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BIOTECH EXPRESS

Volume 6
Issue 70
May 2019

Guest Article:
“Blockade of
immune
checkpoint
therapy for
advanced
cancers” -
A topic of
2018
Nobel
Laureate
in Physiology
or Medicine

Press Release:
Start-up Podium®,
Hyderabad

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Gagandeep Kang
becomes first
Indian woman
scientist fellow
of UK Royal
Society

Guest Article:
RNA silencing
based
new age drug
therapy
approved
by FDA

Editorial News & Interview:

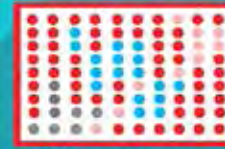
Prof S K Sopory, Padma Shri

**Joins as New Advisory Board Member of
Biotech Express Magazine**

Primary cell solutions Certificate of Analysis

Trade Name:	Trans-MSC
ID:	Trans-MSC14/R
Cells Harvested Date	
Biosafety Level	1
Organism	Homo sapiens (Human)
Growth properties:	Adherent
Morphology	Spindle Shaped, fibroblast like
Volume/Vial:	5ml (2.3 million cells / 1ml)
No. of Vials	As required
Viability	≥92%
Population Doubling Capacity:	≥ 10 in complete growth medium and support differentiation
Shipped	Frozen
Storage	Liquid nitrogen or for short term storage at -80°C
Quality Assurance:	
Testing	Tested for CD73, CD90, CD105, CD34, and CD45. Primary cells display normal karyotype as assessed by G-banding of 20 metaphase cells.
Sterility Tests	Bacteria & Yeast: Negative Mycoplasma: Negative Endotoxin: Negative

Trans-MSC + Test compound



Colormetric Assays



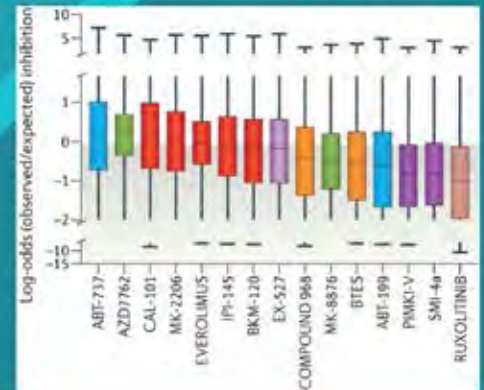
Turbidity Measurements



Cell Marker Expression



Colony Growth & Cell Death



Use Case

STEM CELLS FOR EVERY USE

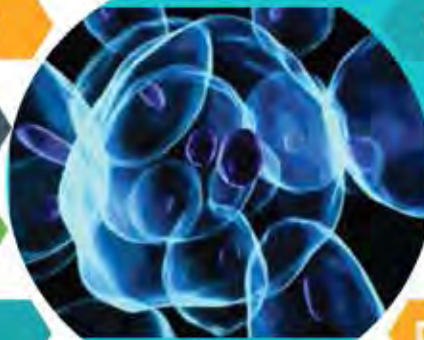


Acute Toxicity

Chronic Toxicity

Repeat Dose Toxicity

Ic50



Carcinogenicity

Mutagenicity

Draize Test

Developmental Toxicity

Plot No. 70A/B, Door No:8293/ 82/ 2,
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BIOTECH EXPRESS

From the desk of Editor



Kamal Pratap Singh
Managing Editor

Dear Readers!

Biotechnology in India was started in 1986, and since then many Indians have come up with many notable discoveries in plant and animal Sciences. One such personality is Prof Sudhir Kumar Sopory, a plant molecular biology specialist and a plant biotechnologists. His research led to many discoveries that finds application for wider common population.

For his discoveries and scientific contributions, he was awarded prestigious awards like SSB in 1987 and Padma Shri in 2007.

Prof Sopory has recently joined Advisory Board of Biotech Express Magazine and we all Board Members are grateful to him to have with us and for giving us valuable suggestions to cover plant biotechnology. We are sure that his vast knowledge and experience will help us to promote Indian plant sciences to much larger audience.

Taking this opportunity we have Interviewed Prof Sopory to know more about him and publishing here his biography and answers of some questions which are related to field of his specialization and useful for common people, students, researchers, scientists and budding generation.

On behalf of Biotech Express Board I am grateful to Prof Sopory and like to thank him whole heartily and wish for his lifelong accord and support in promoting Indian Science and its people.

Best wishes
Enjoy Reading and stay with us for updates

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Dr. Seema P. Upadhye
(Former Principal,
Biochemist)

Managing Editor:

Kamal Pratap Singh

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May 2019

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Gagandeep Kang becomes first Indian woman scientist to receive UK Royal Society

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Glenmark Appoints Dr. Yasir Rawjee as CEO of Glenmark Life Sciences its Subsidiary Glenmark Pharmaceuticals Ltd.,

Merck & Company is planning a \$1 billion expansion

Pfizer announced it intends to buy Therachon, a rare disease biotech company based in Basel, Switzerland for \$810 Million

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Advisory & Editorial Board

From the very first issue, Biotech Express team has been delivering what's best for Biosciences community. The audience of this magazine includes students, researchers, faculties and executives of highly prestigious organizations of India. In year 2016, BEM has made new editorial Board combining experience of eminent Advisory Board Members who have been into Award winning Research and head prestigious Administrative positions.

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Vice -Chancellor, JNU, Delhi, 2011-16
Director, ICGEB 2014-15



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Prof S K Sopory Joins as New Advisory Board Member of Biotech Express Magazine



Photo: Prof Sopory(right) with Dr Abdul Kalam,(left) the president of India in 2007

Prof S K Sopory

Padma Shri-2007; S.S.B-1987

Sudhir Kumar Sopory or S K Sopory or known by few just as Sopory is an Indian educationist, plant physiologist, scientist and former vice chancellor of Jawaharlal Nehru University, New Delhi. Prof Sopory is an elected Fellow of several major Indian science academies including four major science academies i.e. IAS, INSA and NASI and NAAS and International 'The World Academy of Sciences' (TWAS) and is a recipient of many honours, including the 1987 Shanti Swarup Bhatnagar (SSB) Prize, the highest Indian award in the science and technology categories and The Government of India awarded him the India's fourth highest civilian honour of the Padma Shri, in 2007, for his contributions to science and technology.



