaharlal Nehru Centre for Advanced Science Research, Bangalore

The human genome consists of 3,200,000,000 pairs of DNA and 20,000-25,000 genes of which less than 2% code for proteins and more than 50% are "junk" repeated sequences. The pregenomic era was followed by an international effort to sequence the complete genome and with the completion of the Human Genome project the genomic era was born.

Genomic medicine will have a huge impact on human life and diseases. For an example genomics was used to rapidly identify the pathogens involved in severe acute respiratory syndrome(SARS), to assess prognosis in cancer as in breast cancer and stratify the development of myocardial infarction to name a few. The use and response to drugs is another important field and its role in hereditary disease is unparallel.

Glioblastomamultiforme is the most common and aggressive brain tumor in humans. The occurrence is 10 to 12 per 100,000 in USA and Europe. It is classified into two broad categories primary and secondary. Primary GBM (accounting for >90% of cases and most of the TCGA cases profiled) manifest *de novo* without prior evidence of preexisting tumor in older patients of mean age of 55 years. Secondary GBM develop through malignant progression from lower grade astrocytomas and is usually seen in younger patients of mean age of 40 years.

Prognosis for GBM patients remains dismal, with a median survival of 14 months. Current treatments include surgery, radiation therapy and chemotherapy. About 20% live more than 2-3years.

Glioblastomamultiforme is the first cancer type identified for comprehensive genomic characterization by The Cancer Genome Atlas (TCGA). The potential roles of genomics are many fold. Firstly, do the different types of GBM belong to a sub category and would it be possible to identify them by gene signatures. The conventional treatment for Glioma is surgery with chemo and radiation therapy but all do not respond to chemo in the same way.

So would these gene signatures help predict the prognosis or recurrence or can prognostic markers be developed. Genomics can further be be used to identify new therapeutic targets that help develop serum biomarkers, proteomics detections and development of ELISA based quantification.

From the study done to assess prognostic signature markers in GBM, 14 protein signatures were identified that classified them in to high or low risk as given in the table below.

Table: 14 Gene prognostic signature.

The candidate genes and their respective multivariate Cox proportional regression coefficient score is given. The expression pattern of these genes in the present cohort in low risk and high risk groups is tabulated.

	Gene symbol	Gene name	Regression co-efficient (Cox PH score)	Low risk			High risk		
				Median	Mean	SD*	Median	Mean	SD*
1	AGT	Angiotensinogen	0.0319	-0.801	-2.335	4.366	0.1767	-0.290	2.319
2	EGFR	Epidermal growth factor receptor	-0.05152	1.106	1.261	3.409	2.850	3.105	2.947
3	CHI3L1	Chitinase 3-like 1	0.00442	3.600	3.782	2.965	6.934	6.168	2.624
4	SOD2	Superoxide dismutase 2, mitochondrial	-0.08050	0.839	0.919	1.669	2.827	2.443	2.07
5	CCL2	Chemokine (C-C motif) ligand 2	0.13690	-0.153	-0.574	1.911	1.560	1.219	2.037
6	IGFBPL1	Insulin-like growth factor binding protein-like 1	-0.07953	2.413	2.586	3.168	-0.017	-0.236	2.576
7	MBP	Myelin basic protein	0.07308	-6.881	-6.791	2.851	-5.010	-4.964	3.077

8	CPE	Carboxypeptidase E	0.03070	-1.591	-2.224	2.462	-1.101	-1.241	1.258
9	OLFM1	Olfactomedin 1	0.09206	-4.885	-4.837	2.446	-3.387	-3.736	1.769
10	MCF	MCF.2 cell line derived transforming sequence	-0.20973	-2.592	-1.954	2.528	-3.281	-3.569	2.475
11	PACSIN1	Protein kinase C and casein kinase substrate in neurons 1	0.01182	-6.411	-6.648	2.219	-6.085	-6.071	2.586
12	CALCRL	Calcitonin receptor-like	-0.08132	2.569	2.300	1.802	1.438	1.204	2.353
13	SNCA	Synuclein, alpha	0.17266	-4.633	-4.572	1.554	-3.588	-3.572	1.626
14	TOP2A	Topoisomerase (DNA) II alpha	-0.12357	9.692	8.922	1.860	8.385	8.108	2.137

* SD - Standard deviation

The above 14 gene prognostic signature helps to categorize GBM into high and low risk groups.

Before mapping out the disease network in glioma there is a need to understand the role of genes and their products in development of disease, that has been much discussed and the lessons learned are very clear. They do not act alone. They network with other genes and their products in context with an environment. This is observed in the fact that Mendelian diseases are rare and complex disorders develop as a result of multiple gene defects in many genes and often associated with defective regulatory genes. Hence there is a need for Genome biology to understand dysregeulation of proteins and their role in development of diseases.

As a result there should be a network based approach to diseases. Most cellular functions occur as a result of interactions of cellular components within the cells, across cells and organs. In the humans as a result there is highly complex network with ~25,000 protein coding gene, ~1000 metabolites, and undefined number of distinct proteins and functional RNA molecules, the number of cellular components that serve as the NODES of the interactome easily exceeding 100,000.

This network implies that the defect in a single gene will not be restricted to it's product alone, that through it's links in the network affect the activity of other non defective genes or their products. Thus, the phenotype of a disease is rarely due to single gene defect but as a consequence of the interaction of this complex gene network.

Network Medicine may be explained by several hypotheses. Among them are

- Hubs: Non-essential disease genes (representing the majority of all known disease genes) tend to avoid hubs and segregate at the functional periphery of the interactome. *In utero* essential genes tend to associated with hubs.
- *Local hypothesis:* Proteins involved in the same disease have an increased tendency to interact with each other.
- *Corollary of the local hypothesis:* Mutations in interacting proteins often lead to similar disease phenotypes.
- *Disease module hypothesis:* Cellular components associated with a specific disease phenotype show a tendency to cluster in the same network neighborhood.
- *Network parsimony principle*: Causal molecular pathways often coincide with the shortest molecular paths between known disease-associated components.
- *Shared components hypothesis:* Diseases that share disease-associated cellular components (genes, proteins, metabolites, mRNAs) show phenotypic similarity and comorbidity.

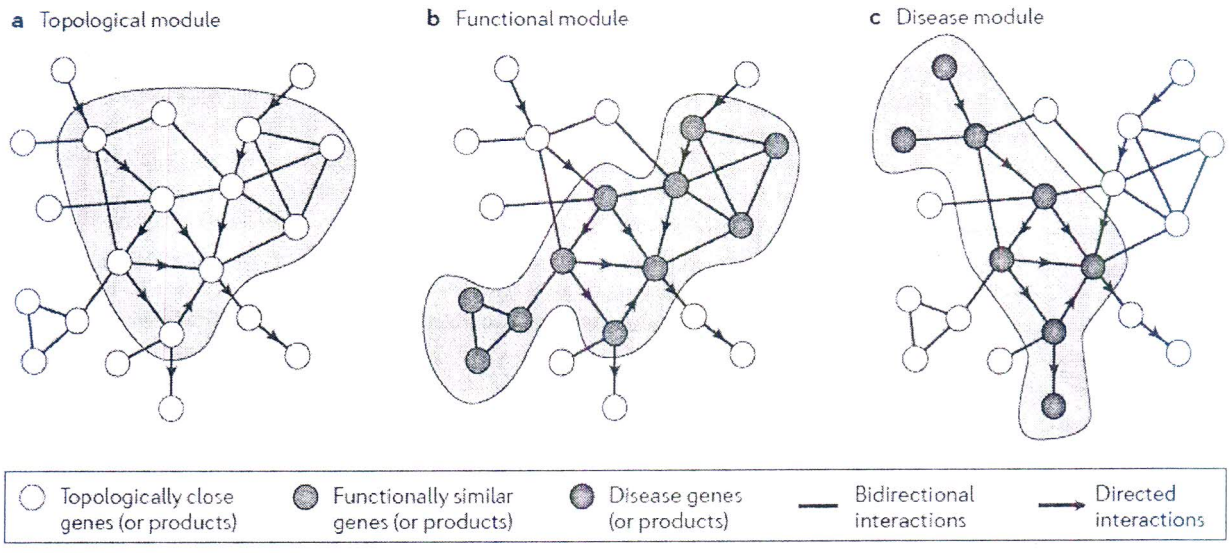


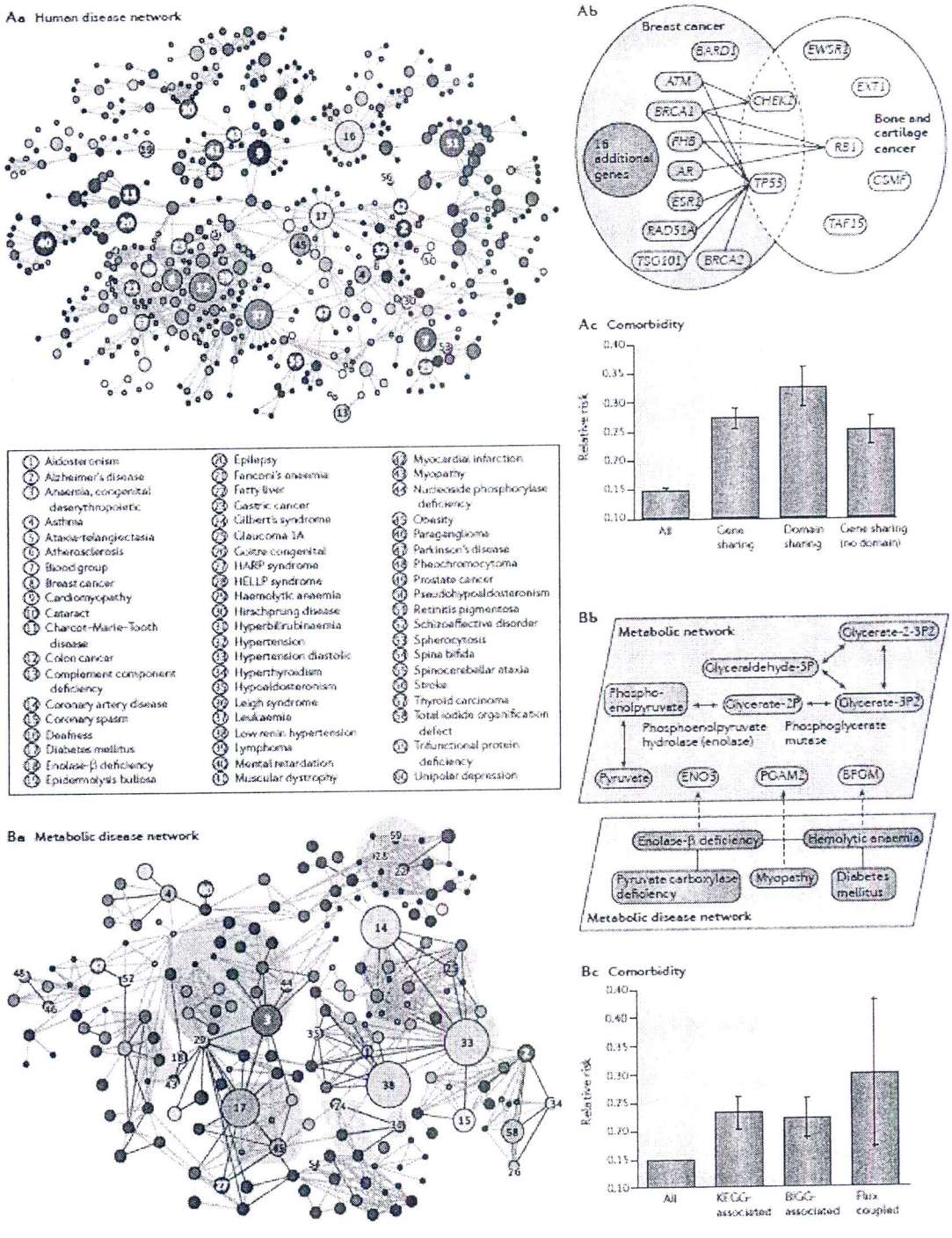
Figure 2 | **Disease modules.** Schematic diagram of the three modularity concepts that are discussed in this Review. **a** | Topological modules correspond to locally dense neighbourhoods of the interactome, such that the nodes of the module show a higher tendency to interact with each other than with nodes outside the module. As such, topological modules represent a pure network property. **b** | Functional modules correspond to network neighbourhoods in which there is a statistically significant segregation of nodes of related function. Thus, a functional module requires us to define some nodal characteristics (shown as grey nodes) and relies on the hypothesis that nodes that are involved in closely related cellular functions tend to interact with each other and are therefore located in the same network neighbourhood. **c** | A disease module represents a group of nodes whose perturbation (mutations, deletions, copy number variations or expression changes) can be linked to a particular disease phenotype, shown as red nodes. The tacit assumption in network medicine is that the topological, functional and disease modules overlap, so that functional modules correspond to topological modules and a disease can be viewed as the breakdown of a functional module.

The three distinct phenomena here are the *topological module* that represents a network where nodes have a high tendency to link to nodes within the same neighbourhood than to the nodes outside and not to the function of individual nodes. By contrast, a *functional module* represents the link of nodes with similar function in same network neighborhood. Finally, a *disease module* represents a group of network components that together contribute to a cellular function whose disruption results in a particular disease phenotype.

Cellular networks are modular, and consist of inter-connected proteins responsible for specific functions. In Cancer, functional gene modules cannot carry out their basic functions

and they become critical in the development of cancer that necessitates self sufficiency in growth signals, evasion of apoptosis, sustained angiogenesis, tissue invasion and metastasis. Different defective genes can incapacitate each module. Each tumor can perturb individual genes via multiple mechanisms including sequence mutations, copy number alterations, gene fusion events or epigenetic events.

The Human disease network (HDN) nodes represent disorders. And two disorders are connected if they share at least one defective gene associated with the disorder. There is also disease gene network (DGN) where 2 genes are connected with the same disorder. Understanding of these networks is important in understanding disease phenotype and gene association.


Aa Human disease network
1 Aldosteronism
2 Alzheimer's disease
3 Anaemia, congenital dyserythropoietic
4 Asthma
5 Ataxia-telangiectasia
6 Atherosclerosis
7 Blood group
8 Breast cancer
9 Cardiomyopathy
10 Cataract
11 Charcot–Marie–Tooth disease
12 Colon cancer
13 Complement component deficiency
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17 Diabetes mellitus
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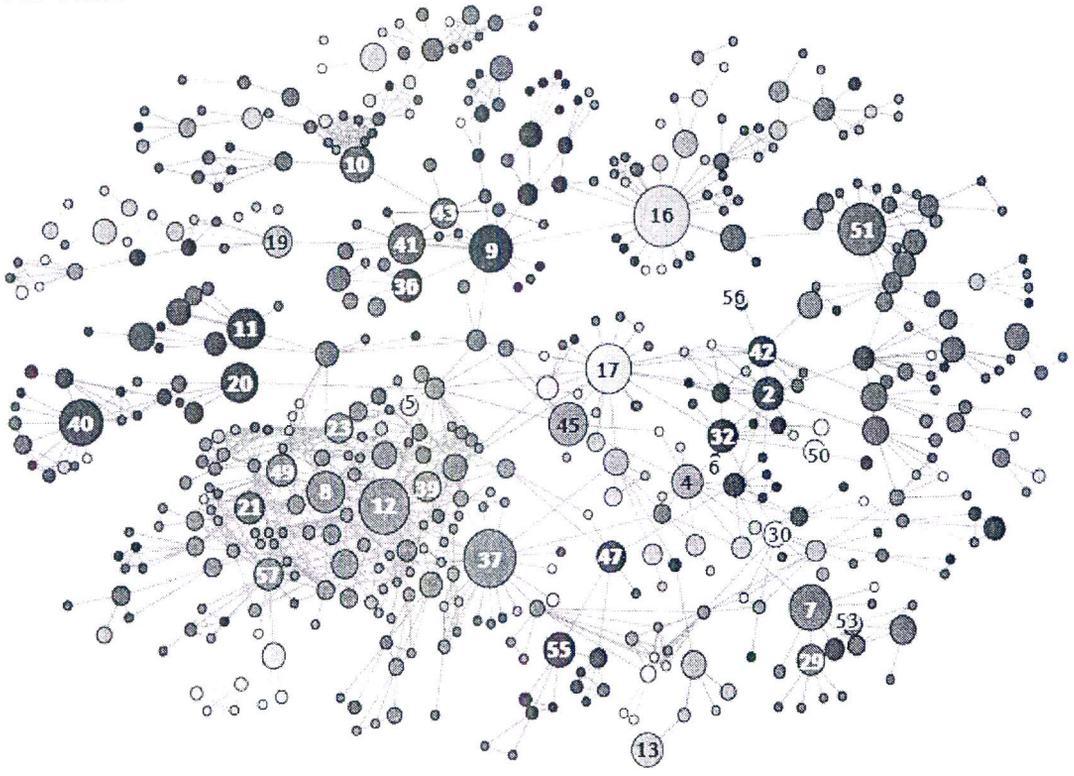
41 Muscular dystrophy
42 Myocardial infarction
43 Myopathy
44 Nucleoside phosphorylase deficiency
45 Obesity
46 Paraganglioma
47 Parkinson's disease
48 Pheochromocytoma
49 Prostate cancer
50 Pseudohypoaldosteronism
51 Retinitis pigmentosa
52 Schizoaffective disorder
53 Spherocytosis
54 Spina bifida
55 Spinocerebellar ataxia
56 Stroke
57 Thyroid carcinoma
58 Total iodide organification defect
59 Trifunctional protein deficiency
60 Unipolar depression
Ab
Breast cancer
BARD1
ATM
BRCA1
PHB
AR
ESR1
RAD51A
TSG101
BRCA2
CHEK2
TP53
EWSR1
EXT1
RB1
CSMF
TAF15
18 additional genes
Bone and cartilage cancer
Ac Comorbidity
Relative risk
0.40
0.35
0.30
0.25
0.20
0.15
0.10
All
Gene sharing
Domain sharing
Gene sharing (no domain)
Bb
Metabolic network
Glycerate-2-3P2
Glyceraldehyde-3P
Phospho-enolpyruvate
Glycerate-2P
Glycerate-3P2
Phosphoenolpyruvate hydrolase (enolase)
Phosphoglycerate mutase
Pyruvate
ENO3
PGAM2
BPGM
Enolase-β deficiency
Hemolytic anaemia
Pyruvate carboxylase deficiency
Myopathy
Diabetes mellitus
Metabolic disease network
Ba Metabolic disease network
Bc Comorbidity
Relative risk
0.40
0.35
0.30
0.25
0.20
0.15
0.10
All
KEGG-associated
BIOG-associated
Flux coupled

Aa Human disease network



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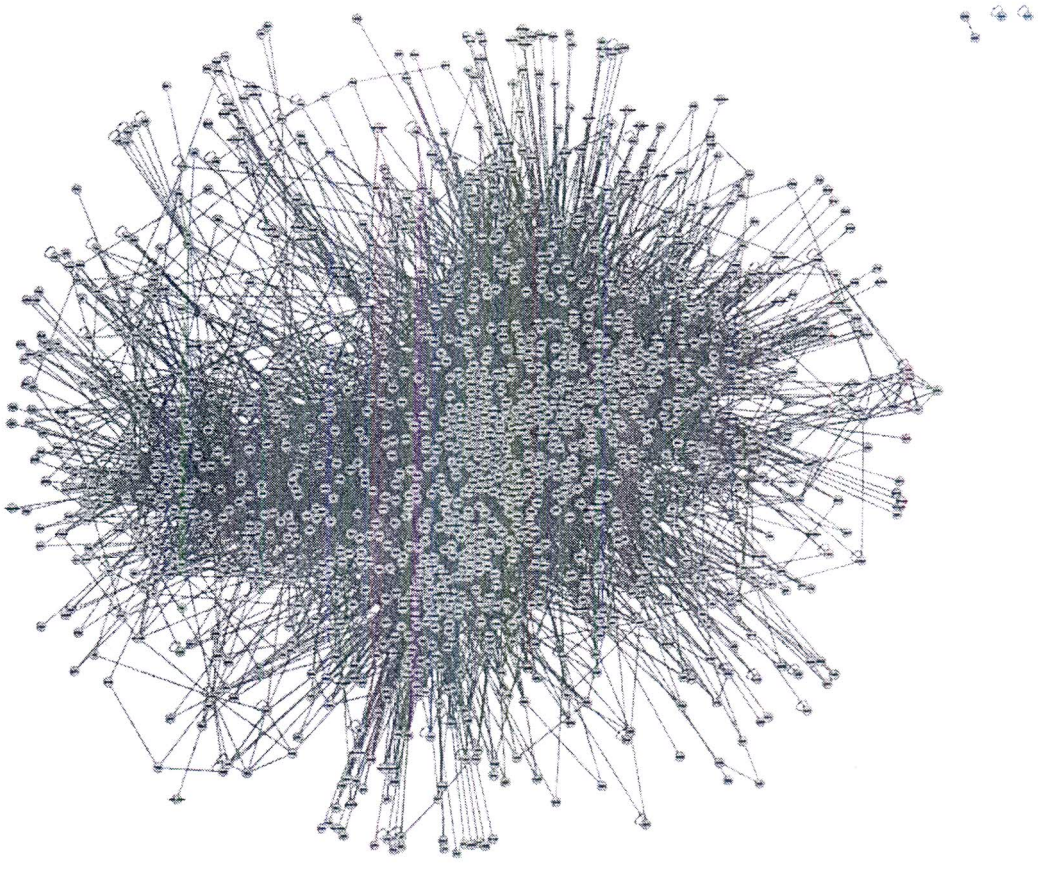
57. Thyroid carcinoma
58. Total iodide organification defect
59. Trifunctional protein deficiency
60. Unipolar depression

In system approach to understanding GBM, literature show over 124 expressed genes in GMB. 62 genes were identified in their upregulations and whole network was constructed with the identified 1447 genetic nodes and 11752 edges as shown here.