Prof Sopory is currently holding position of SERB Distinguished professor in International Center for Genetic Engineering and Biotechnology (ICGEB), New Delhi, India.

Prof Sopory was born on 7 January 1948, secured his graduate degree (BSc) in 1966 and postgraduate degree (MSc, Botany Hons.) in 1968 from Sri Pratap College, Sri Nagar of the University of Kashmir. Subsequently, he moved to Delhi to start his career by joining University of Delhi as a member of faculty and pursued his doctoral studies there to obtain a PhD in plant molecular biology in 1973.

After securing the doctoral degree, he joined Jawaharlal Nehru University in 1973 as an Assistant professor and worked there till his superannuation in 1996, holding positions such as associate professor (1978–1984), professor (1985–1996) and Vice-Chancellor.

Professor Sopory has many notable awards to his name and been member of several national committees of DBT, DST, ICAR, CSIR, UGC, academic bodies of over two dozen universities and institutions, Science and Engineering Research Council of DST; and Council Member of the Indian Academy of Sciences, Bangalore. He served(s) on the Editorial boards of many national/international journals. He was Vice President, INSA (2004-06), Society of Plant Physiology and Biochemistry and Secretary, Plant Tissue Culture Association of India.

Career at glance

1. University of Delhi, 1968-1972
2. At the Jawaharlal Nehru University, New Delhi (Assistant Professor 1973-78), (Associate Professor 1979-84), (Professor 1985- 1996), 1973 -1996
3. Max-Planck-Institute fur Zuchtungs-forschung, Koln, Germany, 1976-1978
4. Dept. of Botany, University of Texas, U.S.A. (Visiting Fulbright Fellow), 1981-1982
5. Plant Molecular Biology Lab, U.S. D.A., Maryland, USA, 1987-1988
6. Botanisches Institute der Universitat Munich, Germany, (Visiting Humboldt Professor), 1991-1992
7. Group Leader, Pl. Mol. Biol., International Centre for Genetic Engineering & Biotechnology, New Delhi, 1997 - 2010
8. Vice –Chancellor , Jawaharlal Nehru University, 2011- 2016
9. Director, International Centre for Genetic Engineering & Biotechnology, New Delhi, 2014-15
10. Arturo Falaschi Emeritus Scientist, ICGEB, 2016-2018
11. SERB Distinguished Fellow, ICGEB, DST, Govt. of India, 2018.....

Honorary Fellowships

- i. Fellow, Indian Academy of Sciences, Bangalore, 1992
- ii. Fellow, Indian National Science Academy, Delhi, 1992
- iii. Fellow, National Academy of Sciences, Allahabad, 1994
- iv. Fellow, National Academy of Agricultural Sciences, 2002
- v. Fellow, The World Academy of Sciences, Trieste, Italy, 2005
- vi. Fellow, Guha Research Conference, 1989
- vii. Max Planck Society Fellow, 1976
- viii. Fulbright Fellow, USEFI, 1982
- ix. Humboldt Foundation Fellowship, 1991

Prof Sopory is among the few 4615 Padma Awardees and one of the 3005 Padma Shri awardees, who has received the fourth highest civilian award of India. Research of Prof Sopory has led to the rapid development in the field of Agriculture Sciences that has vast applications and has been able to monetize soon. Today he has to his credit a whole stress tolerance pathway and many varieties which could stand in harsh salinity conditions. In this way we would grow crops even in the areas like 'The Rann of Kutch' which is a large area of salt marshes where salinity in soil goes upto pH 10.2.

President/Vice-President of Organizations

- i. Vice-President, Indian Society for Plant Physiology and Biochemistry 2001-2003
- ii. Secretary(Elected), Plant Tissue Culture Association of India, 2001-2010
- iii. Vice – President , Indian National Science Academy , 2004-2006
- iv. Vice-President ,Society for Plant Biochemistry and Biotechnology, New Delhi, 2009-2011
- v. President, Indian Society of Plant Physiology, 2013-2016
- vi. Vice-President, National Academy of Sciences, Allahabad, 2015-2016

Prof Sopory has also been awarded Shanti Swarup Bhatnagar Prize in 1987 work in the field of physiology of plant growth and development for his researches that led to a better understanding of the mode of action of phytochrome, and the possible involvement of calcium as a second messenger in higher plant cells. SSB Prize carries the value of Rs 5,00,000 (Rupees five lakh) and a citation and the purpose of the award is to recognise outstanding Indian work in science and technology.





Awards Given to Prof S K Sopory

- i. Padamshree, Govt. of India, 2007 (civilian honour given by the President of India)
- ii. Shanti Swarup Bhatnagar Award, (CSIR) 1987 (given by The Prime Minister of India).
- iii. H.L. Chakravorty Award, Indian Science Congress, 1986. (given by The Vice-President of India)
- iv. Career Award, University Grant Commission, 1985
- v. Salgram Sinha Award, National Academy of Sciences of India, 2001
- vi. Birbal Sahni Medal, Indian Botanical Society, 2001
- vii. Birbal Sahni Centenary Gold Medal Award for Life Time Achievements in Plant Sciences, Indian Science Congress Association, 2005 (given by the Prime Minister of India)
- viii. S.S. Katiyar Award , Indian Science Congress Association, 2010
- ix. Corresponding Membership Award for Non-USA scientists 2010 American Society of Plant Biology. (given first time to an Indian Plant Scientist since its inception in 1932)
- x. Prof. R.N. Tandon Memorial Award, National Academy of Sciences, India, 2012.
- xi. B.M. Johri Memorial Award, Society of Plant Research, India, 2012.
- xii. Jawaharlal Nehru Birth Centenary Award, Indian National Science Academy, New Delhi 2014.
- xiii. T.N. Khoshoo Memorial Award, Orchid Society of India, 2014.
- xiv. Conferred D.Sc (Honoris Causa) by Banaras Hindu University, Varanasi, 2012 and Rani Durgawati Vishwavidyalaya, Jabalpur, 2014.
- xv. Life Time Achievement Award, Biotechnology Society of India, 2017



Award lectures of Prof S K Sopory

- i. Gadgil Memorial Award Lecture, Plant Tissue Culture Association, 2000
- ii. R. N. Singh Memorial Lecture, Banaras Hindu University, Varanasi, 2000
- iii. P. Maheshwari Award Lecture, Indian National Science Academy, 2000
- iv. Panchanan Maheshwari Memorial Lecture, Delhi University, 2001
- v. N.B.Das Memorial Award Lecture, Society of Plant Biochemistry and Biotechnology, 2002
- vi. Platinum Jubilee Award Lecture, Indian Science Congress Association, 2003
- vii. Tenth Godnev Award lecture of the Belarus Academy of Sciences, Institute of Photobiology (delivered at Minsk, Belarus; 7th April 2003)
- viii. N. Narayana Memorial Award Lecture, Biochemical Society, Indian Institute of Sciences, Bangalore, 2005.
- ix. S.P. Ray-Chaudhuri 75th Birthday Endowment Lecture Award; Indian Society of Cell Biology, 2009 (first time to a plant scientist).
- x. Dr Yellapragada Subba Row Award Lecture, Indraprastha University, Delhi 2009
- xi. G.V. Joshi Lecture Award : Indian Society of Plant Physiology, 2010
- xii. Sisir Kumar Mitra Memorial Lecture Award, 2011-2012, Indian National Science Academy, New Delhi.
- xiii. First H.C. Arya Lecture Award, Plant Tissue Culture Association (India), 2011
- xiv. Dr. Gopinath Sahu Memorial Award Lecture; Rice Research Institute, Cuttack, 2014
- xv. 45th Lal Bhadur Shastri Award Lecture, IARI, New Delhi, 2015
- xvi. H.S.Srivastava Memorial Award Lecture, BHU, 2016 (Science Society Lucknow).
- xvii. R.D. Asana, Award lecture, Plant Physiology Division, IARI, 2017
- xviii. Pran K Parija Award lecture, Cuttack University, Bhubaneshwar, Orissa, 2019
- xix. VI Kashyap Award lecture, Panjab University, Chandigarh, 2019





Major Scientific Contributions

His journey in scientific world has been fascinating because whenever he joined any institute he made a discovery and showed how quick learner he is. From 1973 to 2010 he visited many labs in different countries to get higher and diverse knowledge.

After, PhD he did researches at Max Planck Institute for Plant Breeding Research, Cologne, where he developed a plant breeding methodology to produce monohaploids of potato, in 1978.

During early 80s, his researches at University of Texas assisted in the discovery of the “role of calcium and calmodulin” in higher plants.

In Maryland, he worked on D1 protein to find the mechanism behind it. In the early 90s, he worked under R. Hermann on promoter analysis of light regulated genes encoding proteins involved in photosynthesis.

Prof Sopory made notable contributions to the mechanism of light and stress regulation of gene expression. Studying the expression and activity of nitrate reductase, he found that light, via phytochrome perception, affects the turnover of phosphoinositide cycle thereby releasing two second messengers, IP3 and DAG. Thus, the role and involvement of this pathway was demonstrated in light signal transduction in plants.

He further characterized calcium dependent kinases which were found to be regulated by light. A protein kinase C like activity was also purified for the first time from plants and this enzyme was found to be regulated also by PMA, an analog of DAG.

He also identified topoisomerase I as a substrate of PKC in plants.



PHOTO:
Prof Sopory(right) with PM of Japan, Shinzō Abe(left), awarding him Honorary Doctorate degree at JNU.



Based on his work on dehydration stress and salinity-related gene regulation, he is known to have developed a new methodology for gene amplification and a Polymerase chain reaction-based protocol for manipulating differentially-expressed genes and their promoters. Working on rice (*Oryza sativa*) and Pennisetum, he evolved new methodologies for producing stress tolerant transgenic plants.

He also identified glyoxalase system in plants and showed its role under stress environment. The glyoxalase system comprises of two enzymes, glyoxalase I and II which are involved in the detoxification of methylglyoxal whose level increases in response to stress. By manipulating the expression of these genes, he propounded a process how transgenic plants capable of growing in conditions of high salinity could be developed by manipulating glyoxalase I and glyoxalase II.

All his work lead to another discovery like after Studying the expression and activity of nitrate reductase, it was found that light, via phytochrome perception affects nitrate reductase gene expression via calcium and phosphoinositide mediated signaling pathways involving protein kinase c and calcium/calmodulin dependent protein kinases. Then his group worked on gene regulation in response to salinity and dehydration stress which led to the development of strategies for getting stress tolerant transgenic plants.

The glyoxalase system identified by him in plants showed its role under stress environment. The glyoxalase system comprises of two enzymes, glyoxalase I and II which are in-

volved in the detoxification of methylglyoxal whose level increases in response to stress. His group identified many novel members of glyoxalase I and II. By manipulating the expression of these genes, transgenic plants could be developed which could be grown under high saline conditions.

Research of Prof Sopory has been published in many high impact journals like PNAS, USA; Plant Physiology, Plant Journal, Journal of Experimental Botany, Plant and Cell Environment, Plant Molecular Biology, J. Biol. Chem., Nucl. Acid Res, Sci . Reports, Front. Pl. Sci, Int. J. Plant Physiology and many many others.