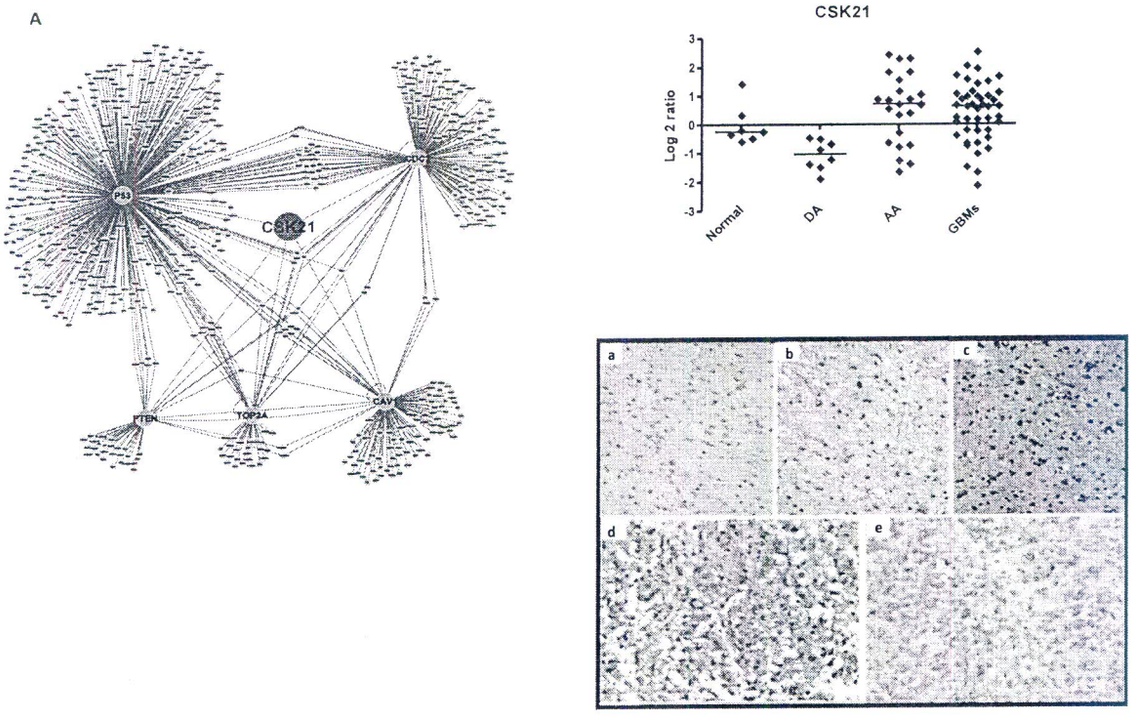
Specific Protein-Protein Interaction Network



. 1447 Nodes and 11752 edges

Two very important subnetworks identified is the CSK 21 module and PP1 a module.

CSK 21 Sub-network Module and Expression Pattern of CSK 21



Casein Kinase(CSK)21 Subnetwork module contains 569 nodes. Casein kinase2 is a tetrameric protein formed by the association of homodimeric regulatory subunit beta and homodimeric or heterodimeric catalytic subunit alpha (CSK21) or alpha' (CSK22). CDC2 phosphorylates CSK21 in a cell cycle dependent manner during mitotic prophase and metaphase. CSK21 phosphorylates p53, phosphorylates PTEN and regulates AKT pathway, phosphorylates Topoisomerase IIa and phosphorylates CAV1

PP1A Sub Network Module and Expression pattern of PP1A

PP1A Sub Network Module contains contains 661 Nodes. PP1A is a multifunctional protein phosphatase (Ser/Thr) that is involved in regulating various cellular processes. At the turn of

M-G1 phase, several mitotic proteins should be dephosphorylated to promote timely dephosphorylation of mitotic substrates.As cyclin B is destroyed at mitotic exit, cdc 2 kinase activity drops, allowing auto dephosphorylation of PP1A resulting in its partial activation.

This is followed by PP1A mediated dephosphorylation of Inh1 and its dissociation, allowing full activation of PP1A that can then dephosphorylate other mitotic proteins to allow mitotic exit. So the question arises can PP1A, be a potential therapeutic target for Glioma . Synthetic and Natural inhibitors of PP1A have been identified which are being tried for possible therapeutic intervention of other types of cancer. In the development of disease it was often thought a derangement of physiology lead to disease.

With the advent of molecular biology, the role of physiology took a back seat and the role of proteins and molecular changes in a gene took precedence. In the genomic era, the role of genes in the disease network and its influences physiology and the phenotype of the disease is highlighted.

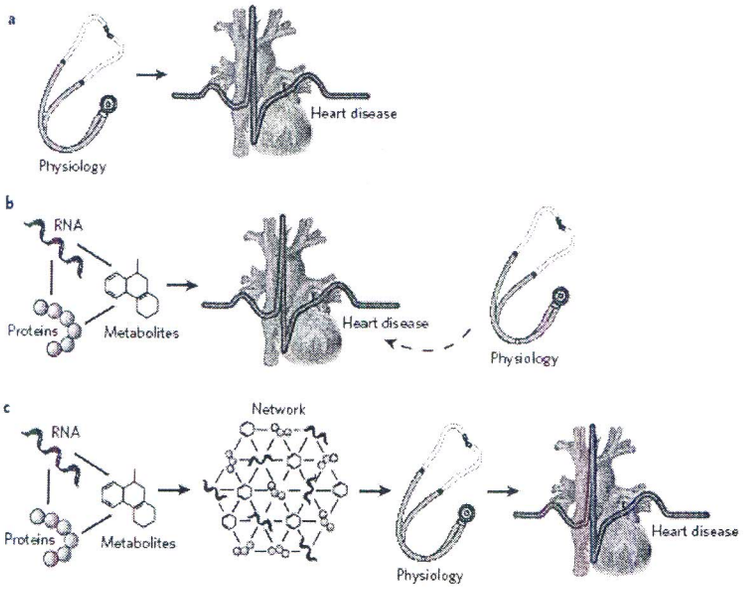
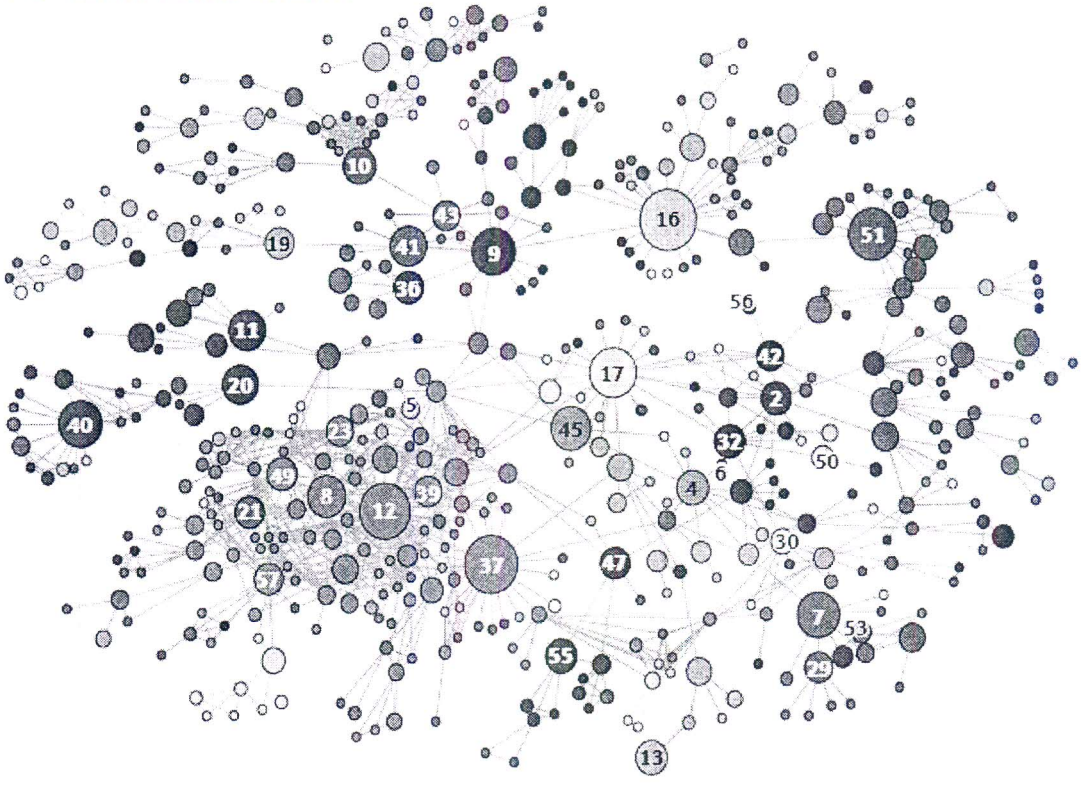


Figure 2 | Linking molecular biology to physiology through molecular networks. **a**, Before the molecular biology revolution, disease was studied primarily in the context of physiology. **b**, As a result of the molecular biology revolution, physiology has played a less prominent role in the study of the molecular bases of disease, given the reductionist push to associate molecular changes in a given gene (affecting protein levels, activity or function) directly with changes in disease states. **c**, The complexity of molecular biology — given the ability to monitor DNA variation, RNA variation, metabolite variation and protein variation in populations on a comprehensive scale — has driven a systems view of disease, in which networks of interacting molecular entities are constructed to define physiological states of the system associated with disease. In this way, the molecular networks allow a direct link between molecular biology and clinical medicine by connecting molecular biology to physiology.

Aa Human disease network



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If each human disease or disorder has a distinct genetic orgin, than HGN would consist of a disconnected network of single nodes or small clusters. But there is a huge network with connections across disorders. Of the 1,284 disorders, 867 show at least one link with other disorder showing that genetic origin of diseases share other genetic diseases. Most diseases are associated with a few genes, but some like leukemia, colon cancer and deafness are associated with a large number of genes. The prominence of cancer among the most connected disorders arises in part from the many clinically distinct cancer subtypes tightly connected with each other through common tumor repressor genes such as *TP53* and *PTEN*.

Genetic epidemiology is another fascinating area of study. 25% of global mortality and more than 50% of deaths in children under the age of 5 is due to infectious diseases prominent among them being, HIV –AIDS, malaria, pneumonia and tuberculosis. The genetic study here would be very complex as it involves not only the genomes of individuals but also of pathogens, vectors and their interaction. The genomic details would help track their evolution over time and space and understand infection behavior.

Genetic disorders are medical conditions caused by mutations in a gene or a set of genes. Mutations are changes in the DNA sequence of a gene. There are three types of genetic diseases: Monogenic those that are pure genetic diseases caused due to mutations in single gene. They do not require any environmental factors to elicit them like cystic fibrosis, sickle cell anemia, Huntington's disease, SCID, Albinism. Oligogenic diseases are conditions produced by the combination of two, three, or four defective genes as in Schizophrenia, Bipolar disorder, Autism etc and polygenic where many mild defects conspire to produce a chronic disease like Cancer, Type II diabetes, heart disease, high blood pressure, Alzheimer's disease, Arthritis. Genetic diseases result from inborn errors in the genetic code or from mutations that occur post-fertilization. And Genes can "predispose" susceptibility to infectious and genetic diseases, but environment also influences the outcome and symptom severity.

Evidence Based Medicine - Using Research in Clinical Practice

Dr.P.F.Kotur, MD,PhD
Vice-Chancellor,
Sri Devaraj Urs Academy of Higher Education & Research,
Kolar

The findings of research, needs to be translated into practice and the scientific publications are the 'Tools of Translation'. A study published in Annals of Internal Medicine quotes that of the 6 million medical articles published only 15% of them are useful. The Average Quality Score of Randomized clinical trials are less than fifty percent. Publications are important to convey research finding which can be utilized in patient care, but of late publications are of low quality because they have become criteria for determining competence and academic position. Doing research leads to innovations and helps in gaining new knowledge which in turn helps in better health care. It also helps in the career advancement of the researcher and is considered as one of the tool of measurement of an individual and of an institutional growth.

Arguably China had used the term "Kaozeng" - Practicing Evidential Research" and traces of evidence based medicine (EBM) can be found in ancient Greece also. Following the French Revolution - Pierre Louis was seeking truth through systematic observation. Professor Archibald Leman Cochrane during (1909–1988) promoted increasing acceptance of the concepts behind evidence-based practice. Methodologies of EBM were established by the McMaster University research group led by David Sackett and Gordon Guyatt.The term "evidence based" was first used in 1990 by David Eddy. In 1992 Gordon Guyatt et al coined the term EBM which was more formally defined by Sacket et al in 1996.

EBM is best defined as optimal integration of best research evidence with clinical expertise and patient's unique values and circumstances. It is also defined as the explicit use of valid external evidence combined with the prevailing internal evidence. External evidence can be obtained from valid literature and the internal from the clinician in the form of his expertise, pathophysiological understanding of a disease and also his intuition.The knowledge and skills of medicine, obtained during the course of study are insufficient to carry on life long

successful / competent clinical practice.In the present day scenario doctors are no longer considered as Gods by the patients as it was in the earlier days. They have to be prepared to provide the best treatment to their patients.

We must learn and teach EBM to improve clinical decision making and for incorporating the best available evidence into the clinical practices. It has been said that 'medical science attracts brightest minds but does not challenge their brains'. The curriculum of yesterday is being taught today, to prepare the professionals for tomorrow. Efforts are being made for inclusion of EBM in post graduate medical curriculum by several regulating councils and universities. Medical education requires ongoing curricular development to incorporate new scientific knowledge and competencies.

Competence addressed by EBM

Competence	**Component of EBM**
Medical Knowledge	Demonstrate investigatory and analytic thinking approach to clinical situations
Patient Care	Make clinical decisions based on patient preferences, up-to-date scientific evidence and clinical judgment Use computer technology to support patient care decisions
Practice Based Learning and Improvement	Locate, appraise, and assimilate evidence from scientific studies. Apply knowledge to the appraisal of clinical studies. Access on-line sources
Systems Based Practice	Practice cost effective health care and resource allocation that do not compromise quality of care
Professionalism	Demonstrate respect, compassion, integrity sensitivity and responsiveness to patients' values
Interpersonal/Communication Skills	Create and sustain a therapeutic and ethically sound relationship with patients

The initial goal of EBM was to minimize the use of non-documentary knowledge and reasoning in clinical practice. It is now attempting to augment rather than replace individual experience and understanding of basic disease mechanisms. Some forces driving the EBM movement are the daily need for valid information about diagnosis, prognosis, therapy and prevention of diseases; inadequacy of traditional sources like text books being outdated, experts being wrong frequently and CMEs being ineffective; disparity between clinical skills and clinical judgment and updating knowledge and clinical performance; lack of time to gather evidence by traditional methods and inability to afford sufficient time per patient for assimilating evidence.

Five-Step Approach for Practicing EBM

Step-1: Converting the need for information into an answerable question using PICO model (P–Patient problem, I–Interventional strategy, C–Comparison, O–Out come).

Step-2: Answer to the question can be obtained by tracking the evidence utilizing journal, databases like PubMed, Science Direct, INDmed, Ovid, Cochrane, textbooks, patient profiles, practice guidelines. EBM reviews can also be used.

Step-3: In a critical appraisal, published research article will be assessed in an objective and structured way for its validity and authenticity. The strengths and weaknesses will be analyzed with an intention to identify how much near it is to the truth. Clinicians must critically appraise published research articles to decide the validity of new information and whether to incorporate it to their clinical practice. Stronger the statistics, more valid and reliable is the article for the practice of EBM.

Step-4: Integrating the evidence with clinical expertise and patient's biology, values and circumstances.

Step-5: Evaluating the effectiveness and efficiency in executing the above steps and seeking ways to improve them.

Some benefits of EBM are that it minimizes errors in clinical decisions, there is a continuous improvement in quality of patient care and identifying and promoting optimal medical practices which are scientifically valid and effective. It also enables lifelong and self directed learning, enhances critical thinking and encourages researchers to focus on evidence and

outcomes that are important to clinicians and patients.The relevant outcomes of EBM could be changes in the attitude, behaviour, clinical outcomes optimized, knowledge and skills enhanced. Some challenges in adopting EBM are availability of IT infrastructure, internet connectivity for online information, ability to search evidence and critically appraising it, critical thinking and attitude.

Impact of EBM are number of articles indexed in MEDLINE with the word 'evidence based' in the title has grown dramatically over the past decade, from 295 in 1997 to 1162 in 2005 to 14602 in 2011. Further experiences gained through EB practice leads to the development of management protocols. Pooling the outcomes of the implementation of these protocols and their systematic evaluation by expert's results in the establishment of practice guidelines by professional organizations.

Limitations of EBM are infrequent application of available resource, the sheer volume of research-based evidence and inability of clinicians to afford time for finding and assimilating evidence and task of teaching clinicians the basic skills of EBM .

Is Evidence-Based Medicine Relevant to the Developing World?

Most of the reviews produced to date address health conditions that are priorities in the developed world and not the major health concerns of the developing world. Doubts exist about the relevance, suitability and transferability of evidence evolved in the developed countries for application in the developing countries. What is needed is, not the best evidence but the most appropriate one.

Because of paucity of related RCTs, many decisions in ICUs/ERs are based on pathophysiologic processes, studies on animal and healthy volunteers. Lot of literature pertaining to this is dispersed across journals. This diversity demands efficient methodologies to access literature. In procedure oriented specialties such as surgery and anaesthesiology, the skill of the provider and hospital level factors may affect the risk and should be considered in risk/benefit analysis

Philosophical barrier

No amount of empiric evidence can tell us what we ought to do in any particular situation as decisions are value based. The necessary gap between clinical research and medical practice means that evidence can never directly dictate care; evidence cannot tell us when it has to be best to ignored. The current boundaries of EBM are generally defined in relation to obstacles to the development, dissemination and incorporation of medical evidence. Finally, despite its ancient origins, EBM remains a relatively young discipline whose positive impacts are just beginning to be validated, and it will continue to evolve.

Community Based Interventions for Preventing Maternal and Neonatal Mortality in Resource Poor Settings: Experiences of Jawaharlal Nehru Medical College, Belgaum

Dr Shivaprasad S Goudar *MD MHPE*

Professor of Physiology & Research Coordinator,

Women's and Children's Health Research Unit,

KLE University's Jawaharlal Nehru Medical College,

Belgaum

Introduction

India has the highest burden of maternal and neonatal deaths in the world. Postpartum hemorrhage and birth asphyxia are the leading causes of maternal and neonatal mortality. Leading Causes of death among pregnant women are haemorrhage, sepsis, unsafe abortion and eclampsia and among neonates are due to birth asphyxia, prematurity, low birth weight and infection.

The Global Network for Women's and Children's Health Research was established in 2001 by National Institute of Child Health and Human Development, USA and the Bill & Melinda Gates Foundation to expand scientific knowledge, develop sustainable research infrastructures and improve health outcomes for pregnant women and young children in developing countries. KLE University's J N Medical College, Belgaum is one of the GN sites and has conducted community based research studies to test interventions to accelerate achievement of Millennium Development Goals 4 and 5 in low and middle income countries.

Methods

Randomized, double blind, placebo-controlled trial of oral Misoprostol 600 mcg for prevention of postpartum haemorrhage was carried out from 2002-05. Our landmark trial of oral Misoprostol produced a wealth of evidence, regarding PPH identification and prevention and stimulated both national and international policies. As visual estimation of blood loss is inaccurate, the study team developed and validated the BRASSS-V calibrated blood collection drape to measure postpartum blood loss. The trial also led to the selection and subsequent participation of JNMC in the WHO evaluation of controlled cord traction (CCT) to reduce postpartum blood loss among women receiving active management of the third

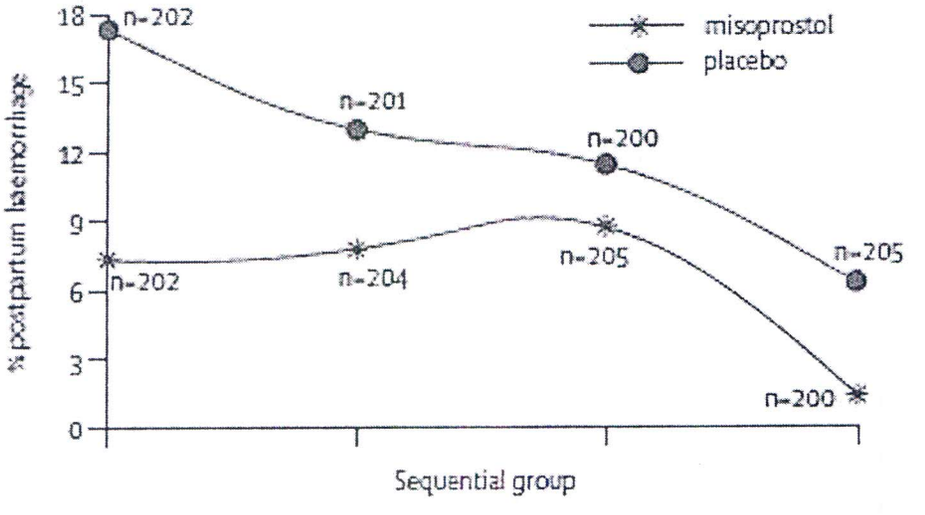
stage labor (AMTSL). This trial, conducted in 16 hospitals and two primary healthcare centers in 8 countries provided compelling evidence that may facilitate PPH prevention by simplifying AMTSL implementation.

Results

Table: Misoprostol to Prevent PPH

Primary Outcome	*Misoprostol (N= 812) N (%)*	*Placebo (N=808) N (%)*	*Relative Risk (95% CI)*	*P-value*
PPH (blood loss ≥ 500 ml)	53 (6.5%)	97 (12.0%)	0.53 (0.39, 0.74)	**<0.0001**
Severe PPH (blood loss ≥ 1,000 ml)	2 (0.2%)	10 (1.2%)	0.20 (0.04, 0.91)	**<0.0001**

Fig: Secular trend in rates of PPH



Conclusions:

Oral Misoprostol

One case of PPH prevented for every 18 women who received Misoprostol.

Decreases need for transfer to higher medical facility, blood transfusion, additional uterotonic drugs and surgical procedures.

Impact on Public Health Policy

Government of India Guidelines for Antenatal Care and Skilled Birth Attendance by ANMs/LHVs

- 2005: Oral Misoprostol for prevention of PPH
- 2010: Oral Misoprostol for prevention of PPH in the absence of refrigeration

Misoprostol included in:

- WHO List of Essential Medicines
- UN Life-Saving Commodities for Women and Children

Active Management of the Third Stage of Labour without Controlled Cord Traction: A Randomized Non-Inferiority Controlled Trial

Dr Shivaprasad S Goudar *MD MHPE*

Professor of Physiology & Research Coordinator,

Women's and Children's Health Research Unit,

KLE University's Jawaharlal Nehru Medical College,

Belgaum

Rationale

- ❑ AMTSL associated with 60% reduction of risk of PPH
- ❑ AMTSL components:
  - administration of oxytocin soon after delivery of the baby
  - controlled cord traction (CCT)
  - delayed cord clamping and cutting & uterine massage
- ❑ WHO guidelines recommend full AMTSL package
- ❑ Lack of evidence on effectiveness of individual components.
- ❑ CCT requires manual skills
- ❑ *CCT recommended for use by skilled birth attendants only*
- ❑ If CCT does not have meaningful impact on blood loss, it could be omitted
- ❑ *Can a Simplified Package focusing mainly on the uterotonic be recommended?*

Primary Objective

- ❑ To determine whether the simplified package of oxytocin 10 IU IM/IV, without CCT, is not less effective than the full AMTSL package with regard to reducing blood loss ≥ 1000 ml in the third stage of labour
- ❑ The hypothesis was that of non-inferiority within a (risk difference) margin of 0.45

Study design

- ❑ Hospital-based, multicentre, randomized, non-inferiority controlled trial.
- ❑ Participating countries:
  - Argentina, Egypt, Kenya, Uganda, South Africa, India, the Philippines and Thailand

- 16 hospitals, 2 Primary Health Centres

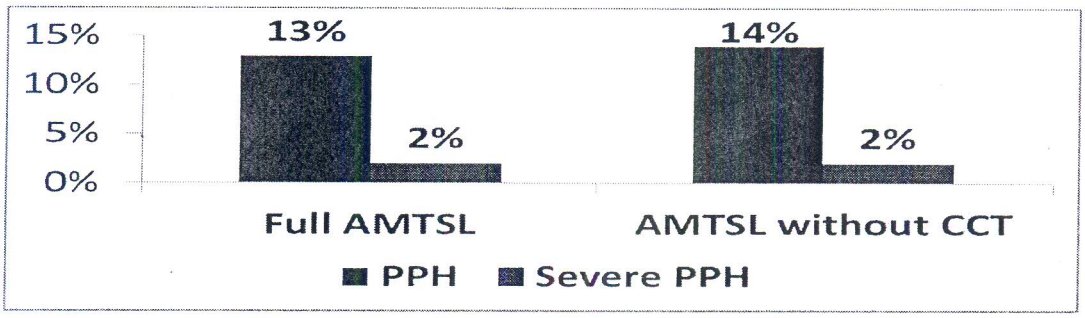
- Sample size ~ 25,000 women
- Recruitment period: June 2009 – November 2010
- Interventions:
  - experimental arm:
    - "Simplified package": *Placental delivery WITHOUT controlled cord traction. i.e. maternal effort, gravity*
  - control arm:
    - "Full package": *Placental delivery WITH controlled cord traction*

Outcome measures

- Primary outcome
  - Severe PPH (blood loss ≥ 1000 ml) at one hour or up to 2 hours for women who continue to bleed beyond one hour

- Secondary outcomes
  - Blood loss ≥ 500 ml
  - Blood transfusion
  - Additional uterotonics
  - Maternal death
  - Manual removal of the placenta
  - Additional surgical procedures
  - Maternal death or severe morbidity
  - Initiation of breastfeeding

Effectiveness of AMTSL with and without CCT on PPH prevention



Main findings

- CCT has minimal added value in terms of reducing blood loss over and above the uterotonic
- Oxytocin 10 IU IM injection after delivery of the baby should be the primary intervention for prevention of PPH
- In settings where SBAs are not available and oxytocin is used as routine uterotonic for prevention of PPH, CCT could be safely omitted during the third stage of labour

FIRST BREATH Trial - Community-based Training and Intervention in Neonatal Resuscitation, 2005 - 2008

Dr Shivaprasad S Goudar *MD MHPE*
Professor of Physiology & Research Coordinator,
Women's and Children's Health Research Unit,
KLE University's Jawaharlal Nehru Medical College,
Belgaum

The "FIRST BREATH" study was a pre-post assessment of the effectiveness of providing the WHO Essential Newborn Care (ENC) course and AAP Neonatal Resuscitation Program (NRP) training promoting clean delivery practices, stimulation and bag-and-mask resuscitation as needed, skin-to-skin contact and early initiation of breastfeeding to birth attendants to reduce neonatal mortality. The First Breath study findings, of a reduction in early neonatal mortality and fresh stillbirth rates following resuscitation training of community level birth attendants, led to the American Academy of Paediatrics development of a resuscitation training curriculum that could be implemented in community and lower level health care facilities, called Helping Babies Breathe (HBB). Pre-post assessment of field testing of the HBB training curriculum demonstrated a reduction in stillbirths secondary to birth asphyxia. The First Breath and Helping Babies Breathe studies provided the critical evidence in support of the Government of India's Navajat Shishu Suraksha Karyakram (NSSK) basic newborn and resuscitation program.

To address the concern that asphyxiated survivors that revived newborn resuscitation do not end up with long term neurological deficit, between 2006 and 2011 under the auspices of the Global Network, JNMC participated in a multi-site RCT of a community-based early developmental intervention in infants with birth asphyxia. Over a 3 year period, parents in the intervention group received bi-monthly home-based training, initiated within the month after birth. The intervention significantly improved the cognitive and psychomotor outcomes of children resuscitated at birth.

Additionally, a community based maternal and newborn health registry permits the site to track the outcomes of all pregnancies in the study clusters and monitor trends of maternal and neonatal mortality over time. JNMC's current research initiatives are focused

on testing interventions aimed at preconception maternal nutrition supplementation to improve newborn growth, reducing pre-term births, improving survival among pre-term low birth weight babies, and determining optimal uterotonic regimes for prevention of postpartum haemorrhage. This presentation will provide an overview of JNMC's research in the past decade focused on the leading causes of women's and neonates' death and its notable effect on both national and global programs and policies to avert perinatal and neonatal mortality, stillbirth and on disability in surviving vulnerable infants.

Trial Objective and Design

- Comparing effectiveness of training birth attendants by WHO-Essential Newborn Care Course and AAP-Neonatal Resuscitation Program in decreasing Early Neonatal Mortality Rate
- Cluster randomized trial
    - Total 80 communities at 7 Global Network Sites
    - India (Belgaum & Orissa), Pakistan , Zambia, DR Congo, Guatemala, Argentina
    - > 40,000 births per year monitored

First Breath Communities

Clusters / Primary Health Centers 26

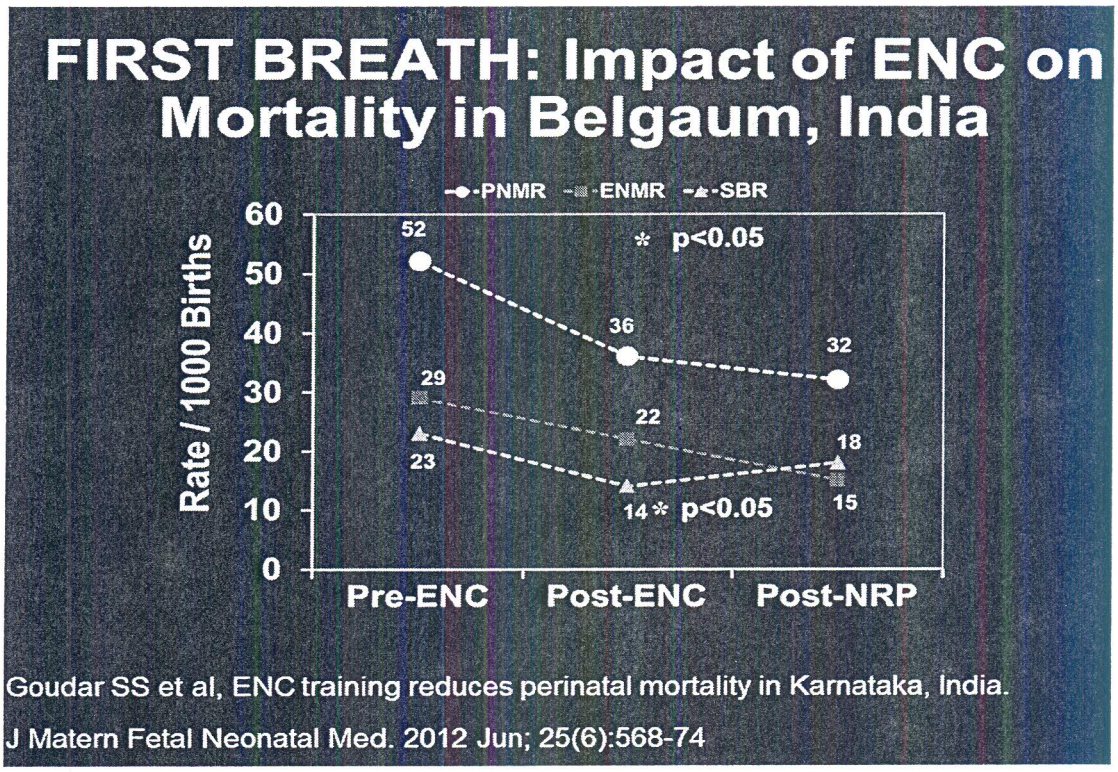
Villages 298

Population 856,985

ENC Training Components

- WHO Essential Newborn Care course
    - Clean delivery practices
    - Resuscitation with bag and mask
    - Skin-to-skin contact
    - Early initiation of breastfeeding

FIRST BREATH: Impact of ENC on Mortality in Belgaum, India



American Academy of Pediatrics

Field Implementation of the *Helping Babies Breathe® Initiative* in Belgaum, Karnataka INDIA 2009-2011

BRAIN HIT

Home-based, early intervention to promote neurodevelopment among infants requiring resuscitation

2006 – 2011

RCT of Early Developmental Intervention in Infants with Birth Asphyxia

BSID Results at 36 Months

	Intervention	Control	p value
	N=59	N=64	
MDI (m±SD)	102.6±9.8	98.0±14.6	0.02
PDI (m±SD)	108.7 ± 12.0	103.3±17.0	0.04

Impact on Public Health Policy

- Ministry of Health,Govt. of India Initiative 2009
  - Basic Newborn Care & Resuscitation Program:

Navajat Shishu Suraksha Karyakram

  - Integrated package of:
    - WHO Essential Newborn Care
    - AAP Helping Babies Breathe
- Revision of:
  - WHO Essential Newborn Care Course
  - AAP resuscitation (HBB) guidelines
- Curriculum for combined revised HBB/ENC

Current Research Initiatives

- Community Level Intervention for Pre-Eclampsia
- Primary vs Secondary Prevention of PPH
- Clindamycin for Reducing Preterm Birth
- Antenatal Corticosteroids for Improving Survival among Preterm Births
- Evaluation of Helping Babies Breathe®
- Preconception Maternal Nutrition and Infant Growth
- Ultrasound use to improve pregnancy outcomes

References:

1. Derman RJ, Kodkany BS, Goudar SS, Geller SE, Naik VA, Bellad MB, et al. Oral misoprostol in preventing postpartum haemorrhage in resource-poor communities: a randomised controlled trial. Lancet 2006;368(9543):1248-53. Accessed from PubMed PMID: 17027730.
2. Patel A, Goudar SS, Geller SE, Kodkany BS, Edlavitch SA, Wagh K, et al. Drape estimation vs. visual assessment for estimating postpartum hemorrhage. Int J Gynaecol Obstet; 93: 220–4;
2006.
3. Goudar SS, Chakraborty H, Edlavitch SA, Naik VA, Bellad MB, Patted SS, et al. Variation in the postpartum hemorrhage rate in a clinical trial of oral misoprostol. J Matern Fetal Neonatal Med. 2008;21(8):559-64. Accessed from PubMed PMID: 18609354.
4. Gülmezoglu AM, Lumbiganon P, Landoulsi S, Widmer M, Abdel-Aleem H, Festin M, et al. Active management of the third stage of labour with and without controlled cord traction: a randomised, controlled, non-inferiority trial. Lancet 2012;379(9827):1721-7. Accessed from Epub 2012. Erratum in: Lancet. 2012 May 5;379(9827):1704. Lancet. 2012 Jul 21; 380(9838):218. PubMed PMID: 22398174.
5. Goudar SS, Dhaded SM, McClure EM, Derman RJ, Patil VD, Mahantshetti NS, et al. ENC training reduces perinatal mortality in Karnataka, India. J Matern Fetal Neonatal Med. 2012;25(6):568-74. Accessed from Epub 2011 Jul 27. PubMed PMID: 21793707.
6. Carlo WA, Goudar SS, Jehan I, Chomba E, Tshefu A, Garces A, et al. First Breath Study Group. Newborn-care training and perinatal mortality in developing countries. N Engl J Med 2010;362(7):614-23. Accessed from PubMed PMID: 20164485.
7. Goudar SS, Somannavar MS, Clark R, Lockyer JM, Revankar AP, Fidler HM, et al. Stillbirth and Newborn Mortality in India After Helping Babies Breathe Training. Pediatrics. 2013;131(2):e344-52. Accessed from Epub 2013 Jan 21. PMID:23339215
8. Carlo WA, Goudar SS, Pasha O, Chomba E, McClure EM, Biasini FJ, et al. Brain Research to Ameliorate Impaired Neurodevelopment-Home-based Intervention Trial Committee; National Institute of Child Health and Human Development Global Network for Women's and Children's Health Research. Neurodevelopmental outcomes in infants requiring resuscitation in developing countries. J Pediatr 2012;160(5):781-5. Accessed from Epub 2011 Nov 17.PubMed PMID: 22099522; PubMed Central PMCID: PMC3309169.
9. Goudar SS, Carlo WA, McClure EM, Pasha O, Patel A, Esamai F, et al. The Maternal and Newborn Health Registry Study of the Global Network for Women's and Children's Health Research. Int J Gynaecol Obstet 2012;118(3):190-3. Accessed from Epub 2012 Jun 26. PMID: 22738806

Diabetes Epidemic in India – Why and what can be Done?

Dr. V. Mohan,
Chairman & Chief Diabetologist,
Dr.Mohan's Diabetes Specialities Centre,
WHO Collaborating Centre for Non Communicable Diseases Prevention & Control & IDF Centre of Education &
Director & President, Madras Diabetes Research Foundation,
Chennai.

The International Diabetes Federation (IDF) had estimated that the total number of diabetic subjects was 50 million in India in the year 2010 and that this was further set to rise to 87 million by the year 2030. However, these data are based on small studies done in some parts of the country and have several methodological constraints. Therefore, there is an urgent need for a large well-planned national study, which could provide reliable nationwide data, not only on prevalence of diabetes, but also of pre-diabetes, hypertension and dyslipidemia. Thus was born the **I**ndian **C**ouncil of **M**edical **R**esearch, **In**dia **Diab**etes (ICMR–INDIAB) study which is one the first of its kind to provide accurate and comprehensive state and national level data on diabetes prevalence in India. The results of the first phase of the ICMR - INDIAB study involving 3 whole states and one union territory of India covering a population of 218 million people, was recently published. The prevalence of diabetes and pre-diabetes in adults in Tamil Nadu are 10.4% and 8.3%, Chandigarh are 13.6% and 14.6%, Jharkhand are 5.3% and 8.1% and Maharashtra are 8.4% and 12.8% respectively. This translates to 62.4 million adults with diabetes and 77.2 million with pre-diabetes in India. Thus, effective preventive programmes need to be urgently implemented to tackle the diabetes epidemic threatening our country.