Photo:
Prof Sopory(left)
with Shri Pranab
Mukherjee(2nd from
right)

Prof Sopory has
travelled as
Member of
delegation with the
President of India,
Sh. Pranab
Mukherjee To
Belgium and
Turkey in 2013
and to Jordan,
Palestine and
Israel in 2015.



PHOTO: UP
Prof Sopory(right) with David Ho,
the president of Americal Society
of Plant Biologists at the felicita-
tion ceremony of election of Dr
sopory as corresponding member.



PHOTO: LEFT
Prof Sopory(2nd from right) with
Shri Ram Nath Kovind.

He was invited to become a part
of committee which was set up to
select Vice Chancellors of Uni-
versities in Bihar. Shri Ram nath
Kovind was Governor of Bihar at
the moment.



Interview Questionnaire

Sir, would you like to share some personal background?

I belong to a family of Kashmiri Pandits. My grandfather was an engineer and father had done Master in English, from the University of Lahore, and served the Govt of J& K, as Deputy Commissioner. I was around four years old when my father passed away. We were raised up by my mother with support from my Uncle and elder brother. After finishing my Masters from J&K University, I came to Delhi to look for a job, that was the need for the family at that time.

However, having failed in a few competitive tests, and some interviews, I finally took up my research work at DU and finished Ph.D under the supervision of Prof. S.C Maheshwari. For some reasons I also had to take a break from DU and joined Meerut College where I taught for about 5 months. I felt proud that my Ph.D viva exam was conducted by Prof M.S. Swaminathan, with whom I maintained communication all through, and had an opportunity to visit him, at his invitation, when he was DG at IRRI, Phillipines. After my studies I joined JNU and in between I visited many Institutes to upgrade my skills and knowledge.



PHOTO:

Prof Sopory(left) with Prof M S Swaminathan whom with he has still maintain communication



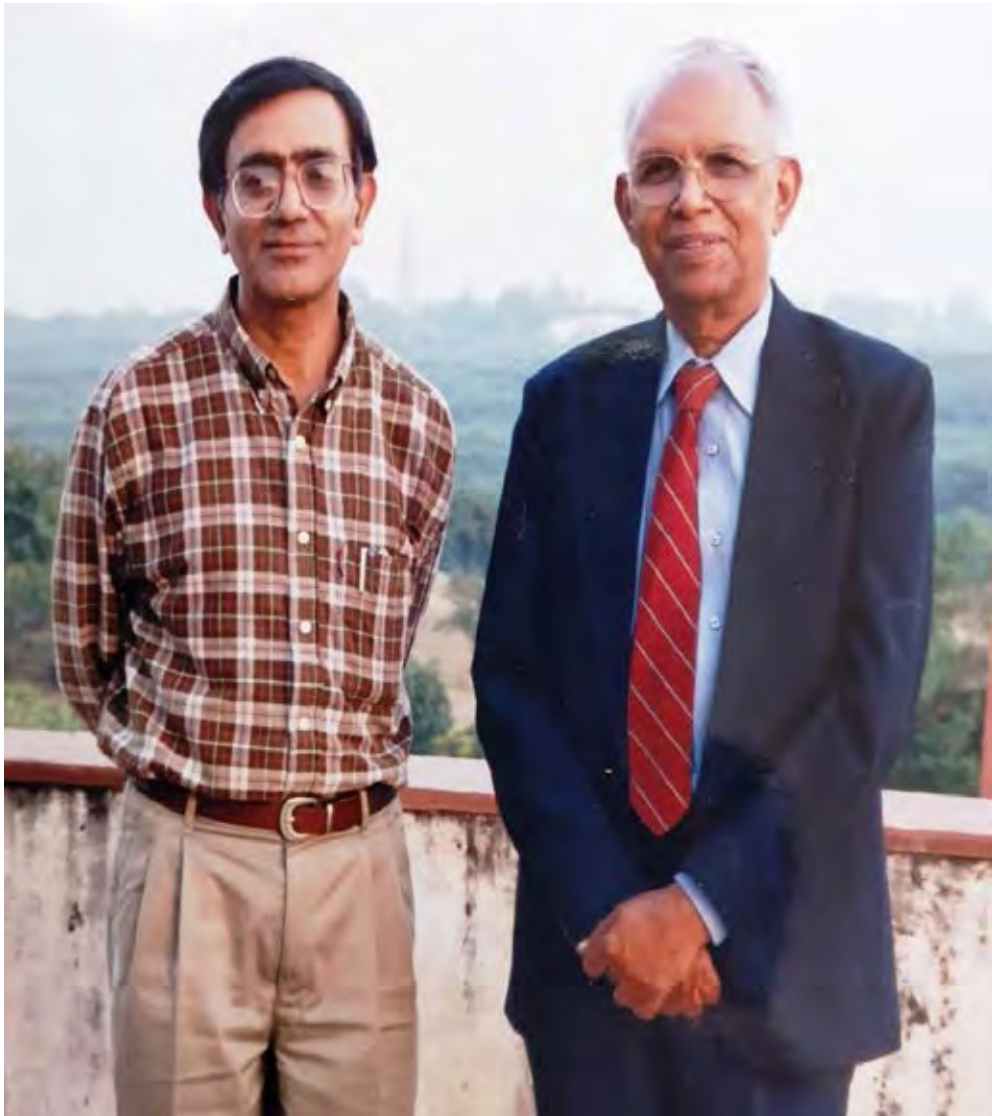
Sir, were you determined to do research or some other circumstances took you in?

At the time I was doing B.Sc at the Sri Pratap College, Srinagar, they opened a one year simultaneous course in Botany honours. I took it along with my regular B.Sc course. This was tough, nevertheless, this course did invoke some interest in me for plants. However, even after my Master in Botany, where I met some good teachers, I was not sure if I should go for Ph.D, and in which area in plant sciences.