Large population based genetic studies done by us on some of the candidate genes have shown interesting results. We have carried out genetic studies on PPAR γ gene where we compared the frequencies of the common Pro 12 Ala polymorphism in South Indians living in Chennai with South Asians and White Caucasians living in Dallas. We demonstrated that this polymorphism which is known to be protective against diabetes in White Caucasians does not offer protection to Indians. Another genetic study in the same study groups on Plasma Cell glycoprotein PC-1 gene polymorphism K121Q, showed it was a diabetic gene in all 3

populations studied. We also observed that the Thr394Thr (G→A) polymorphism in PGC-1 gene was strongly associated with diabetes as well as body fat in Indians and this has not been reported in other ethnic groups. Perhaps, the most important gene implicated in type 2 diabetes is the TCF7L2 gene. Our work showed that subjects with TCF7L2 gene G->T polymorphism at rs 12255372 have a 1.5 fold higher risk of having diabetes confirming the association in Asian Indians and this appears to be similar to studies in several European populations and another study from Pune and Hyderabad. Very recently our study on genome wide association studies (GWAS) in individuals of South Asian ancestry published in **NATURE GENETICS** identified six novel type 2 diabetes in South Asians which were not seen among Europeans. Our findings provide insight into the genetic mechanisms underlying T2D and show the potential for new discovery from genetic association studies in populations such as Asian Indian.

Though genetic factors undoubtedly play a major role in the predisposition of diabetes in Indians, environmental factors contributes to over 50% of the risk. The economic growth has resulted in nutritional transition that is inadequacy replaced with more food and this is accompanied by a change in physical activity from more laborious jobs to reduced physical work. Physical inactivity and family history of diabetes add a cumulative effect on the risk of diabetes. Recently, the report showed that two environmental factors, physical inactivity and intake of refined grains (white rice) contribute greatly to the diabetes epidemic in India. Thus, it has helped to explain why Indians are prone to diabetes and also shows that a combination of some unique factors in combination with genetic environmental factors is responsible for this.

Publications in Medical Research and Present Challenges

Dr. Subarna Roy, *Ph D,*
Scientist, Regional Medical Research Centre,
Belgaum

Academic publishing describes articles which distribute academic research and scholarship. It is mostly done in the form of journal articles and books. Publications are done to register a discovery, to get their research quality stamped by publication in a journal of known quality, to attract lasting recognition, reward and to qualify for a degree or a job. The bulk of research and scientific publishing traditionally remained confined to developed countries with USA contributing to 31% of total publications across the globe in 1996 and India contributing only 1.9%. Developing countries like China, India and Middle East in recent years have shown significant rate of growth in publication numbers. China for example is expected to overtake USA before 2020. Even the quality of publications have improved substantially in countries like China but India is still lagging behind as evident by the fewer number of citations. Discipline wise medical field registered the highest number of publications in 2011. Publications and scientific literature is now being digitalized with a decline in the use of print media as observed in a study done in 2005 where a major portion of literature was available only in electronic format. Access to free digital information also has escalated.

The journal publication process consists of various stages including soliciting submissions followed by peer review, editing, production and dissemination of information. This is achieved by the use of gateway and editorial systems, production tracking system and electronic warehousing. All of which is overviewed by an editorial board headed by the editor in chief who is the public face of the journal. He decides on board members and the final acceptance of each paper. The board members provide advice on specialized areas and arrange for reviews. The next methodological check for the authenticity of any publication is the peer review done by two anonymous academics. On an average 30% more papers are reviewed than published. Lastly the publisher manages production, sales and marketing. There are certain guidelines to follow before a publication is made. They include reviewing

the originality of the idea at the very beginning of the research, so that time is not wasted on dead or dying topics. These topics usually lack newer or recent references. Hence hot topics should be identified. The type of manuscript like a full or original article compared to a limited article like a case report should be identified. Then the type of audience should be considered as topics of local/national relevance are sometimes not interesting to an international audience and hence may get rejected. Choosing the right journal is imperative and so all candidate journals should be scrutinized – their aims and scope, the type of article accepted, readership and current hot topics. Journals are judged by parameters like the citation index and impact factor to know their level of acceptance among researchers. They can be accessed on internet sites like Pubmed, Google Scholar, Index Copernicus etc. But then each of these parameters have their own limitations and should be viewed carefully as they further depend on other factors like the area of research involved, journal policy and can be plagued by bias. Lastly approach to different types of journals is necessary to enhance the chances of acceptance.

Why do papers get rejected? Because it is of limited interest, covers local issues only, is limited in scope or has been prepared poorly. But rejection is not the end of the world! Every effort should be made to understand the causes for rejection in order to revaluate and resubmit articles. Shorter articles are preferred by editors as they are reported faster and the chances of detecting an error reduce. Choosing different areas to publish articles is more fruitful. Author guidelines should be strictly adhered to avoid rejection. Beware of fake journals and fake publishers that vanish after 3 to 4 issues!

Finally ethical problems with scientific articles are on the rise globally. Unethical behavior like multiple submissions, plagiarism and data fabrication can earn rejection and even a ban from publishing in the journal. Thus ethical rules must be obeyed. Attention to details, considering reviews, acknowledging contributors and critical valuation of manuscripts are vital for acceptance into a journal and hence into the world of publishing and scientific research.

Novel Research Approaches to Unravel the Brain's Plasticity and Repair Mechanism: New Challenges in Treating Neurological and Psychiatric Disorders

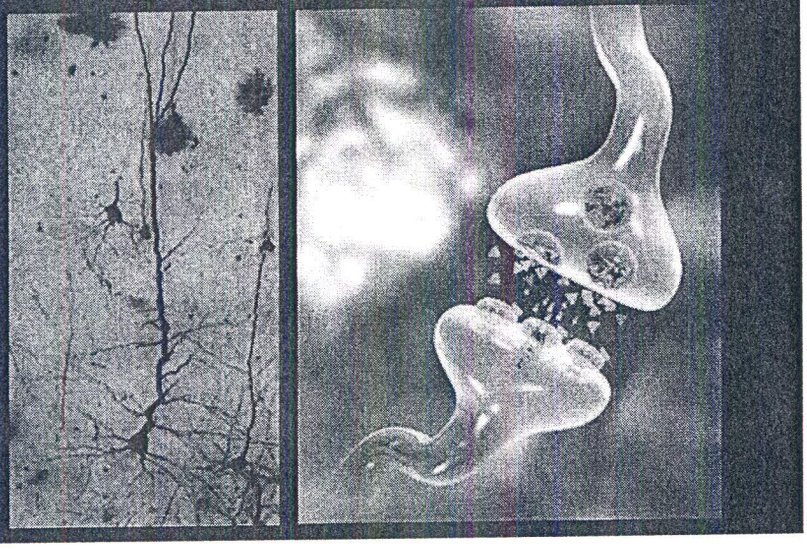
Dr. B.S.Shankaranarayana Rao,
Professor,
Dept. of Neurophysiology,
NIMHANS, Bangalore

Brain is an organ of mind. It interacts with external world, processes the information using different components and is responsible for cognition, attention and other different complex behaviour.

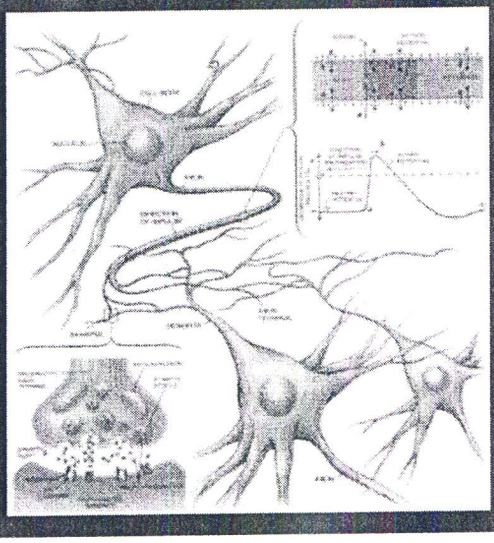
Human beings are advanced as they have a well-developed neocortex which controls the behavioural aspect. Complex cytoarchitectural organisation of different regions of the brain is thought to be responsible for different brain behaviour. Both serial and parallel neuronal connections are responsible for this complex behaviour. Behaviour is mostly modulated by the environment both external and internal.

Complex development of different patterns of behaviour is due to remodelling and rewiring of different neural circuits. At birth, a child has numerous neural circuits which get refined based on sensory inputs the child receives. As the child grows, development of grey matter occurs and connectivity of the brain increases. Specific connections useful for the child are retained and rest are discarded. The types of connections between neurons determine the complex behaviour.

Communication between neurons determine the Intelligence of an Individual



Communication between neurons determines brain's ability to process the information



Neuronal plasticity

Throughout life there is extensive reorganisation and remodelling of these circuits based on external and internal environmental inputs. A positive environment results in positive plasticity and perturbations leads to regressive plasticity and disease condition. Plasticity occurs at various levels of organisation. Hippocampus is a highly plastic region of the brain, extremely susceptible to various forms of insults. This is involved in declarative learning and memory.

Stress

It is a condition which perturbs physiological and psychological homeostasis resulting in disorders ranging from anxiety to Post Traumatic Stress Disorder (PTSD). Stress results in regressive plasticity of the brain. Longer duration of stress, severe in nature leads to inescapable anxiety, depression, presenile dementia and accentuated neurodegeneration. The potential damage stress can cause at the neuronal level include: loss of neuronal cell density in CA3 region of the hippocampus, dendritic atrophy, decrease in dendritic hormones, loss of connections and hampering of information processing in hippocampus.

In normal individuals, new information excites hippocampus. This enhanced active stimulus if maintained for a long time converts short term memory to long term memory (long term potentiation), which is the basis for learning and memory.

In stressful conditions, there is no enhanced information processing. Hence one cannot remember anything newly read during stressful situations and the performance deteriorates. Stress leads to hippocampal dependent loss of memory and defective spatial learning.

Hippocampus and frontal cortex help in decision making. In chronically stressed individuals, both hippocampus and frontal cortex undergo degeneration and hence are unable to take decisions during times of stress. During stress, there is decreased synaptic processing ability in hippocampus accompanied by decreased dopaminergic and cholinergic neurotransmitters.

In normal people, whenever a new thing is learnt, new cells are formed in hippocampus and their remodelling/ rewiring of circuits are essential for learning and memory. In stress, the

number of new cells formed is very less and also formed cells do not differentiate into neurons. Decrease in formation of proliferative cells leads to decreased survival of cells.

Is it possible to reverse these deficits associated with stressful conditions?

Stimulating brain directly and activating particular cortical area of brain helps restore neural circuits to some extent. Brain stimulation produces rewarding behavioural experience and induces progressive plasticity in multiple regions of the brain. Some of the types of stimulation include: enriched environment, locomotor and physical activity, sensory stimulation, social stimulation etc. Novel environment can interact with the brain and modulate the circuit progressively.

Treatment with bromocriptine restores dopamine in hippocampus and frontal cortex. Hence synaptic activity is restored back in the hippocampus leading to recovery of learning in stressed individuals.

Amygdala is responsible for fear, anxiety and emotions. Chronic stress induces cortisol release and increased growth & connections in the amygdala. On the other hand hippocampus degenerates in chronic stress. By selective suppression of the basolateral amygdala during and before stress, hippocampal degeneration is not seen and hippocampal transmission activity is restored. Untreated prolonged stress leads to depression. Due to aging or disease, there is a decrease in neurotropic factors. BDNF (Brain Derived Neurotropic Factor) increase by transgenic approach can help in preventing degenerative changes.

And finally, Yoga and meditation can induce progressive plasticity by increasing the dopaminergic neurons, increasing the cortical thickness of brain and the normal neurodegenerative disorders can be minimised.

IMPLICATIONS

- These studies throw light on the vulnerability and plasticity of hippocampal neurons to insults like stress and possible mechanisms for reversing the degenerative changes of these neurons
- Our studies provide cellular and molecular mechanisms of neuronal plasticity in response to different experiences. This information is critically important, because hippocampal neurons are affected in conditions like depression, stroke/ischemia, Alzheimer's disease, aging and epilepsy
- Understanding these plasticity mechanisms may have implications for treatment and in development of new strategies to prevent /ameliorate neurodegeneration and associated cognitive deficits

Gene Expression Studies and their Utility in the Management of Cancer Patients

Dr.Paturu Kondaiah
Professor,
Dept. of Molecular Reproduction, Development & Genetics,
IISc, Bangalore

Most human chronic diseases are correlated to defects in genes or expression of genes. Quantitative differences in the expression of genes in disease conditions have been used to evaluate the prediction of prognosis. New high throughput approaches have been of tremendous utility in the estimation of the expression of multiple genes.

There are many challenges in the management of cancer patients like early diagnosis of cancer, identification of tumours that show invasive phenotype by molecular markers (Gene expression, IHC). Many cancer patient show poor prognosis due to resistance to conventional therapy, hence they require prediction of the prognosis by gene expression signatures. To minimize the systemic side effects of chemotherapy we need to develop Targeted therapy by Identifying possible genetic lesion and design inhibitors (enzyme inhibitors or antibodies).

Cancer biomarkers can aid in diagnosis, prognostication, staging of cancers, monitoring response to treatment, identifying novel therapeutic targets. We Need to identify biomarkers involved in Oncogenic pathways (driving the tumor growth), Apoptosis (tumor initiation/progression), Angiogenesis (tumor progression), Tumor immunology (escape from immune surveillance), EMT, Cell migration & Invasion (tumor spread), etc.

Approaches to identify Cancer biomarkers includes Gene expression signatures methods , Gene amplifications methods, miRNA profiles, Methylation patterns of genes and Proteome analysis.

Our aims are to identify

- Differential gene expression signatures between diseased tissue compared to normal tissues

- Signatures/pathways that predict prognosis
- Targets that could be developed for therapeutic intervention

Global gene expression analysis study was performed on Breast cancers and Oral Submucous Fibrosis tissues .

Gene expression signatures in breast cancers of Indian patients was undertaken in collaboration with Dr Geetashree Mukerjee, Kidwai Memorial Institute of Oncology and Vaijayanti Gupta, Strand Life Sciences along with Surekha, D; Neeraj Kumar; Prasson Agarwal; Shwetha.

Worldwide, breast cancer is the fifth most common cause of cancer death (after lung, stomach, liver and colon). WHO Fact sheet no. 297, 2007. Women in the USA have 1 in 8 lifetime chance of developing invasive breast cancer (American Cancer Society, 2006). In India, breast and cervical cancer are the two most important types of cancers in females. Breast cancer is on a rise and is already the most prevalent cancer in women of urban India. There is a significant increase in the incidence of breast cancers in young women in our country. Presently 75,000 new cases are diagnosed in Indian women every year (Delhi Breast Unit, Apollo Clinic). Multiple factors are associated with an increased risk of developing breast cancer.

Challenges in the management of breast cancer patients

- ✓ Prediction of recurrence and Metastatic spread
- ✓ Personalized treatment options with patient centric targeted approaches
- ✓ Reliable prognostic predictions for better therapeutic management

Gene signature based prognostic predictions are being advocated for a more reliable management of recurrence and disease. There are at least two gene signature based prognostic assays for breast cancer, Mammaprint and OncotypeDx .

Signaling Pathways and Molecules Involved in the Progression of Breast Cancer include the followings

- Nuclear receptors – ERα, ERβ, PR etc.
- Growth Factors and Receptors – EGF, PDGF, TGFβ, IGF, etc.
- Proliferation markers – Cyclin E, Cyclin D1, p27 etc.
- Signaling molecules – PI3K, AKT, MAPK, mTOR etc.
- Her2 amplification.

Our aim of the study is

- Expression profiling of genes in breast carcinomas of various subclasses based on Node status, ER, PR, HER2, Triple negatives etc. in Indian patients
- Build gene networks that distinguish breast tumor that proceed to metastasis
- Identify and functionally characterize therapeutic targets

Identification of gene signatures in Indian patients is important because the behaviour of the disease is some what different from the western patients. Breast cancer gene profiling worldwide reveals variation in gene expression signatures indicating heterogeneity in breast cancers. Higher frequency of ER $^{-ve}$ /PR $^{+ve}$ breast cancers in Indians as compared to western population and more incidence of aggressive breast cancers in younger women(<30 yrs) in India.

Tumor and normal samples are collected from KMIO, Bangalore along with Pathological evaluation. RNA isolation, quality check Selection of tumor samples were done.

A total of 80 arrays were hybridized and analyzed on breast tumors representing various categories.

S.NO.	TYPE	NODE +ve	NODE -ve
1	ER -ve	18	27
2	ER + ve	12	7
3	PR -ve	14	24
4	PR + ve	17	9
5	HER -ve	13	19
6	HER + ve	16	14
7	TRIPLE -ve	7	13

S.NO	Sample type	Numbers
1	NODE -ve	35
2	NODE +ve	34
3	ER -ve	47
4	ER +ve	21
5	PR -ve	41
6	PR +ve	27
7	HER -ve	35
8	HER +ve	32
9	TRIPLE -ve	22
10	TRIPLE +ve	12

Pooled RNA from some 8 Non- tumorigenic regions of breast tissues served as Reference RNA

- 21 genes for OncotypeDX and 70 gene signature genes (Mammaprint Breast Cancer) were used for the analysis.
- All the Unique Caucasian dataset genes were matched in both cases.

- GSA Analysis was done for Indian data & Caucasian data, taking OncotypeDX (21 genes) & 70 gene signature gene data sets.
- Some genes matched with LN status in Indian Patients with respect to 70 Gene signature
- No match with the Oncotype Dx or Mammaprint genes with Indian recurrent patients
- Oncotyhe Dx matched with Cacausian patients

Summary of breast cancer findings.

- Micro array based expression profiling revealed several common and differentially expressed genes in DCIS and various categories of breast cancers
- Over expression of several novel transcription factors in Triple negative tumors was identified
- There are several unique genes that are expressed in Indian patients compared to Caucasian patients
- Most importantly, there is a great deal of discordance between Indian patient gene expressions with respect to OncotypeDx and Mammaprint
- Prognosis data revealed differntially expressed genes in the primary tumors of those patients that showed distant metastasis; this data also validates in a caucasian data set
- There is a need to develop prognostic predictors for Indian Patients since both the available diagnostic tests are for ER+ve patients and good number of Indian patients are ER-ve.

Molecular pathology of Oral Submucous Fibrosis

Oral Submuous Fibrosis (OSF) is a chronic inflammatory disease resulting in progressive juxta-epithelial fibrosis of the oral soft tissues that leads to difficulty in chewing, swallowing, speaking, and mouth opening (Henry *et al.*1987) . Epidemiological studies have shown that

OSF is a precancerous condition (Pindborg *et al.*, 1984) and carries a risk of 2-8% for malignant transformation (Angadi PV *et al.*) . This disease affects >0.5% (5 million people) of the population in the Indian subcontinent and is now a public health issue in many parts of the world, including the United Kingdom, South Africa, and many south east Asian countries (Chiu CJ *et al.*, 2002) .Habit of chewing betel nut (*Areca catechu*) in the form of quid was found to be the major risk factor associated with OSF (Sinor et al., 1990; Maher *et al.*,1994). Areca nut is used as a masticator substance by approximately 600 million people worldwide.

Various pathways showing differential expression in Oral Submucous Fibrosis as revealed by KEGG pathway analysis

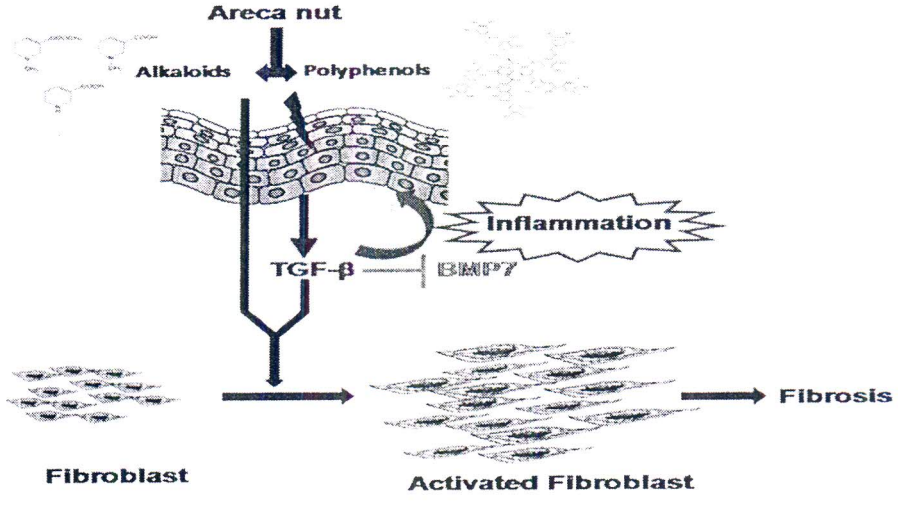
KEGG Pathway Name	**No of Genes**	**KEGG Pathway Name**	**No of Genes**
LEISHMANIA INFECTION	22	NATURAL KILLER CELL MEDIATED CYTOTOXICITY	27
ECM RECEPTOR INTERACTION	26	TOLL LIKE RECEPTOR SIGNALING PATHWAY	21
CYTOKINE CYTOKINE RECEPTOR INTERACTION	54	LEUKOCYTE TRANSENDOTHELIAL MIGRATION	35
FOCAL ADHESION	55	T CELL RECEPTOR SIGNALING PATHWAY	23
VIRAL MYOCARDITIS	22	CELL ADHESION MOLECULES	31
SYSTEMIC LUPUS ERYTHEMATOSUS	24	PARKINSONS DISEASE	15
HYPERTROPHIC CARDIOMYOPATHY	24	VASCULAR SMOOTH MUSCLE CONTRACTION	32
MELANOMA	23	REGULATION OF ACTIN CYTOSKELETON	60

CHEMOKINE SIGNALING PATHWAY	40	TGF BETA SIGNALING PATHWAY	22
COMPLEMENT AND COAGULATION CASCADES	20	ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY	21
DILATED CARDIOMYOPATHY	24	KEGG OXIDATIVE PHOSPHORYLATION	15
HEMATOPOIETIC CELL LINEAGE	18	KEGG AXON GUIDANCE	35

Activation of TGF-β pathway by areca nut constituents: A possible cause of Oral submucous fibrosis study shows that areca Nut extracts induces Genes that overlap with TGF-β regulated genes in epithelial cells . Pure compounds of areca nut induce TGF-β and down regulate anti fibrotic cytokine, BMP7.

Working model of mechanism of Oral Submucous Fibrosis

Figure 6.



"Epigenetics and Cancer: Targeted for New Generation Therapeutics"

Prof. Tapas K Kundu

Professor,

Jawaharlal Nehru Centre for Advanced Science Research,

Bangalore

Epigenetics is one of the emerging areas for studying the pathogenesis for cancer in oral cavity, HIV and CNS disorders. Its components are chromatin which is a complex three-dimensional organization of the eukaryotic genome composed of DNA, histones, nonhistone proteins and RNA components, which are intricately packed within the nucleus. Chromatin modifying enzymes (lysine (K) acetyl transferases for acetylation, lysine and arginine (R) methyl transferases for methylation) by virtue of their modifying abilities of both histones and the non histone components, are vital regulatory factors for gene expression both in physiological as well as pathophysiological conditions. Hence the modulators (inhibitors/activators) of these enzymes, which are capable of altering the gene expression globally, could also be useful in understanding the epigenetic mechanism of gene expression as well as for therapeutic purposes.

Role of Acetylation in Modulating NPM1 function: NPM1 gets acetylated by p300at its C-terminus. Acetylated NPM1 has enhanced histone chaperone activity and interaction ability with acetylated histones. Acetylation of NPM1 is a prerequisite for it to activate acetylation dependent transcription from chromatin template. Loss of acetylation of histone HAT is hypothesized in cardiac hypertrophy, diabetes, inflammatory lung disease like asthma, neurodegenerative like Huntingtons' disease and liver cancer, breast cancer and leukemia.

Acetylation and deacetylation process maintain activation and deactivation process in chromatin and thus the homeostasis in nucleus. In cancer normal cell is hyperacetylated or acetylated but a cancer cell is hypoaceylated. Exception is breast and thyroid cancer where the cells are hyperacetylated.

Oral Cancer in India

(OSCC) Oral squamous cell cancer originates in the tissues that line the mouth and lips or the tongue. It may also occur on the floor of the mouth, cheek lining, gingiva or palate. It is the most prevalent among Indian men. Most cases are not detected in the early pre-cancerous stage. Although, NPM1 has been reported to be overexpressed in several cancers there is no information about its status in oral cancer. Oral cancer is the topmost killer in India.

Role of NPM1 in oral cancer:

Samples from a major Oncology institute in Bangalore showed that as the grade of oral cancer on histopathology examination increases the expression of NPM1 is over expressed i.e, NPM1 is predominantly acetylated in malignant tumors.

p300 is hyperacetylated in oral cancer whereas SIRT is not acetylated. All proteins expressed by p300 including H3 protein is upregulated. NPM1 enhances the autoacetylation of p300 and hence it's HAT(histone acetyl transferase) activity. Futuristic drugs should be designed on p300 which is autoacetylated and has HAT activity.

GAPDH is an inducer of autoacetylation of p300 along with NPM1 in oral cancer. NPM1 c-terminal is involved in enhancement of expression of autoacetylation of p300. Mechanistically, over expression, as well as enhanced autoacetylation of p300 induced by nucleophosmin (NPM1) and glyceraldehyde 3-phosphate dehydrogenase (GAPDH) causes the hyperacetylation, which is nitric oxide (NO) signal dependent through IFN-γ will lead to HAT activity and upregulation of genes in oral cancer. The acetyl transferase inhibitors are potential drugs for treatment of cancer for e.g. curcumin, plumbagin, garcinol and lysyl CoA. Inhibition of the histone acetyltransferase (HAT) activity of p300 by a water-soluble, small molecule inhibitor, Hydrazinocurcumin (CTK7A), substantially reduced the xenografted oral tumor growth in mice. These results, therefore, not only establish an epigenetic target for oral cancer, but also implicate a HAT inhibitor (HATi) as a potential therapeutic molecule. Garcinol found in fruit rind of garcina indica has potential inhibitory activity of HAT. Luteolin has also HAT inhibitory activity substantially reduced the xenografted mice implanted with oral tumor.

Further the micro RNA modulation is seen through p300 inhibition. Combination of chemotherapy and miRNA has been tried in liver cancer.

Another aspect is lysine methylation by CARM1 in oral cancer. H3R17 is tremendously upregulated at protein level and RNA levels in oral cancer. Another potential chemical is TBBD from pomegranate fruit inhibits CARM1 though proline presence in TBBD perfectly fits the substrate i.e CARM1(Coactivator associated arginine methyl transferase) mediated inhibition of H3.

The multiple target levels in oral cancers are

1. TBBD – CARM1. CTK7A – P300

Herbal Medicine: Challenges and Research Needs

Dr Sanjiva D Kholkute
Director,
National Institute for Research in Reproductive Health (ICMR),
Mumbai

WHO defines traditional medicine as "health practices, approaches, knowledge and beliefs incorporating plant, animal and mineral based medicines, spiritual therapies, manual techniques and applied singularly or in combination to diagnose treats and prevent illnesses or maintain well-being."

Herbal medicine and traditional medicine are not the same. Herbal medicine is a "medicinal product consisting of a substance produced by subjecting plants to drying, crushing or any other processes, or of a mixture whose sole ingredients are two or more substances so produced."

There is a misconception that herbal medicine and Ayurvedic medicine are the same but they are two different entities. The codified systems of traditional medicine are Ayurveda, Unani, Siddha and Homeopathy. AYUSH constituted Ayurveda, Yoga, Unani, Siddha and Homeopathy which is now called as indigenous systems of medicine. The non codified system was started before Ayurvedic medicine and it constitutes folk medicine or ethnomedicine. Ayurveda does not comprise only medicines obtained from herbs.

Herbal medicine is one of the oldest forms of health care. It evolved even before agriculture had started. About 80% of world population rely on traditional / herbal medicine for primary health care and 30% of the worldwide sales is based on natural products. Herbal medicine provided modern medicine with drugs like morphine, quinine, cocaine, tubocurarine, pilocarpine, reserpine etc. and also provided new lead structures, templates and scaffolds for drug discovery.

There are 47000 different plant species in India and among them 15000 are designated as "medicinal". 1500 medicinal plants are mentioned in Ancient Indian literature and currently 800 plants are used as sources for Herbal Medicine. Natural products play a role in drug development by:

- Drug leads/pathfinder compounds
- Greater structural diversity

- Economical source of chemical diversity than synthesis of equivalent numbers of diverse chemicals
- Source of novel low molecular weight agents
- Capable of being absorbed & metabolized also orally active
- 39% out of 520 new approved drugs are from natural products
- 60-80% of antibacterial & anticancer drugs are from natural products
- Only less than 10% world biodiversity has been screened for biological activity

Secondary metabolites are compounds produced by plants which are not useful to them but are useful to human beings and to reproduce these products in lab may take several days.

The resurgence in traditional/herbal Medicine are due to the factors such as side effects of modern drugs, problems with drug – resistant microorganisms, emerging diseases (AIDS) where no suitable medicines are available, need for effective drugs for chronic / difficult to treat diseases such as cancers, cardiovascular diseases, diabetes, rheumatism, socioeconomical, cultural aspects and difficulty in identifying new lead structures. Traditional medicines if used appropriately are associated with lesser side effects, for example if basma is prepared properly it does not produce toxicity by metals as highlighted in New England Journal of Medicine.

There are many success stories from botanical medicines, like use of Artemisinin in malaria, Rauwolfia alkaloids (reserpine) in hypertension, Psoralens in vitiligo, Guggulsterones in hypolipidemia, Mucuna prurieus in parkinson's disease, and certain plant products like Picrosides as hepatoprotectant, Cucurmine with anti-inflammatory activity useful in arthritis, Steriodal lactones as immunomodulators and Piperidines as bioactivity enhancer.

The positive features of herbal medicines are their easy availability or accessibility, socioeconomical, cultural & spiritual aspects, cost effectiveness, low level of technological inputs, lesser side effects and may serve as a source of leads for the following:

- Drug resistant microorganisms
- New emerging diseases
- Chronic / lifestyle diseases like cancer, diabetes, cardiovascular diseases, rheumatism, viral diseases

There are some constraints existing with the use of herbal medicines such as use of plant for a treatment mainly based on clinical experience i.e., wide-spread use even before "scientific" evaluation, formulation contains a variety of "active substances" in various concentrations whose mode or mechanism of action is not established, raw material is from wild source and is dependent on supplier, problem of correct identification of plant. There is comparability between plant preparations and parts used such as fresh plant or part of the plant or dried or extract/decoction and hence the active components may vary depending on the preparation / part used. There is lack of certification of raw material, adulterations/substitutions, lack of stringent regulations for the process materials, manufacturing processes, shelf life or stability of the finished product and no stringent regulations for packaging and labeling.

The reason for research needs in the field of herbal medicine are standardization & quality control of herbal medicines, potential toxicity when high dose or prolonged usage, teratogenicity, efficacy, mode of action, herb-drug and herb-herb interactions, sensitive subpopulations, effect on developing fetus, young ones, elderly, awareness among users and practitioners. Standardization is adjustment of given contents of phytoconstituents or chemical markers, maintaining consistency in quality and able to reproduce.

Why Standardization?

1. Herbal medicines are complex mixtures and active ingredients may not be known and may constitute only a small percent of total product.
2. Dried parts commercially available may be cross contaminated and can be misidentified and there may be batch to batch variations.
3. Active ingredient may vary based on the part of the plant used, season of collection, weather, and soil.
4. Combined actions of several ingredients.

Quality control is required to ensure uniform potency, increase reliability, avoid batch to batch variations, assure predictable therapeutic response or efficacy, avoid toxicity or adverse effects and for comparison with other standard drugs. Factors affecting quality are

environment, geography, soil, place, season, maturity, time of harvesting, subspecies, varieties, wild and cultivated (secondary metabolites) sources.

Standardization of herbal medicine can be done by identification and authentication of species with macroscopic and microscopic evaluation, parts of plants with medicinal value to be collected based on season and geographical location, shade drying or drying at moderate temperature depending on chemical constituents, processing depending on chemical nature of constituents, stored at 25^0 to 30°C in dry and ventilated place to prevent fungal or bacterial growth, infestation by insects and rodents.

Physico-chemical evaluations based on ash value, extractive value, moisture content, chemical evaluations for identification of marker compounds, DNA finger printing, pesticide residue, heavy metal contents and microbial contaminations should be under specified limits

Herbal medicines may be toxic and documentation of adverse effects is largely limited/scanty, preclinical safety data are not available, data on safety associated with prolonged use lacking and minimal research on possible adverse effects on reproductive systems, teratology, carcinogenicity etc. Medicinal plants cannot be assumed safe because they are "natural" eg., aflatoxin, pulegone, etc.

Herb/Herb and Herb/drug Interactions are not systematically documented. Herbs as therapeutic agents can cause synergistic or antagonistic interactions with other pharmacologically active compound, medicinal plants may have similar or opposite therapeutic effects. For ex., warfarin may delay blood clot formation; garlic, ginger, ginseng has similar effects, St. Johns Wort may affect metabolism of drugs. Package insertion may not have adequate information. So it is important to identify these interactions and create consumer awareness. Data should be compiled based on age, gender, nutrition, allergic response, contraindications etc.

Increased awareness or education can be created in general public about their unawareness of adverse health effects as only positive aspects are mainly highlighted, about lack of clinical trial data on herbal medicines, contraindications being not mentioned, and shelf life /stability data not made available. Thus information on efficacy, safety, quality control of the herbal formulations and both beneficial as well as adverse effects should be provided to the consumer.

Way ahead

- India is sitting on a gold mine of well-recorded and well-practiced knowledge of traditional herbal medicine
- Both experimental and clinical studies are needed to expand the validity and value
- Skepticism about unconventional practices higher than conventional practices, hence a demand for rigorous multi-disciplinary research involving experts in basic, clinical and traditional medicine is required before acceptance
- The continuing interface between conventional and traditional medicine provides the opportunity for new strategies and methodologies to emerge in the age of global medicine

Summary

- Oldest system of medicine still in practice: testament to real and perceived beneficial effects
- Increased interest in recent years as an alternative/substitute to modern medicine
- Medicinal plants are "natural" : no assurance for safety
- Information regarding adverse effects associated with high dose/chronic use/sensitive subpopulations lacking
- Active ingredients not known in many cases
- Lack of information on herb/herb and herb/drug interactions and mechanism of action

"An Editorial in New England Journal of Medicine 1998 opines that there cannot be two types of medicine- conventional and alternative. There is only medicine that has been adequately tested and medicine that has not, medicine that works and medicine that may not work. Once a treatment has been tested rigorously, it no longer matters whether it was considered alternative at the outset".

Research Design and Grant Writing - Eight Steps Approach

Shivaprasad S Goudar
Director, Dept. of Medical Education
Research Coordinator, Women's & Child Health Unit,
KLE University's JNMC,
Belgaum

Post Graduate scholar's and young faculty often will need vital information on how to plan a research design and to write a research project for extra mural funding from national and international funding agencies. The "Eight steps – 28 questions" of Prof Georges Bordage, Department of Medical Education, University of Illinois at Chicago essentially focuses on Research Design and Grant writing and includes,

1. Transform an idea into a question (1-9)
2. Select instrumentation (10-11)
3. Select the best study design (12-15)
4. Select statistics (16)
5. Determine sample size & sampling (17-20)
6. Monitor data quality (21)
7. Set timetable and budget (22-25)
8. Write a grant proposal (26-28)

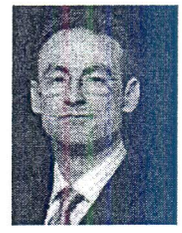
	Eight Steps	(28) Questions
1	Transform an idea into a question (1-9)	1. What is the topic (idea) of study? 2. What has been done before? The literature 3. What is the major outcome of the study? 4. What is the intervention? 5. Looking for a difference or an association? 6. What population to apply results? 7. What is the specific research question? 8. What is the expected answer? Hypotheses 9. Why do this study? Importance,

		Relevance
2	Select instrumentation (10-11)	10. Will you use or modify an existinginstrument or develop a new one? 11. What are the psychometricqualities of the scores?
3	Select the best study design(12-15)	12. Do you want to observe orintervene? 13. Do you need a control group? 14. How will you control forconfounding variables? 15. What is "best" study design toanswer your question?
4	Select statistics(16)	16. Which statistics best fits theresearch question, hypotheses,design, and variables?
5	Determine sample size & sampling (17-20)	17. What are the criteria for inclusion /exclusion? 18. How to obtain subjects? 19. How to assign subjects if anexperiment? 20. How many subjects are needed?
6	Monitor data quality (21)	21. How to- collect data & - monitor data quality?
7	Set timetable and budget (22-25)	22. What is the timetable (schedule)? 23. Who will be doing what(personnel)? 24. What equipment will you need? 25. How much will it cost (budget)?
8	Write a grant proposal (26-28)	26. How will you keep track of thestudy, including schedule, personnel,and budget? 27. What is the granting agency interested in funding? 28. What forms and application process will you have to follow?

There is a need to emphasize on following issues related to research design and grant writing,

- Ethical Guidelines for Biomedical Research (IRB / IEC approval)
- Grant Proposal – Elements
- Four successive ingredients to obtain funds

Matching the study design to the research question



Dr. Stephen Brett
Head for Research, Directorate of Anaesthetics & Critical care,
Imperial College Health Care, NHS Trust,
London, UK

Research is defined as "formal work undertaken systematically to increase the knowledge, including knowledge about humanity, culture and society and use of this stock of knowledge to devise new applications". The history of research can be traced to as early as Aristotle and the medical research to the time of Hippocrates.

There are various reasons for the conduct of research in medicine. It helps us to acquire new knowledge for improving the health of individuals and thus of the whole population. It is through research that we are able to make new innovations be it in diagnostics or therapeutics. Now a day's research is mandatory for career advancement. Also it seems that academic health care is better health care as they have more resources and have lower morbidities and mortality rates.

The main focus of research in medicine is to learn about the natural history of disease like why it occurs, what the disease does to the body, the susceptible population and ways of diagnosis, the treatment options and also regarding the care delivery system. For answering all these queries, different types of research is done. Types of research could be quantitative, qualitative, and translational. Most recent areas of research are bioinformatics, which includes genomics, transcriptomics, proteonomics and metabanomics.

Origin of an idea to carryout research can be raised out of curiosity, concern, opportunity, novel information, new diagnostic or therapeutic innovation. Research in the clinic can be carried out by first understanding of current local situation, importance of local epidemiology, availability of the stake holders like patients, doctors, nurses and funding sources and regulatory requirements.