My initial interest was to continue to stay in the state for job or further studies but this did not mature. It is only after coming to Delhi and having met Prof Maheshwari (with Prof Sopory in photo on this page), under whose supervision I finished my doctorate, that I developed keen interest in plant biology. He induced me to read about research going on in different areas, other than my own immediate area of research, and said that in future we should move into an understanding of the biochemical and molecular mechanisms of plant development and physiological processes.

I have remained in close contact with him, and more so when he moved to ICGEB after his retirement, where I joined in 1997 and continued there till 2011(Jan). As I am answering this question of yours, I talked to Prof Maheshwari, who is now in Jaipur, I found that he is not keeping well. I pray for his good health.

In 1966, Professor S C Maheshwari's group made the landmark discovery of the anther culture technique for the production of haploid plants, which leads to rapid production of homozygous pure lines, a boon for agriculture. At Delhi University, Professor Maheshwari established the first unit of Plant Cell and Molecular Biology and later the first Department of Plant Molecular Biology in the country.





BOX: Grant/ Review Panels in National Agencies served by Prof Sopory

(I) Council of Scientific and Industrial Research, India

Plant Agriculture & Forest Committee, 1990-1995; Plant Science Committee, 1998-2001; Travel Grant Committee, 1990-1991; RA/SRF Selection Committee; CSIR-NET, examination committee; Bhatnagar Award Committee; Young Scientist Award Committee; Member, Project Review committee for New Millennium Indian Technology Leadership Initiative Program; Member, Research Council, CIMAP, Lucknow, 2001-2006; Co-chairperson: CSIR Recruitment Board 2003-2011; Member, Research Council, RRL, Jammu, 2004-2006; 2010-2012; 2013-2015; Chairman, Research Council, Institute of Himalayan Bioresource Technology, Palampur; 2004-; Member, Research Council, National Chemicals Laboratory, Pune, 2007-2010; Member Search /Selection Committee for CSIR Director like CCMB/ NBRI/ CIMAP/IHBT; Member, 12th Plan Committee 2011; Member, Governing Council, 2014; Chairman, Research council, NBRI, Lucknow 2013-; Chairman, Plant Science committee, 2015 to date.

II Department of Science and Technology, Govt. of India

MAC for Young Scientist, 1990-1995; PAC for Plant Sciences, 1994-1999; Member, Committee for selection of Swarnajanti Fellowships, 2000- 2007; Member, PAC, ILTP, Indo Russia and Other Foreign Programs, 2001; Member, FIST program committee, 2002—2007; Member, Committee for BOYSCOST selection 2005-2007; Member, SERC, 2004-2007; Chairman, PAC, Plant Science, 2004-2007

(III) Department of Biotechnology, Govt. of India

PAC 1991-1992; PAC for Human Resources Development, 1997-99; PAC for Patent Screening Committee, 1998-2002; PAC, Agriculture Biotechnology, 2000-2003, 2008; PAC, Bioprospecting and Biodiversity, 2000-2003; Chairman, Overseas fellowship committee, 2000; Member, Indian Delegation DBT to visit China to develop Sino- Indian Collaboration Programmes, 1994; Member

from DBT on NBPGR, New Delhi monitoring committee (1999- 2007); Member from DBT on Rajiv Gandhi Centre, Trivandrum, monitoring committee, 2000-2005; Member on Scientific Advisory Committee of National Centre for Plant Genome, New Delhi (1999- 2006 , 2009-); Member, Review Committee Genetic Modified Organisms, 2002. Member, Task Force, Plant Biotechnology, 2003; Member, Working Group on Biosafety Regulations, 2003; Chairman, PAC, Bioprospecting and Biodiversity, 2005-2011; Member, PAC for Centres of Excellence, 2005—2008; Member, Technical Screening Committee of SIBRI 2005—2010; Member, Bioscience National Award Committee, 2005—2010; Member, Basic Science Committee, 2006-2010; Co-Chairman, Agricultural Biotechnology PAC 2006-2010; Co-Chairman, Interdisciplinary Research Committee (IDRC) in Biotechnology, 2006-2010; Member, Committee for selection of Tata Innovative prize and Ramalingaswamy Fellowships, 2007-2010; Member, Bioresource Board, 2007-2012; Chairman, Task Force, Plant Biotechnology 2012-2014; Chairman, RNAi technology task force, 2012-1014; Member, Task Force and Apex Committee, BIRAP, Co-Chair, Scientific Advisory Committee, NIPGR, 2013-; Chairman, Fast track committee on Agricultural Biotechnology 2010-2013

(IV) University Grants Commission, India

Member, Molecular Biology and Biotechnology Panel; Nominated member, visiting committees to evaluate different Universities; Course Development Committee for Plant Sciences (2001); Course Development Committee for Biotechnology (2001); Member, Committee for Formulating the Xth Plan Profile of Higher Education in India(2001); Member, visiting committee for NEHU; Member, special committee to evaluate Univ. of Hyderabad, Excellence Program

(V) National Science Academies

Member, Biology Committee, INSA 1998; Member, Library Acquisition Committee, INSA, 1998; Representative of INSA 26th Gen. Assembly of IUBS held at Taipei in 1998; Representative to the Royal So-

ciety London, 1999, 2000: was member of a team along with the US Academy President and his team, Royal Academy President and his team, Chinese Academy, Brazil Academy, Third World Academy, and Mexican Academy that brought out a document on Transgenic Plants and World Agriculture Member; Sectional Committee, Indian Academy of Sciences, Bangalore (1993-1997); Convenor, Sec. Common Plant/Animal Sciences, Indian Academy of Sciences(2002-); Member, Section Committee, Indian National Science Academy (1996-1998, 2000, 2001, 2002-2004); Council Member, of Indian Academy of Sciences (2001 -2003; 2004-2006); Member, Screening committee for fellows, National Academy of Sciences, Allahabad, 2004-; Vice-president, Indian National Science Academy (INSA) 2004-2006; Member, Inter-Academy committee, INSA, 2004-; Chairman, ICSU, INSA 2004-; Team leader of INSA delegation to Hungary for Cooperative programs, and joint workshops, 2004, 2006; Chairman, Section committee, on Plant Science, INSA, 2008; Member, Screening committee, NAAS, 2009; Member, NAAS Committee to prepare the chapter on “Agricultural Research Preparedness” for the document on State of Indian Agriculture (2009). Released by the Minister of Agriculture, GOI; Member, Int committee on Biosecurity, 2011-

(VI) Member, Board of Studies/ Academic Council

Indore University, 1992; NEHU, Shillong, 1994-; Kurukshetra University, 1989-1991; Banaras Hindu University, 1994-95; Delhi University, 1997-1999; G.J.University, Hissar, 1999-2001, 2004- (AC); Poorvanchal University 2000-2002; SAC, Bose Institute, Calcutta 2001; Member IGNOU Course Design Committee, Plant Physiology; Member, Academic Committee, National Centre for Plant Genome Research. New Delhi, 2001-2006; Member Governing Board, Netaji Institute of Technology, New Delhi (nominated by Delhi Govt.)2004; Academic Committee, National Institute of Immunology, Delhi, 2004-; Member Governing Board, GB Pant Institute Almora 2005-2008; Member Academic Council, In-

draprashta University, New Delhi 2008-2010; Member, Planning Board, GGS Indraprastha University, New Delhi, 2015..

(VII) Indian Council of Agricultural Research, India

Member, Working group for formulation of National Syllabus of Genetics and Plant Breeding(2000); Panel Member, for review of work at IARI, Delhi (2001); Member of the Board for Biotechnology Research of the Fisheries Institute, Bhubaneswar, Orissa(1998-2000); Member, Quinquennial Review Team to review work of IARI from 1990 to 2000; Member of ICAR Society (highest body, Chaired by the Minister of Agriculture) 2007-; Member, Research Program Committee of NAIP, ICAR 2009-;

(VIII) Ministry of Health

Member, Committee on food safety of GM-foods

Planning Commission:

Member, Xth plan Working Group on Agricultural Research and Education Constituted by Planning Commission for ICAR, 2001; Member, Review committee on Biodiversity and GM crops 2006; Member, Sub-group on Adoption and generation of relevant technologies and their; dissemination to the farmers, 2007; Member, sub-group on higher education, 2011

Countries he has visited so far for academic and managerial activities

USA, Germany, France, Italy, England, Spain, Netherlands, Belgium, Denmark, Sweden, Switzerland, Bulgaria, China, Taiwan, Singapore, Vietnam, Australia, Vanezuela, Nepal, Phillipines, Hongkong, BeloRus, Russia, Chile, Austria, Canada, Hungary, UAE, South Africa, Mexico, Bangladesh, Korea, Turkey, Jordan, Palestine, Israel, Rwanda.





Sir who is your role model?

To be very frank with you, I do not have any single role model. To idolize one, there is danger to get caged in “monoculture”. During the last 40 years of my journey, I have learnt many things from different contacts; my professors, collaborators, colleagues and even students.

Sir what is the role of technology in your research?

When I did Ph.D in early 70’s, my only tools were microscopes, spectrophotometers, and tissue culture facilities. Today, the imaging facilities have vastly enhanced. Similarly, the omics platforms that can bring out huge data in very short time are available. We can measure hormones, metabolites with high accuracy and presently it is possible to look at the functioning of single cells. Tremendous advancements in instrumentation, techniques and technologies have been made, and these are still evolving .We require these to answer precise question, as also to utilize the data for practical purpose.



PHOTO:

Prof Sopory(right) with Prof Arturo Falaschi(left), the then DG, ICGEB at U.N, Economic Forum Convention.



PHOTO: Prof Sopory(left) with his colleagues at USDA, Maryland in 1988.

PHOTO: RIGHT
Prof Sopory during one of his visits to Russia



Sir, how was the experience as VC-JNU when it is known as top political hotspot in the country?

I was in JNU as a teacher from 1973 to 1996 and as Vice Chancellor from January 2011 to January 2016. There is a wide gap between perception of reality about JNU. Here over 90% of faculty and students are seriously engaged in research and teaching or learning. In JNU, only 2-3% of over 1 lakh applicants can find admission, and students compete for space to sit in the library; we had to open it for 20 hours to meet the demand. Faculty and students publish regularly. As VC, I encouraged academic activity in all its dimensions and tried my best to interact with each and every faculty and student. I personally benefited a lot and learnt about the kind of work going on in non-natural science schools.

Yes, there is politics of all thoughts in the campus. But more than political activism there is academic activism and that is the reason why JNU stands top in all the national rankings in the country. If the uppermost functionaries in the University are apolitical, and non-partisan and selfless, rest of the things fall in place.



PHOTO: Prof Sopory(right) with Dr Abdul Kalam(center) and Prof SK Brahmachari (2nd left) at 75th Anniversary Celebration of National Botanical Research Institute (NBRI) in 2002.

Sir how research done by you can be useful to common people?

My research has basically revolved around an understanding of the mechanism of light and stress mediated gene expression and in turn the physiology and development in plants. Having identified many genes and pathways that can be linked to these processes, especially to abiotic stress etc., we can use this knowledge to develop transgenic approaches to manipulate gene expression or develop markers to improve crops which can be grown under unfavourable environmental conditions or plants which can overcome the impact of stress that may come during their life cycle.

Sir, how do you think scientific research, which contains a lot of technical language and data, can be more accessible to the general public, specially of India?

Science communication is an important area that has not been well nourished in this country. We need to bridge the gap between knowledge producers and technocrats with the consumers of the data, and the general public. This gap can be filled up by persons like you and the magazine like Biotech Express.