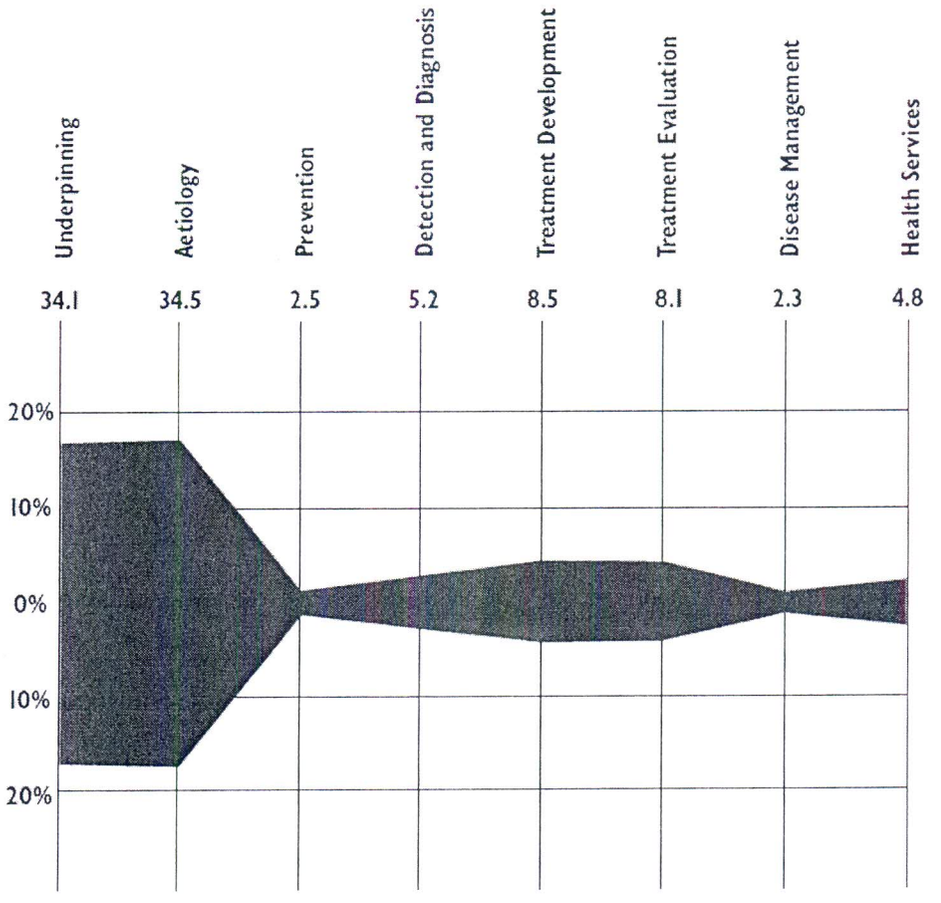
Levels of research starts with case reports, case series, case control (look backwards), cohort studies (look forward), randomized clinical trials, systematic review

and meta analysis. For carrying out systematic review and meta analysis the search engines which can be used are Pubmed, EMBASE, Cochrane library, clinical trials govt., current clinical trials and national library of medicine. Such studies can be vulnerable because of flaws in the original studies and heterogenicity of original study designs.

The study quality dependence on the design, sample size, randomization, blinding, size effect and follow up rate. The Hawthorne effect is a psychological phenomenon which produces an improvement in human behavior or performance as a result of increased attention by clinicians. 'Hawthorne Effect' may have a role in clinical trials and it is an important factor affecting the generalisability of clinical research to routine practice

Importance of rolling clinical information helps in national clinical audit program, identifying outliers, relating the process to outcome, to secure data on the current picture, outcomes/ endpoints of the study. Outcome measure of the study could be in the form of exposure and outcome, intervention related like response to treatment, identifiable confounders or sources of bias (allocation, enrolment, ascertainment, reporting) and disease free intervals/time to worsening.

Chart 2.3: Proportion of combined total UK spend by research activity (expressed as percentage of total spend)



Source: UKCRC Health Research Analysis.
Note: Data excludes R&D support for NHS providers funded by the UK Health Departments, core support costs and research taking place outside the UK.

Innovation research in the pipeline are, Bench to bedside, Early phase or translatable, Translational, Clinical and Applied research. Seeming tensions are in clinical versus non-clinical, translational versus non translational, observational versus interventional and quantitative versus qualitative. Laboratory studies are undergoing changes as previously, it was disease description, drug and device discovery and biomarker discovery.

Clinical trials - Drug trials are being carried out in four different phases (Phase 1-4). Drug and device development needs clinical trials, better phenotyping of populations

needed to offset risk in the form of focused enrollment, adequate power, adaptive trial design.

Qualitative Research - the methods used here are observations, interviews, questionnaire, survey, document analysis, narrative and focused group discussions. It will give the researcher rich data about the experiences and attitudes. The strength of qualitative research lies in validity.

Research Collaborations in India

Imperial College London- Indian Institute of Science, Bangalore

Adaptive Security Network Scheme

Dr Jeremy Pitt -Investigate and develop an innovative approach to security in mobile computer networks.

Imperial College London-All India Institute of Medical Sciences (AIIMS), Delhi

Genetic basis of ischaemic stroke in an Indian population

Dr Pankaj Sharma -Establish the first and largest collection of DNA in Indian ischaemic stroke victims. This repository will be invaluable for future researchers.

Imperial College London- Indian Institute of Science, Bangalore

Shape Memory Alloys

Dr David Dye-Develop new high temperature shape memory alloys, and to develop the tools of combinatorial materials.

International Partnerships with India

Rajiv Gandhi Centre for Innovation and Entrepreneurship

Acts as the point of reference between Indian and British collaborators in innovation and entrepreneurship.

Research projects monitor technology trends in energy, study business model innovation practices globally, and benchmark public-private partnerships in the UK and Indian contexts, among others.

Grantham Institute- Divecha Centre

The Grantham Institute for Climate Change collaborates with its sister institute, the Divecha Centre for Climate change at the Indian Institute for Science in Bangalore. This

collaboration has focussed on understanding the impacts and risks associated with climate change and the changing water cycle.

MoUs with IIT Delhi, IIT Ropar, Bhabha Atomic Research Centre and CII

Pathogenesis of Neurological Disorders

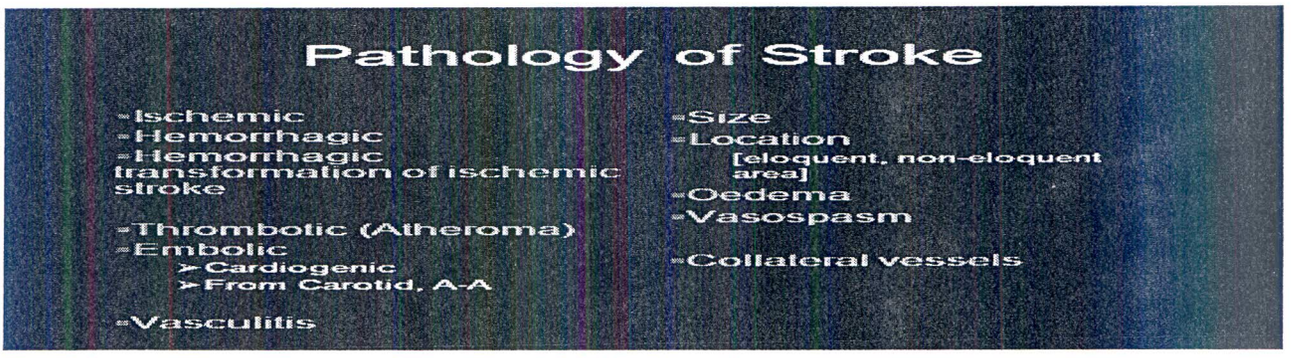
Dr. Chandran Gnanamuthu
Formerly Professor & Head
Dept. of Neurology
CMC, Vellore

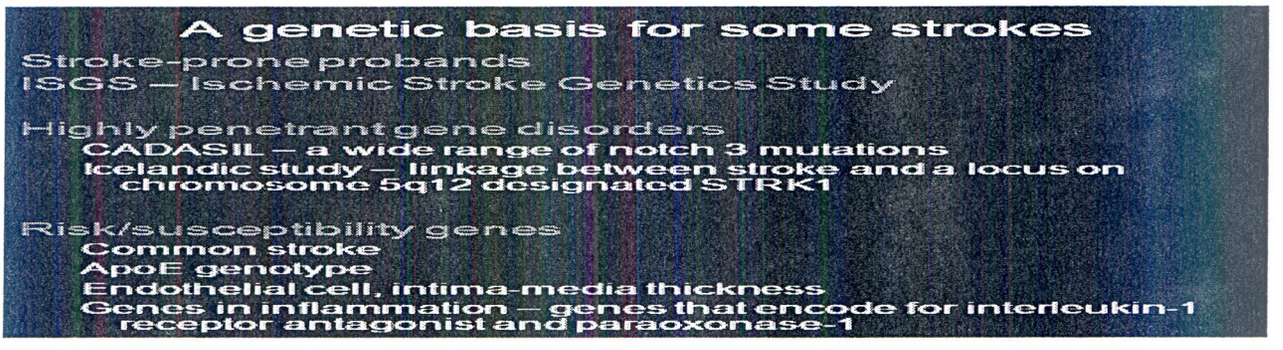
General causes of diseases:

- Genomic
- Proteomic –conformational changes in the tertiary structure of neuronal proteins: taupathies (AD, PSP), synucleopathies (PD), etc.
- Trauma – CNS / PNS
- Neoplasia – benign, malignant
- Vascular – blood vessel changes (intima, media, adventitia),
- Hematologic – pro-thrombotic (infarct), deficient coagulants (hemorrhage)
- Aging

Stroke - Presentation

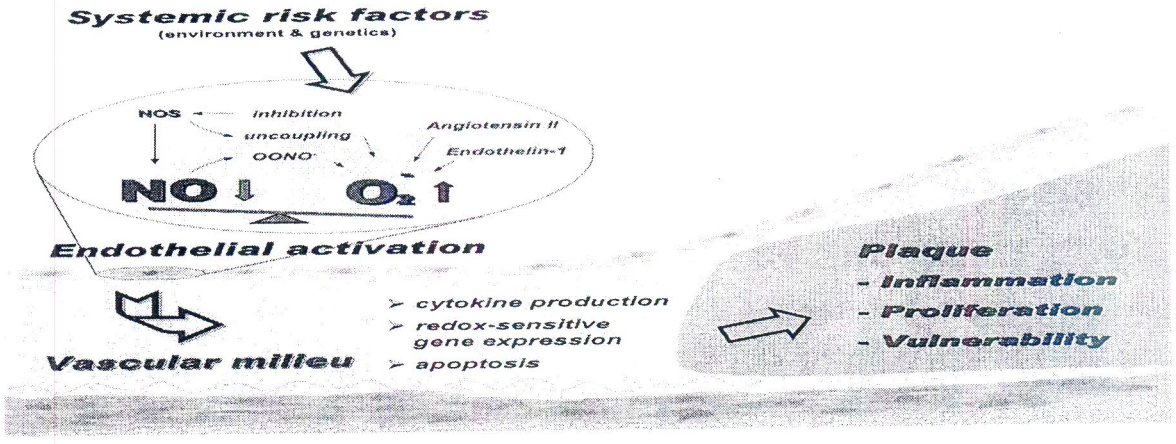
- TIAs only
- TIAs progressing to a persistent neurologic deficit - major or minor
- Stepwise development of a stroke, with or without TIAs
- Stroke developing as a single event:
  - Abrupt (mins / hrs), with or without fluctuations
  - Slow, gradual (few days), with or without minor fluctuations
- Limited stroke followed by TIAs
- Small stroke-like events, recurrent over a period of time, with progressive deficits





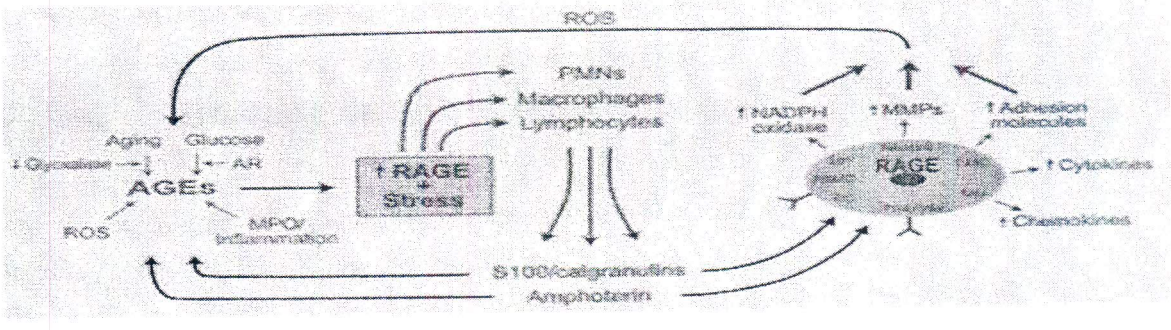
Genetic:

1. CCR5 gene
2. Hypercholesterolemia
3. LDLR
4. Secondary hyperlipoproteinemia
5. Optimal serum lipid levels
6. Oxidative stress



The **pathogenesis of atherosclerosis** and the role of the following in atherosclerosis:

1. Reaction to injury hypothesis
2. Monoclonal hypothesis
3. Inflammatory response
4. Role of interleukins and cytokines
5. Role of macrophages and monocytes
6. TLR/ LXR/RXR receptors
7. Advanced glycation end products (AGE)
8. Age cell receptors (RAGE)



Causes of cervical artery dissection:

Ehlers Danlos syndrome type IV (autosomal dominant), Marfan's syndrome (autosomal dominant), osteogenesis imperfecta (autosomal dominant [types I, II, IV] and recessive [type III]) and pseudoxanthoma elasticum (autosomal dominant and recessive forms described)

Causes of intracranial arterial occlusive disease:

Pseudoxanthoma elasticum and neurofibromatosis type 1.

Fabry's disease (X-linked recessive inheritance) is a lysosomal storage disorder characterised by angiokeratoma corporis diffusum - dark red papules found on the lower trunk, perineum and thighs. Deficiency of a-galactosidase leads to accumulation of trihexosyl ceramide in blood vessels. Patients die in the fourth and fifth decades from cerebrovascular, cardiovascular or renal disease.

CADASIL: Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy

MELAS: mitochondrial encephalopathy with lactic acidosis and stroke-like episodes

- A3243G mutation in the tRNA gene of mitochondria
- Relapsing, remitting course in the young (teenage / young adult)
- Can mimic herpes encephalitis
- Short stature, bilateral ptosis, (mild) elevation of serum lactate
- Brain ischemia not following a specific arterial territory. Bilateral basal ganglia calcification.

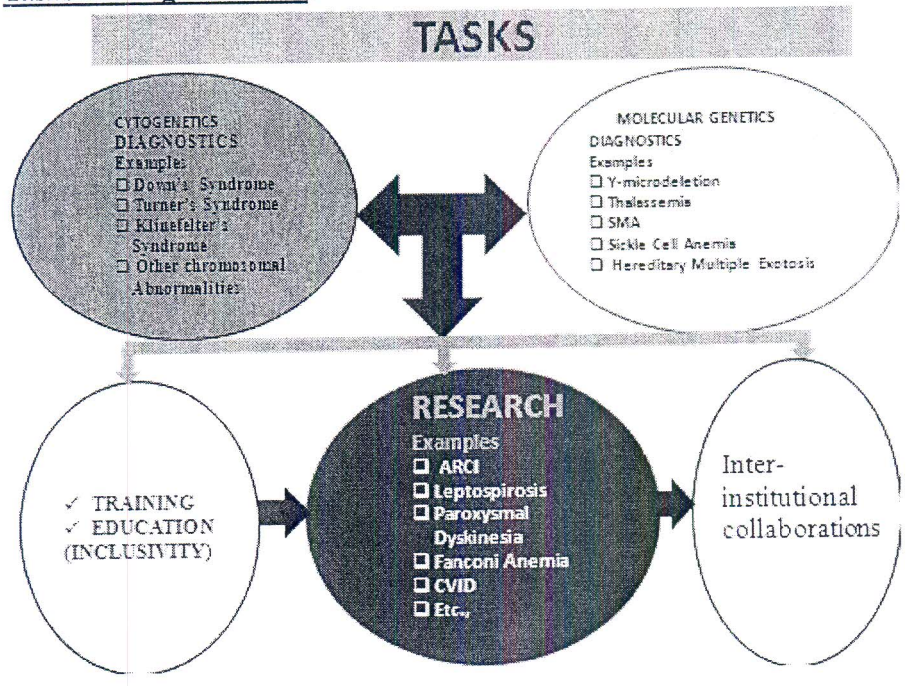
Anti-Phospholipid Antibody syndrome (APLA syndrome):

Homocysteinuria: Upward dislocation of the lens.

The Kolar Experience in Laboratory Driven Medical Research – Some Anecdotes

Dr. P.R.Krishnaswamy
Research Advisor,
Sri Devaraj Urs Academy of Higher Education & Research,
Kolar

Tasks of the genome lab:



KARYOTYPING AND CYTOGENETICS AT SDUAHER

No. of cases :	189
Total No. of Cases Completed :	147
Total No. of Cases Processing:	42

No of interesting and rare cases	6
No of cases with NO phenotypic and genotypic corelation	47

Dysmorphic Features and Congenital Anomalies	11
Down's syndrome	3
Repeated spontaneous abortions	3
Trisomy- 13,18,21	1
3pter-p25 Deletion Syndrome	1
Pataus Syndrome	1

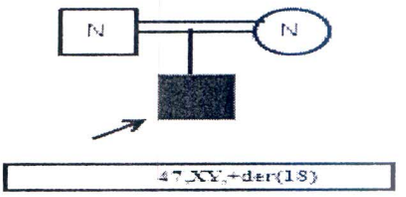
A novel micro-duplication 8q24.3 (924.381 kb) characterized by array CGH and 47,XY,+mar[der (18)]in a newborn with clinical features of Trisomy 18

- 1 month old (newborn male baby)
- Normal delivery, Vertex presentation
- Dept of Pediatrics(NICU), R.L.Jalappa Hospital, KOLAR
- Referral Diagnosis: Dysmorphic features, MCA/?Trisomy 18

ON EXAMINATION:
- Birth Wt. 1.82 kg
- Admitted NICU
- Facial dysmorphism, Clinical features of Trisomy 18 syndrome – Short palpebral fissure, Low set ears, Micrognathia, prominent occiput, Rocker bottom feet, Clinodactyly, overlapping fingers, Laryngomalacia, CHD – PDA, Hydronephrosis (PUJ obstruction).

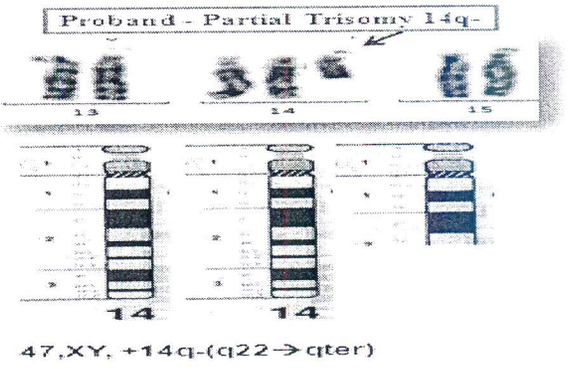
CYTOGENETIC STUDIES:
Provisional report:
KARYOTYPE : 47,XY,+der(18)(mos)
Comments: Mosaicism for derivative chromosome 18 was observed.

Karyotype of parents confirmed normal 46,XX (Mother) and 46,XY(Father).



Partial Trisomy 14 q- in a 5 year old Proband: resulting from balanced maternal translocation 46, XX, t(12p:14q)(p11:q22)

- **5 yrs old Male child**
- **Clinical findings :**
  Low set ears, Prominent pinna, Retrognathia, Beaked nose, Microcephaly
- **Clinical Diagnosis:**
  Global developmental delay with Nutritional anemia with pulmonary stenosis with ? ASD



47,XY, +14q-(q22→qter)

Attempts at Molecular Genetics - Inter Institutional Collaborations

1. Indian Institute of Science, Bangalore
2. Manipal Hospital, Bangalore
3. NIMHANS, Bangalore

Turner Syndrome complex Mosaicism: An unusual case with multiple cell lines in a 16 year old Proband

- **16 yrs old female**
- Brief History : **Patient not attained menarche, No breast development, H/o Short stature, No h/o thyroid disease.**
- Family history : 3rd degree consanguineous marriage, mother – short stature, father- normal & well built, Brother – normal, well built.
- Clinical findings : No axillary hair, no breast development, pubic hair- sparse, USG – **Hypo plastic uterus**
- Clinical Diagnosis : **Turners syndrome.?**

Karyotype Analysis :

- **Total no of cells captured – 102**
- **Total no of cells analyzed – 42**
- **Different Cell lines:**

1.	45,X	- 20
2.	46, XX(IsoXq)	- 15
3.	46, XX, r(X)	- 1
4.	47,XXX (IsoXq)	- 1
5.	45, X(12p–)	- 1
6.	45, X(12q–)	- 2 ?

Clinical workup and differential diagnosis made by Dr. Prabhakar, Dr. Anitha.A and team referred to the genomic laboratory

❖ **A 22 year old male patient presents with**

Major complaints:

- ✓ loose stools-8 years
- ✓ Cough-8years

History of presenting illness:

- ✓ Loose stools since 8years, 4 to 5 episodes per day, watery yellowish, foul smelling, no blood or mucus.
- ✓ passage of worms in stools five years back for which he received treatment.
- ✓ loss of weight since 8years
- ✓ intolerance to milk and milk products
- ✓ knee joint pain since 5years
- ✓ ear discharge since 10days-pus,not blood tinged.