Sir what you think about GMOs when regulations are in favour of scientists?

The technology of genetic engineering or genome editing for creating transgenics that overproduce a useful protein or which do not produce a protein that is of hindrance to plant development and adaptation, is becoming more and more advanced and precise. There are good regulations in place and if anyone obeys these honestly then these biotech plants can provide a vast resource of novel variants, with added advantage, which can be used in our breeding programs to develop crops that produce more, are tolerant to diseases or abiotic stresses and also those that are water and nutrient efficient. There are tremendous opportunities and hence we should go ahead with the safe use of this technology in our agricultural system. Currently, however, unfortunately, ignorance and resistance from some quarters is driving the debate on this technology against its adoption in the country. We will pay a price for this activism in the long run.





Sir, what do you enjoy most about being a scientist?

There is nothing else that I enjoy as much as reading about new developments in science, in teaching, if get an opportunity, and in a small way contributing to science through my research. I enjoy this activity as it allows me to learn and understand a bit more about the vast nature of biological world. Science to me reveals the nature of universal consciousness that pervades all around. It connects me to myself.

I wonder how a human mind functions which on one hand can scan the outer physical world at the Astronomical level, and at the same time voyages into the inner biological and cellular world at the Angstrom level.

Sir, any message to Life Science community of India i.e. to students, researchers and scientists?

Keep the curiosity of a child alive in you. Ignorance follows knowledge and that feeling and realization should become the passion for more discoveries and innovations.

Science is a wonderful activity, remain engaged. But do not overlook other aspects of life. Read philosophy. That helps to sharpen one's thoughts and explanations.





He served(s) on the Editorial boards of many national/international journals. He was Vice President, INSA (2004-06), Society of Plant Physiology and Biochemistry and Secretary, Plant Tissue Culture Association of India.

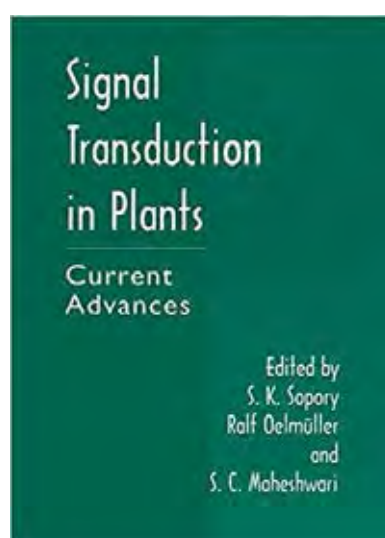
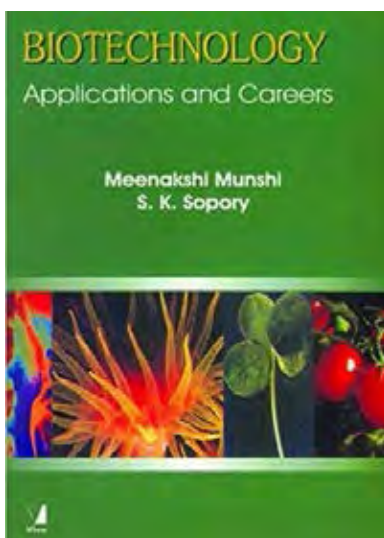
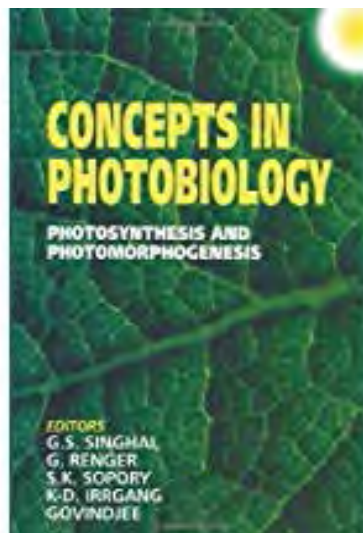
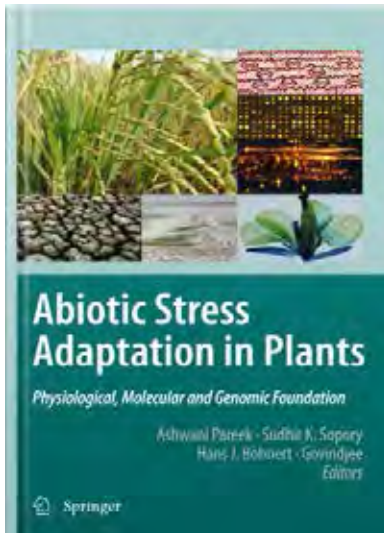


PHOTO:
Some Books written and edited by Prof Sopory

List of Publications:

Total in refereed journals : 230
Book chapters : 57
Books edited : 13

- ## Member of Editorial Boards:
- i. Physiology and Molecular Biology of Plants, 1994-1995, 2003-
 - ii. Journal of Plant Biochemistry & Biotechnology, 1995.-
 - iii. National Science Academy Science Letters 1995-2002
 - iv. Plant Physiology and Biochemistry 1997-
 - v. Plant Biology 1999-
 - vi. Indian Journal of Experimental Biology 2001-2008
 - vii. Indian Journal of Biotechnology 2002-
 - viii. Phytomorphology. (Int. J. of Plant. Sci)-2007-
 - ix. Journal of Food Agriculture and Environment, Finland, 2003-2006
 - x. The Journal of National Science Foundation of Sri Lanka. 2005-
 - xi. Molecular Plant : Blackwell Scientific Publ. England. 2007-2012
 - xii. Member, Consultation Board of IDOSI Journals, Canada 2006-
 - xiii. Tree Physiology, Canada, 2006-2008
 - xiv. J. Plant Physiology, Germany, 2008-
 - xv. J. Biomedicine and Biotechnology (Section Pl. Biotech)(2009-15)

Article by:
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Guest Article

RNA silencing based new age drug therapy approved by FDA

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Patisiron (Onpatro), a RNA-drug based on gene silencing was cleared by the U.S. Food and Drug Administration (FDA) regulations recently. This approval will pave the way for new generation drugs by targeting disease causing genes.