PROVISIONAL DIAGNOSIS

- Chronic diarrhea for evaluation with growth failure
- Cystic fibrosis
- Hypopituitarism
- Congenital heart disease
- Immuno compromised state

ON EXAMINATION

- Poorly built and nourished(fully emaciated),oriented to time place and person
- Lymphadenopathy (submandibular and cervical)+
- Height: 130cms:
  upper segment-59.5cms;lower segment-70.5cms; US/LS=0.84
- Weight =16kgs
- BMI :9.47
- Arm span=128.5cms
- Herpes labialis and Ears: Bilateral CSOM(TTD)
- Respiratory System: Trachea central, Bilateral basal area –impaired note, coarse crepitations heard.
- Cardio vascular system:S1 ,S2 heard ,no mummurs
- Per abdomen examination: soft, non tender, no organomegaly
- Nervous system: No focal neurological deficit

INVESTIGATIONS

HAEMOGRAM
Haemoglobin:9.3gm%
WBC:6300cells/cu.mm;DC-N-55%;L-30%;E-13%;M-2%;
Platelets:1,86,000/cu.mm
ESR:20mm/hr.

STOOL ROUTINE
Macroscopic examination:
Formed stools, with no blood, mucus, worms, larvae or segments seen

Microscopic examination:
a)Saline mount:
Strongyloids seen, no pus cells or RBCs or trophozoites seen.
b)Iodine mount: shows no cysts

- HIV –Negative
- HBS Ag-Negative
- Chest X Ray: Bronchiectasis changes

	OBSERVED VALUE		NORMAL RANGE
BLOOD UREA	0.2	mg dl	10-40
SERUM CREATININE	0.2	mg dl	0.6- 1.4
SODIUM	116	mEq l	135 - 145
POTASSIUM	2.4	mEq l	3.5 - 5.0
SERUM TOTAL BILIRUBIN	0.5	mg dl	0.2 - 1.2
DIRECT BILIRUBIN	0.2	mg dl	0.4 - 0.6
SGOT / AST	35	U l	5 - <40
SGPT / ALT	24	U l	5 - 35
ALKALINE PHOSPHATASE	145	U l	100 - 290
GAMMA-GT (R-GT)	32	U l	11 - 45
TOTAL PROTEIN	8.0	g dl	6 - 8
ALBUMIN	3.2	g dl	3.5 - 5.0
GLOBULIN	3.5	g dl	2.5 - 3.7
A/G RATIO	0.9		1.1 - 2.0

TREATMENT

- ✓ IVF
- ✓ Inj.Ciprofloxacin 250mg bid for 5days
- ✓ Tab.Ivermectin3mg od for 1 week
- ✓ Multivitamins

LUTENISING HORMONE	0.1miu/ml	1.0 -10miu/ml
PROLACTIN	9.5ng/ml	3.0 - 24.0 NG/ML
TESTOSTERONE	0.025ng/ml	0.3 - 11.0 NG/ML
CORTISOL 9 am	129nmol/l	100 - 635 nmol/l
hGH (GROWTH HORMONE)	0.57ng/ml	0.00 - 6.00 ng/ml
IGF1	15ng/ml	116 - 358 ng/ml
IgFBP3	346ng/ml	1800-4620ng/ml
ACTH	8pg/ml	5-60 pg/ml
25(OH)VIT D	4.8ng/ml	>30ng/ml
COPPER	88mcg/dl	70 - 140 MCG/DL
ZINC	75 mcg/dl	80 -120mcg/dl
t TG (TISSUE TRANSGLUTAMINASE)	0.1IU/L	0.0 -10.0 IU/L
IGG	404 mgs/dl	550 - 1900 MG/DL
IGA	22mgs/dl	60 - 380 MG/DL
IGM	103mgs/dl	45 - 145 MG/DL
Alphal Antitrypsin	150mgs/dl	80 - 130mgs/dl

DIAGNOSIS
(clinical and laboratory)

- ?HYPOPITUITARISM WITH IMMUNO COMPROMISED STATE AFFECTING GUT AND RESPIRATORY SYSTEM
- COMMON VARIABLE IMMUNO DEFICIENCY SYNDROME WITH LOW IGF-1, IGFBP-3,IgG, IgA with autoimmune GI diseases

SOME HIGH POINTS

- ✓ Common variable immunodeficiency (CVID) (Acquired hypogammaglobulinemia) is a group of approximately 150 primary immunodeficiencies (PIDs), which have a common set of features (including hypogammaglobulinemia)but which have different underlying causes.
- ✓ CVID is shown to be a genetically determined primary immune defect; however, the underlying causes are different.
- ✓ The result of these defects is that the patient doesn't produce sufficient antibodies in response to exposure to pathogens.
- ✓ As a result, the patient's immune system fails to protect them against common bacterial and viral (and occasionally parasitic and protozoan) infections.
- ✓ High incidence of autoimmune diseases and malignancy

Predisposition to range of infections

- ✓ Helicobacter pylori, Giardiasis, Cryptosporidiosis, Small bowel bacterial overgrowth syndrome, etc.
- ✓ Atrophic gastritis with pernicious anemia and achlorhydria.
- ✓ Nodular lymphoid hyperplasia of the GI tract.
- ✓ Villous atrophy of the small intestine, which can resemble celiac disease.
- ✓ Inflammatory bowel disease.
- ✓ Aphthous stomatitis.
- ✓ Increased intestinal permeability.
- ✓ Polyarthritis, or joint pain, spread across most joints, but specifically fingers, wrists, elbows, toes, ankles and knees. In some cases, Mycoplasma can be the cause.
- ✓ Children may show a "failure to thrive" - they may be underweight and underdeveloped compared with "normal"peers.
- ✓ Candida infection of the lungs.
- ✓ Anxiety and depression, usually as a result of dealing with the other symptoms.

ANNEXURE

Registered External Delegates

	Name	Designation	Institute
1	Dr.K.Venkatesh	Research Director	Genotypic Technology Pvt. Ltd, Bangalore
2	Dr. Krishnaprasad	Vice-President	Genotypic Technology Pvt. Ltd, Bangalore
3	Dr.Vinayak.R.Kumbojkar	Reader in Periodontics	KLE VK Inst. Of Dental Sciences, Belgaum
4	Dr.Bhagyashri.R.Hunugund	Asso. Prof. in Pathology	JNMC, KLE Univ, Belgaum
5	Dr. Manjunath.D	Asst. Prof in ENT	KIMS, Hubli
6	Dr. M.Basavaraju	Prof. in Surgery	SSIMS & RC, Davangere
7	Dr.Anjali Ghanekar	Professor	S. VYASA Univ, Bangalore
8	Monali Madhusudhana	Ph.D Scholar	S. VYASA Univ, Bangalore
9	Padmavathi Mahanana	Ph.D Scholar	S. VYASA Univ, Bangalore
10	Dr.E.Amaravathi	Ph.D Scholar	S. VYASA Univ, Bangalore
11	Dr.T.Indira Rao	Ph.D Scholar	S. VYASA Univ, Bangalore
12	Kuldeep Kushwah	Ph.D Scholar	S. VYASA Univ, Bangalore
13	Surendra Singh Sankhra	Ph.D Scholar	S. VYASA Univ, Bangalore
14	Dr.Kruthika.N	PG in Community Medicine	RRMCH, Bangalore
15	Dr.Sudha	PG in OBG	MVJMC, Bangalore
16	Dr.Doddabadre Gowda	Medical Director	Nursing Home, Mulbagal
17	Dr.D.Somashekaraiah	Chairman	K.M.C C.M.E Trust, Karnataka
18	Dr.Savitha.S	Professor	SJMC
19	Dr.Shashak	Deputy Registrar	KLE Univ, Belgaum
20	Dr.Nilgar	Prof. & Controller of Exams	KLE Univ, Belgaum
21	Dr.Syed Ali	Asst. Prof	
22	Dr.Anand Jayarama		
23	Dr.Ashok Vardhan	Director	Shyam Hospital, Bangarpet
24	Dr.N.Bharathi	Specialist in Anaesthesia	ESIC Model Hospital, Bangalore

LIST OF REGISTERED DELEGATES, SDUMC, Kolar

sn	Name	Designation	Department	Institute
1	Dr.Venkateshu	Prof & HoD	Anatomy	SDUMC, Kolar
2	Dr.Sangaeetha	Asso Prof	Anatomy	SDUMC, Kolar
3	Dr.Ashwini	Asst Prof	Anatomy	SDUMC, Kolar
4	Dr.Shashi.P.K	Asst Prof	Anatomy	SDUMC, Kolar
5	Dr.Krishnaveni	Lecturer	Anatomy	SDUMC, Kolar
6	Dr.Kumarawamy.R	Lecturer	Anatomy	SDUMC, Kolar
7	Dr.T.Suresh	Tutor	Anatomy	SDUMC, Kolar
8	Dr.B.H.Shiny Vinila	Tutor	Anatomy	SDUMC, Kolar
9	Dr.Vinay Kulkarni	Tutor	Anatomy	SDUMC, Kolar
10	Dr.Roshni.S	Tutor	Anatomy	SDUMC, Kolar
11	Dr.Kathyani Kutty	Prof & HoD	Physiology	SDUMC, Kolar
12	Dr.Vinutha Shankar	Prof	Physiology	SDUMC, Kolar
13	Dr.Sunanda Nayak	Prof	Physiology	SDUMC, Kolar
14	Dr.Raja Reddy	Asst. Prof	Physiology	SDUMC, Kolar
15	Dr.Jagadamba	Asst. Prof	Physiology	SDUMC, Kolar
16	Dr.Geetha	Asst. Prof	Physiology	SDUMC, Kolar
17	Dr.Patil.N.J	Asst. Prof	Physiology	SDUMC, Kolar
18	Dr.Syed Sadat Ali	Asst. Prof	Physiology	SDUMC, Kolar
19	Mrs.Usha Shenoy	Asst. Prof	Physiology	SDUMC, Kolar
20	Dr.Sindhu.R	Post Graduate	Physiology	SDUMC, Kolar
21	Dr.Ashwini Priyanka	Post Graduate	Physiology	SDUMC, Kolar
22	Dr.Sumit Garg	Post Graduate	Physiology	SDUMC, Kolar
23	Dr.Bhanu.R	Post Graduate	Physiology	SDUMC, Kolar
24	Dr.Ramya.C.S	Post Graduate	Physiology	SDUMC, Kolar
25	Dr.S.Parasuraman	Post Graduate	Physiology	SDUMC, Kolar
26	Dr.Sumitra	Post Graduate	Physiology	SDUMC, Kolar
27	Dr.Vineetha	Post Graduate	Physiology	SDUMC, Kolar
28	Dr.Shashidhar.K.N	Prof & HoD	Biochemistry	SDUMC, Kolar
29	Dr.C.D.Dayanand	Assoc Prof	Biochemistry	SDUMC, Kolar
30	Dr.Sumathi.M.E	Asst Prof	Biochemistry	SDUMC, Kolar
31	Mrs.Deena Mendez	Sr. Lect	Biochemistry	SDUMC, Kolar
32	Mrs.Mamatha.K	Sr. Lect	Biochemistry	SDUMC, Kolar
33	Mrs.Shyamali	Sr. Lect	Biochemistry	SDUMC, Kolar
34	Dr.Ganesh	Post Graduate	Biochemistry	SDUMC, Kolar
35	Dr.Nandini	Post Graduate	Biochemistry	SDUMC, Kolar
36	Dr.Esha Mati	Post Graduate	Biochemistry	SDUMC, Kolar
37	Dr.Harish.R	Post Graduate	Biochemistry	SDUMC, Kolar
38	Mr.Pradeep Vegi	Ph.D Scholar	Biochemistry	SDUMC, Kolar
39	Mrs.Munilakshmi	Ph.D Scholar	Biochemistry	SDUMC, Kolar

40	Dr. M.L.Harendra kumar	Prof and HOD	Pathology	SDUMC, Kolar
41	Dr. CSBR Prasad	Prof	Pathology	SDUMC, Kolar
42	Dr.T.N. Suresh	Assoc Prof	Pathology	SDUMC, Kolar
43	Dr. Subashish Das	Assoc Prof	Pathology	SDUMC, Kolar
44	Dr. Gayathri B.N	Asst Prof	Pathology	SDUMC, Kolar
45	Dr. Prathima S	Asst Prof	Pathology	SDUMC, Kolar
46	Dr. Hemalatha	Asst Prof	Pathology	SDUMC, Kolar
47	Dr. Chaitra	Post Graduate	Pathology	SDUMC, Kolar
48	Dr. Lokesh Hoswani	Post Graduate	Pathology	SDUMC, Kolar
49	Dr. Rizwan Jawed	Post Graduate	Pathology	SDUMC, Kolar
50	Dr. Shruthi P.S	Post Graduate	Pathology	SDUMC, Kolar
51	Dr. Gomathi. N	Post Graduate	Pathology	SDUMC, Kolar
52	Dr. Sharita	Post Graduate	Pathology	SDUMC, Kolar
53	Dr.Suraksha Rao	Post Graduate	Pathology	SDUMC, Kolar
54	Dr. Shubam Agarwal	Post Graduate	Pathology	SDUMC, Kolar
55	Dr. Priya T Rajan	Post Graduate	Pathology	SDUMC, Kolar
56	Dr. Manjula K	Staff	Pathology	SDUMC, Kolar
57	Dr. Sarala	Prof &HOD	Pharmacology	SDUMC, Kolar
58	Dr.Bhuvana K	Assoc Prof	Pharmacology	SDUMC, Kolar
59	Dr. Girish M.B	Assoc Prof	Pharmacology	SDUMC, Kolar
60	Dr. JayaKumar J. K	Asst Prof	Pharmacology	SDUMC, Kolar
61	Dr. Smitha Rai	Asst Prof	Pharmacology	SDUMC, Kolar
62	Dr. Meenakshi L	Asst Prof	Pharmacology	SDUMC, Kolar
63	Dr. Dharmishta Patil	Post Graduate	Pharmacology	SDUMC, Kolar
64	Dr. Tejashree	Post Graduate	Pharmacology	SDUMC, Kolar
65	Dr. Harish S	Post Graduate	Pharmacology	SDUMC, Kolar
66	Dr. Vidyalakshmi	Post Graduate	Pharmacology	SDUMC, Kolar
67	Dr.Revathi	Post Graduate	Pharmacology	SDUMC, Kolar
68	Dr. Chethan Kumar G	Post Graduate	Pharmacology	SDUMC, Kolar
69	Dr. Dheepan Nayagam B	Post Graduate	Pharmacology	SDUMC, Kolar
70	Dr.Balamurali	Post Graduate	Pharmacology	SDUMC, Kolar
71	Dr.Nandish	Post Graduate	Pharmacology	SDUMC, Kolar
72	Dr. Beena	Prof HOD	Microbiology	SDUMC, Kolar
73	Dr S.R. Prasad	Prof & Director of PG Studies	Microbiology	SDUMC, Kolar
74	Dr. Jeevan Shetty	Assoc Prof	Microbiology	SDUMC, Kolar
75	Dr. Savita N	Asst Prof	Microbiology	SDUMC, Kolar
76	Dr. Parimala	Asst Prof	Microbiology	SDUMC, Kolar
77	Dr. Mamata Kale	Asst Prof	Microbiology	SDUMC, Kolar

78	Dr. Tanveer	Asst Prof	Microbiology	SDUMC, Kolar
79	Dr. Vidya R	Post Graduate	Microbiology	SDUMC, Kolar
80	Dr. Sudhamani	Post Graduate	Microbiology	SDUMC, Kolar
81	Dr. Bipin Chandra Bhagat	Post Graduate	Microbiology	SDUMC, Kolar
82	Dr. Anitha D	Post Graduate	Microbiology	SDUMC, Kolar
83	Dr. Shwetha K	Post Graduate	Microbiology	SDUMC, Kolar
84	Dr. Archana B.R	Post Graduate	Microbiology	SDUMC, Kolar
85	Dr. Savita P	Post Graduate	Microbiology	SDUMC, Kolar
86	Dr. Kiran J	Prof & HOD	Forensic Medicine	SDUMC, Kolar
87	Dr. Umesh	Assoc Prof	Forensic Medicine	SDUMC, Kolar
88	Dr. Dayananda R	Asst Prof	Forensic Medicine	SDUMC, Kolar
89	Dr. Ajay Kumar T.S	Asst Prof	Forensic Medicine	SDUMC, Kolar
90	Dr. Ranganath B G	Prof & HOD	Community Medicine	SDUMC, Kolar
91	Dr. Muninarayana	Prof	Community Medicine	SDUMC, Kolar
92	Dr. Prasanna Kamath	Prof	Community Medicine	SDUMC, Kolar
93	Dr.Anil N.S	Assoc Prof	Community Medicine	SDUMC, Kolar
94	Dr.Anuradha	Assoc Prof	Community Medicine	SDUMC, Kolar
95	Dr. Deepa L.N	Assoc Prof	Community Medicine	SDUMC, Kolar
96	Dr. Shilu	Assoc Prof	Community Medicine	SDUMC, Kolar
97	Dr. Mahesh	Asst Prof	Community Medicine	SDUMC, Kolar
98	Mr. Ravishankar	Asst Prof	Community Medicine	SDUMC, Kolar
99	Dr. Nagaraj G M	Asst Prof	Community Medicine	SDUMC, Kolar
100	Dr.Achal Shetty	Post Graduate	Community Medicine	SDUMC, Kolar
101	Dr.Naresh Kumar	Post Graduate	Community Medicine	SDUMC, Kolar
102	Dr. Shruthi M.N	Post Graduate	Community Medicine	SDUMC, Kolar
103	Dr. Naveen B.R	Post Graduate	Community Medicine	SDUMC, Kolar
104	Dr. Ananya Lakshmi	Post Graduate	Community Medicine	SDUMC, Kolar
105	Dr. Prabhudeva	PRO	CommMedicine	SDUMC, Kolar

106	Mr. Akshaya Kumar	PRO	Community Medicine	SDUMC, Kolar
107	Ms. Pooja	Intern	Community Medicine	SDUMC, Kolar
108	Ms. Neha Sinha	Intern	Community Medicine	SDUMC, Kolar
109	Ms. Poulami Ghosh	Intern	Community Medicine	SDUMC, Kolar
110	Ms Pooja Gambhir	Intern	Community Medicine	SDUMC, Kolar
111	Ms. Prarthana B	Intern	Community Medicine	SDUMC, Kolar
112	Dr.S M Azeem	Prof & HOD	ENT	SDUMC, Kolar
113	Dr. Khaja Naseruddin	Prof	ENT	SDUMC, Kolar
114	Dr. Vinay Babu S	Assoc Prof	ENT	SDUMC, Kolar
115	Dr. Chandrakala	Asst Prof	ENT	SDUMC, Kolar
116	Dr. Nikhil S. B	Asst Prof	ENT	SDUMC, Kolar
117	Dr. Vishal P	SR	ENT	SDUMC, Kolar
118	Dr. Abhishek Nayak	Post Graduate	ENT	SDUMC, Kolar
119	Dr. Nikhil S. B	Post Graduate	ENT	SDUMC, Kolar
120	Dr. Sheetal	Post Graduate	ENT	SDUMC, Kolar
121	Dr. Harshita	Post Graduate	ENT	SDUMC, Kolar
122	Dr. Shreyas	Post Graduate	ENT	SDUMC, Kolar
123	Dr. Rijo M	Post Graduate	ENT	SDUMC, Kolar
124	Dr. Bunty	Post Graduate	ENT	SDUMC, Kolar
125	Dr. Narendra Datti	Prof & HOD	Ophthalmology	SDUMC, Kolar
126	Dr. Krishnamurthy	Prof	Ophthalmology	SDUMC, Kolar
127	Dr. Kanthamani	Prof	Ophthalmology	SDUMC, Kolar
128	Dr. Prashanth	Assoc Prof	Ophthalmology	SDUMC, Kolar
129	Dr. Guruprasad	Assoc Prof	Ophthalmology	SDUMC, Kolar
130	Dr. Neeraj	Post Graduate	Ophthalmology	SDUMC, Kolar
131	Dr. Joyita	Post Graduate	Ophthalmology	SDUMC, Kolar
132	Dr. Jiya	Post Graduate	Ophthalmology	SDUMC, Kolar
133	Dr. Prarthana	Post Graduate	Ophthalmology	SDUMC, Kolar
134	Dr. Ashwini	Post Graduate	Ophthalmology	SDUMC, Kolar
135	Dr. Shalini	Post Graduate	Ophthalmology	SDUMC, Kolar
136	Dr. Amol	Post Graduate	Ophthalmology	SDUMC, Kolar
137	Dr. Mithila	Post Graduate	Ophthalmology	SDUMC, Kolar
138	Dr. Manasa	Post Graduate	Ophthalmology	SDUMC, Kolar
139	Dr. Tanushree	Post Graduate	Ophthalmology	SDUMC, Kolar
140	Dr. Sangeetha	Post Graduate	Ophthalmology	SDUMC, Kolar
141	Dr. Rashmi	Post Graduate	Ophthalmology	SDUMC, Kolar
142	Dr. Kunal Kishore	Post Graduate	Ophthalmology	SDUMC, Kolar

143	Dr. Subratham	Post Graduate	Ophthalmology	SDUMC, Kolar
144	Dr. Indranath Prasad	Post Graduate	Ophthalmology	SDUMC, Kolar
145	Dr. Raghavendra Prasad	Prof & HOD	Gen Medicine	SDUMC, Kolar
146	Dr. Lakshmaiah	Prof & Med Superintendent	Gen Medicine	SDUMC, Kolar
147	Dr. Prabhakar K	Prof	Gen Medicine	SDUMC, Kolar
148	Dr. Raveesha A	Prof	Gen Medicine	SDUMC, Kolar
149	Dr. P. N. Venkatarathnamma	Prof	Gen Medicine	SDUMC, Kolar
150	Dr. Srinivas Rao	Prof	Gen Medicine	SDUMC, Kolar
151	Dr. Jayaram N	Assoc Prof	Gen Medicine	SDUMC, Kolar
152	Dr. Rateesh R P	Asst Prof	Gen Medicine	SDUMC, Kolar
153	Dr. Vidya Sagar C. K	Asst Prof	Gen Medicine	SDUMC, Kolar
154	Dr. Harish Kumar S	Asst Prof	Gen Medicine	SDUMC, Kolar
155	Dr. Srinivas S.V	Asst Prof	Gen Medicine	SDUMC, Kolar
156	Dr. Mukesh N Bangare	Asst Prof	Gen Medicine	SDUMC, Kolar
157	Dr. Naveen L	Asst Prof	Gen Medicine	SDUMC, Kolar
158	Dr. Santoshi	Asst Prof	Gen Medicine	SDUMC, Kolar
159	Dr. Madhavi Reddy	Asst Prof	Gen Medicine	SDUMC, Kolar
160	Dr. Kiran B J	Post Graduate	Gen Medicine	SDUMC, Kolar
161	Dr. Yashwanth	Post Graduate	Gen Medicine	SDUMC, Kolar
162	Dr. Srtinivas Prasad	Post Graduate	Gen Medicine	SDUMC, Kolar
163	Dr. Gopinath	Post Graduate	Gen Medicine	SDUMC, Kolar
164	Dr. Shiju	Post Graduate	Gen Medicine	SDUMC, Kolar
165	Dr. Ujwal	Post Graduate	Gen Medicine	SDUMC, Kolar
166	Dr. M Anil Kumar	Post Graduate	Gen Medicine	SDUMC, Kolar
167	Dr. Pavithra	Post Graduate	Gen Medicine	SDUMC, Kolar
168	Dr. Krishna Prasad anne	Post Graduate	Gen Medicine	SDUMC, Kolar
169	Dr. Murthy	Post Graduate	Gen Medicine	SDUMC, Kolar
170	Dr. Kishore Kumar	Post Graduate	Gen Medicine	SDUMC, Kolar
171	Dr. Yugendar	Post Graduate	Gen Medicine	SDUMC, Kolar
172	Dr. Anitha	Post Graduate	Gen Medicine	SDUMC, Kolar
173	Dr. Priyanka N K	Post Graduate	Gen Medicine	SDUMC, Kolar
174	Dr. Beere Gowda	Prof & HOD	Paediatrics	SDUMC, Kolar
175	Dr. K. N.V. Prasad	Prof	Paediatrics	SDUMC, Kolar
176	Dr. Krishnappa J	Prof	Paediatrics	SDUMC, Kolar
177	Dr. Sudha Reddy	Assoc Prof	Paediatrics	SDUMC, Kolar
178	Dr. Sreehari A	Assoc Prof	Paediatrics	SDUMC, Kolar
179	Dr. Naveen Kumar	Asst Prof	Paediatrics	SDUMC, Kolar

	B V			
180	Dr. Venkatesh	Asst Prof	Paediatrics	SDUMC, Kolar
181	Dr. N. Yellappa Gowda	Asst Prof	Paediatrics	SDUMC, Kolar
182	Dr. Bharat Reddy	Asst Prof	Paediatrics	SDUMC, Kolar
183	Dr. Venkatadri Babu T	Post Graduate	Paediatrics	SDUMC, Kolar
184	Dr. Jigar Mahendra Kumar Mehta	Post Graduate	Paediatrics	SDUMC, Kolar
185	Dr. S. Mohammed Sohail	Post Graduate	Paediatrics	SDUMC, Kolar
186	Dr. Ching Thang	Post Graduate	Paediatrics	SDUMC, Kolar
187	Dr. Sharath	Post Graduate	Paediatrics	SDUMC, Kolar
188	Dr. Soumya	Post Graduate	Paediatrics	SDUMC, Kolar
189	Dr. Gayathri	Post Graduate	Paediatrics	SDUMC, Kolar
190	Dr. Puneeth	Post Graduate	Paediatrics	SDUMC, Kolar
191	Dr. Shashank	Post Graduate	Paediatrics	SDUMC, Kolar
192	Dr. Aravind	Post Graduate	Paediatrics	SDUMC, Kolar
193	Dr. Vishnuvardhan	Post Graduate	Paediatrics	SDUMC, Kolar
194	Dr. Deepa	Post Graduate	Paediatrics	SDUMC, Kolar
195	Dr. Harisha	Post Graduate	Paediatrics	SDUMC, Kolar
196	Dr. Mohan Reddy	Prof & HOD	Psychiatry	SDUMC, Kolar
197	Dr. Srinivas Reddy V N	Sen Resident	Psychiatry	SDUMC, Kolar
198	Dr. Deepa C	Asst Prof	Dental	SDUMC, Kolar
199	Dr. Manjula	Asst Prof	Dental	SDUMC, Kolar
200	Dr. Sreenath H S	Lecturer	Dental	SDUMC, Kolar
201	Dr. Mallika Reddy	Lecturer	Dental	SDUMC, Kolar
202	Dr. V. Shivakumar	Prof	Dermatology	SDUMC, Kolar
203	Dr. Rajesh	Assoc Prof	Dermatology	SDUMC, Kolar
204	Dr. Rajashekar	Assoc Prof	Dermatology	SDUMC, Kolar
205	Dr. Harish	Post Graduate	Dermatology	SDUMC, Kolar
206	Dr. Jisha Pilai	Post Graduate	Dermatology	SDUMC, Kolar
207	Dr. Muktha Mani	Post Graduate	Dermatology	SDUMC, Kolar
208	Dr. Prakruthi	Post Graduate	Dermatology	SDUMC, Kolar
209	Dr. Christena	Post Graduate	Dermatology	SDUMC, Kolar
210	Dr. An Jose	Post Graduate	Dermatology	SDUMC, Kolar
211	Dr.P Somashekaran	Prof & HOD	Anaesthesiology	SDUMC, Kolar
212	Dr. Ravi	Prof	Anaesthesiology	SDUMC, Kolar
213	Dr.K.S. Savitha	Prof	Anaesthesiology	SDUMC, Kolar
214	Dr. K. Dinesh	Prof	Anaesthesiology	SDUMC, Kolar
215	Dr. Krishnakumar	Assoc Prof	Anaesthesiology	SDUMC, Kolar
216	Dr.Anand	Asst Prof	Anaesthesiology	SDUMC, Kolar
217	Dr. Suresh Kumar	Asst Prof	Anaesthesiology	SDUMC, Kolar
218	Dr. Kiran	Asst Prof	Anaesthesiology	SDUMC, Kolar

219	Dr. Priya Marghavi	Asst Prof	Anaesthesiology	SDUMC, Kolar
220	Dr.Sindhu	Post Graduate	Anaesthesiology	SDUMC, Kolar
221	Dr. Manisha Sharma	Post Graduate	Anaesthesiology	SDUMC, Kolar
222	Dr. Syed	Post Graduate	Anaesthesiology	SDUMC, Kolar
223	Dr.Priya	Post Graduate	Anaesthesiology	SDUMC, Kolar
224	Dr. Jyothi	Post Graduate	Anaesthesiology	SDUMC, Kolar
225	Dr. Manjunath	Post Graduate	Anaesthesiology	SDUMC, Kolar
226	Dr. Archana	Post Graduate	Anaesthesiology	SDUMC, Kolar
227	Dr. Don Sebastan	Post Graduate	Anaesthesiology	SDUMC, Kolar
228	Dr. Sushree	Post Graduate	Anaesthesiology	SDUMC, Kolar
229	Dr.Ananya	Post Graduate	Anaesthesiology	SDUMC, Kolar
230	Dr.M.N.Chandrashekhar	Proff	Neurology	SDUMC, Kolar
231	Ms.Mary shobha rani	Trainee scientific assistant	Allied health sciences	SDUAHER, Kolar
232	Ms.Malini.K	Scientific Assistant	Genome Lab	SDUMC, Kolar
233	Dr. B.N.Kishore kumar	Prof &HOD	Radiodiagnosis	SDUMC, Kolar
234	Dr. Naveen	Asst Prof	Radiodiagnosis	SDUMC, Kolar
235	Dr. Nagaraj. S	Asst Prof	Radiodiagnosis	SDUMC, Kolar
236	Dr.manjunath Y.C.	Asst Prof	Radiodiagnosis	SDUMC, Kolar
237	Dr.Jagadish Basavaiah	Asst Prof	Radiodiagnosis	SDUMC, Kolar
238	Dr. Jilu Joy	Post Graduate	Radiodiagnosis	SDUMC, Kolar
239	Dr.Jayadeva	Post Graduate	Radiodiagnosis	SDUMC, Kolar
240	Dr.Rangaprasad	Post Graduate	Radiodiagnosis	SDUMC, Kolar
241	Dr.Rajkumar	Post Graduate	Radiodiagnosis	SDUMC, Kolar
242	Dr. vinay.N.Raj	Post Graduate	Radiodiagnosis	SDUMC, Kolar
243	Dr.P.Haritha	Post Graduate	Radiodiagnosis	SDUMC, Kolar
244	Dr.Bharath	Post Graduate	Radiodiagnosis	SDUMC, Kolar
245	Dr. Sindhoori	Post Graduate	Radiodiagnosis	SDUMC, Kolar
246	Dr.Aditya	Post Graduate	Radiodiagnosis	SDUMC, Kolar
247	Dr.Sandhya	Post Graduate	Radiodiagnosis	SDUMC, Kolar
248	Dr.Bhargavi	Post Graduate	Radiodiagnosis	SDUMC, Kolar
249	Dr.Prem	Post Graduate	Radiodiagnosis	SDUMC, Kolar
250	Dr. kiranmai	Post Graduate	Radiodiagnosis	SDUMC, Kolar
251	Dr.Shivaraj	Post Graduate	Radiodiagnosis	SDUMC, Kolar
252	Dr.Deepa Das	Post Graduate	Radiodiagnosis	SDUMC, Kolar
253	Dr.K.J.S.S.Raghuteja	Post Graduate	Radiodiagnosis	SDUMC, Kolar
254	Dr. Narayana swamy	Prof&HOD	OBG	SDUMC, Kolar
255	Dr.Pushpa	Prof	OBG	SDUMC, Kolar
256	Dr.Gayathridevi	Prof	OBG	SDUMC, Kolar

257	Dr. Sheela	Prof	OBG	SDUMC, Kolar
258	Dr.sunitha	Prof	OBG	SDUMC, Kolar
259	Dr.Manjula S.J	Asst Prof	OBG	SDUMC, Kolar
260	Dr.Manjula H.M	Asst Prof	OBG	SDUMC, Kolar
261	Dr.Latha G.S	Asst Prof	OBG	SDUMC, Kolar
262	Dr.Raja Munireddy	Asst Prof	OBG	SDUMC, Kolar
263	Dr.Sheebha	Asst Prof	OBG	SDUMC, Kolar
264	Dr Sudha	Asst Prof	OBG	SDUMC, Kolar
265	Dr.Nagashrimath	SR	OBG	SDUMC, Kolar
266	Dr.Nayashri	SR	OBG	SDUMC, Kolar
267	Dr.Seema B..R	Post Graduate	OBG	SDUMC, Kolar
268	Dr Ashwini	Post Graduate	OBG	SDUMC, Kolar
269	Dr.Chandramani	Post Graduate	OBG	SDUMC, Kolar
270	Dr.Ramya	Post Graduate	OBG	SDUMC, Kolar
271	Dr.Latha	Post Graduate	OBG	SDUMC, Kolar
272	Dr.Pooja patil	Post Graduate	OBG	SDUMC, Kolar
273	Dr.Geetha	Post Graduate	OBG	SDUMC, Kolar
274	Dr.Malthi	Post Graduate	OBG	SDUMC, Kolar
275	Dr.Jhansi.K	Post Graduate	OBG	SDUMC, Kolar
276	Dr.Lakshmi.G	Post Graduate	OBG	SDUMC, Kolar
277	Dr.Ambika	Post Graduate	OBG	SDUMC, Kolar
278	Dr.Alekya	Post Graduate	OBG	SDUMC, Kolar
279	Dr.Dheera	Post Graduate	OBG	SDUMC, Kolar
280	Dr.Padmini bhat	Post Graduate	OBG	SDUMC, Kolar
281	Dr.Aditi	Post Graduate	OBG	SDUMC, Kolar
282	Dr.Vidyashree	Post Graduate	OBG	SDUMC, Kolar
283	Dr. Krishna Shetty	Prof&HOD	Urology	SDUMC, Kolar
284	Dr.T.K .Sen	Prof	Urology	SDUMC, Kolar
285	Dr.D.Sreedharan	Assoc Prof	Urology	SDUMC, Kolar
286	Dr.Bhaskaran	Prof&HOD	Gen Surgery	SDUMC, Kolar
287	Dr.M.Madhan	Prof	Gen Surgery	SDUMC, Kolar
288	Dr. Nagaraj	Prof	Gen Surgery	SDUMC, Kolar
289	Dr.Krishna Prasad	Prof	Gen Surgery	SDUMC, Kolar
290	Dr.Mohan Kumar	Prof	Gen Surgery	SDUMC, Kolar
291	Dr.P.N.Sreeramulu	Prof	Gen Surgery	SDUMC, Kolar
292	Dr. Mohan kumar	Prof	Gen Surgery	SDUMC, Kolar
293	Dr.Ambikavathi	Assoc Prof	Gen Surgery	SDUMC, Kolar
294	Dr.Shashikala	Asst Prof	Gen Surgery	SDUMC, Kolar
295	Dr.K.Nishal	Assoc Prof	Gen Surgery	SDUMC, Kolar
296	Dr. Rohith	Asst Proff	Gen Surgery	SDUMC, Kolar
297	Dr.Mahesh	Asst Proff	Gen Surgery	SDUMC, Kolar
298	Dr.Vasanth kumar	Asst Proff	Gen Surgery	SDUMC, Kolar
299	Dr.Shankar Rao	Asst Proff	Gen Surgery	SDUMC, Kolar
300	Dr.Sangamesh	Asst Proff	Gen Surgery	SDUMC, Kolar
301	Dr.shashirekha	Asst Proff	Gen Surgery	SDUMC, Kolar

302	Dr.Pratibha	Asst Proff	Gen Surgery	SDUMC, Kolar
303	Dr.Deepak H	Asst Proff	Gen Surgery	SDUMC, Kolar
304	Dr.Gurucharan	Prof	Plastic surgery	SDUMC, Kolar
305	Dr.Anantharaju	Post Graduate	Gen surgery	SDUMC, Kolar
306	Dr.Srikanth	Post Graduate	Gen Surgery	SDUMC, Kolar
307	Dr.Sathradev	Post Graduate	Gen Surgery	SDUMC, Kolar
308	Dr Avinash	Post Graduate	Gen Surgery	SDUMC, Kolar
309	Dr.Harish kumar	Post Graduate	Gen Surgery	SDUMC, Kolar
310	Dr.Senthil kumar	Post Graduate	Gen Surgery	SDUMC, Kolar
311	Dr.Anupam choudary	Post Graduate	Gen Surgery	SDUMC, Kolar
312	Dr.Pavan Katti	Post Graduate	Gen Surgery	SDUMC, Kolar
313	Dr.SharanBasavaraj	Post Graduate	Gen Surgery	SDUMC, Kolar
314	Dr.Kiran Shankar	Post Graduate	Gen Surgery	SDUMC, Kolar
315	Dr.Jahanavi	Post Graduate	Gen Surgery	SDUMC, Kolar
316	Dr.Jeevanath	Post Graduate	Gen Surgery	SDUMC, Kolar
317	Dr.Gaurav	Post Graduate	Gen surgery	SDUMC, Kolar
318	Dr.Vijay	Post Graduate	Gen surgery	SDUMC, Kolar
319	Dr.Arun H.S	Prof	Orthopaedics	SDUMC, Kolar
320	Dr.Gudi N.S	Prof	Orthopaedics	SDUMC, Kolar
321	Dr.Manohar P.V	Prof	Orthopaedics	SDUMC, Kolar
322	Dr.Venkatesh	Assoc Prof	Orthopaedics	SDUMC, Kolar
323	Dr.Anil	Asst Prof	Orthopaedics	SDUMC, Kolar
324	Dr.Prabhu	Asst Prof	Orthopaedics	SDUMC, Kolar
325	Dr.Maruthi k	Asst Prof	Orthopaedics	SDUMC, Kolar
326	Dr.Anil kumar	Asst Prof	Orthopaedics	SDUMC, Kolar
327	Dr.Naveen	Asst Prof	Orthopaedics	SDUMC, Kolar
328	Dr.Debojyothi	Post Graduate	Orthopaedics	SDUMC, Kolar
329	Dr.Maneesh kumar	Post Graduate	Orthopaedics	SDUMC, Kolar
330	Dr.Satya	Post Graduate	Orthopaedics	SDUMC, Kolar
331	Dr.Abdullah Hadi	Post Graduate	Orthopaedics	SDUMC, Kolar
332	Dr.Gopinath S	Post Graduate	Orthopaedics	SDUMC, Kolar
333	Dr.Praneeth R	Post Graduate	Orthopaedics	SDUMC, Kolar
334	Dr.Samarth Arya	Post Graduate	Orthopaedics	SDUMC, Kolar
335	Dr.Shiva Mahesh	Post Graduate	Orthopaedics	SDUMC, Kolar
336	Dr.K.V.Satyanarayana	Post Graduate	Orthopaedics	SDUMC, Kolar
337	Dr.Girish.L	Post Graduate	Orthopaedics	SDUMC, Kolar
338	Dr.Ashok reddy	Post Graduate	Orthopaedics	SDUMC, Kolar
339	Dr.Aftab Alam	Post Graduate	Orthopaedics	SDUMC, Kolar
340	Dr.Anvesh	Post Graduate	Orthopaedics	SDUMC, Kolar
341	Dr.Awishah	Post Graduate	Orthopaedics	SDUMC, Kolar
342	Dr.Vinodreddy	Post Graduate	Orthopaedics	SDUMC, Kolar
343	Dr.Praneeth reddy	Post Graduate	Orthopaedics	SDUMC, Kolar