The mechanism of RNA interference which involves silencing of target gene by short stretch of complementary RNA molecule has been fascinating the scientific fraternity ever since its discovery. Two scientists *viz.*, Andrew Z. Fire and Craig C. Mello shared the Noble Prize in Physiology or Medicine (2006) for their path breaking finding about RNAi which is the control mechanism that determines the flow of genetic information.

RNAi is outcompeting other small molecule drugs because of its higher targeting capacity for almost all the genes. This technique can be utilized for treatment of various diseases and disorders. Although it is enthralling for scientists, they have a formidable task ahead of them in terms of safe and effective delivery of RNA-based drug in the target tissues. Researchers from University of Massachusetts took up the challenge of developing specific carriers and came up with lipid-based carriers targeting the liver tissues for metabolic disease like hypercholesterolemia, hepatic steatosis and hyperlipidemia. Further, chemical modification of these drugs proved to be safe, effective, stable and potent that aids in reducing the immunogenic response of RNA drug in clinical trials. Approximately every other person in the world is affected by obesity/diabetes mellitus, these therapeutics offers an attractive alternatives for their treatment.

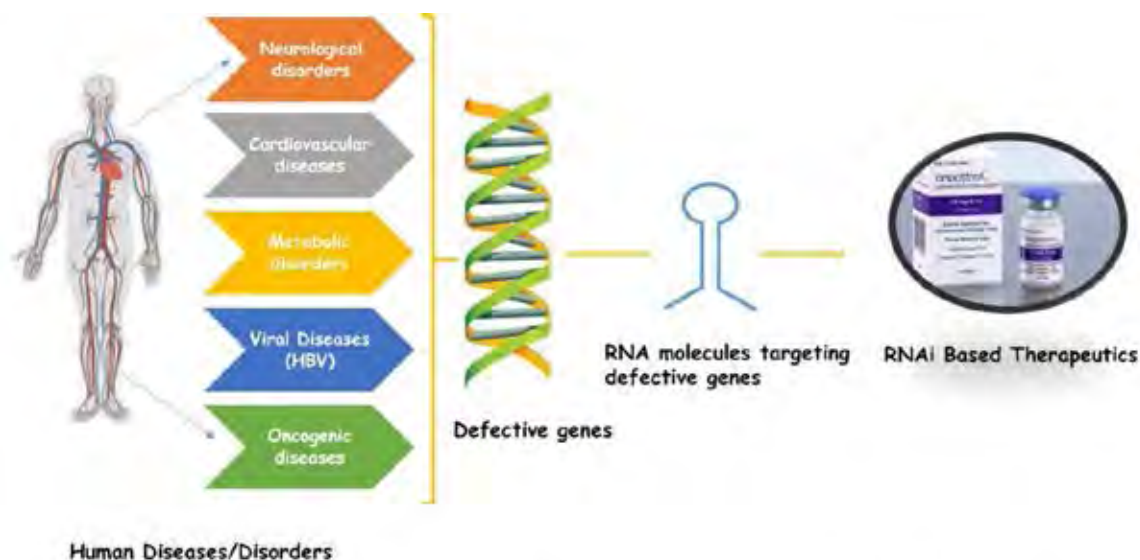


Figure1: Development of RNAi based therapeutics for various human disease and disorders

The potential of this discovery in clinical trials was recognized very early, however the efforts in this direction witnessed a pitfall in terms of stability of RNA molecules and their directional tissue targeting. Douglas Fambrough (Chief Executive of Dicerna, Cambridge, Massachusetts), while working on RNAi based drugs highlighted the problem of delivery of RNA molecules inside human body. Further investigators from Cambridge, Massachusetts-based Alnylam Pharmaceuticals devised a nanoparticle based approach to protect and transport the fragile RNA molecules to target a hereditary rare disease, transthyretin amyloidosis in which the transthyretin protein gets misfolded and accumulates in liver resulting in heart and nerve damage. Different drug delivery routes, different target tissues and encasing for RNA like fatty nanoparticles and chemical modifications were tested by the company but they found that the drug tends to accumulate in liver and kidney. Familial amyloidotic polyneuropathy (FAP) is a rare autosomal dominant disease mainly triggered by amyloidogenic transthyretin (ATTR). This disease is incurable and results in death 10 years after the onset of symptoms. It is estimated to affect approximately 50,000 peoples worldwide. The key step that can be targeted for its treatment is the prevention of conformational changes which result in defective transthyretin, however there was no potential therapeutics targeting this available.

AkshayVaishnaw, the lead researcher from Alnylam Pharmaceuticals group told that they started this project with great enthusiasm as well as hesitation because they were skeptical about the delivery of RNA molecules. Moreover, these nanoparticles were unable to deliver the sufficient amount of RNA molecules to knock down the target gene in liver cells in all the test patients. They further improved the formulation which proved to be potent in human trials as intravenous drug **Onpatro**. Onpatro encompasses patisiran that is a double-stranded small interfering ribonucleic acid (siRNA) encased in the form of a lipid complex. Further this complex attaches to the transthyretin protein and averts its distortion with the help of RNAi mechanism. This results in reduced level of transthyretin protein built in liver and the subsequent amyloid deposition in the tissues.

Alnylam filed the marketing authorization application (MAA) for **Patisiran** to the U.S. FDA in the year 2017 and got the approval in 2018. In 2018 this drug got clearance from U. S. FDA and EU regulators, with a list price

of a \$450,000 per year for market release. Apart from that Arrowhead Pharmaceuticals, Inc.(CA, USA) are also developing different RNAi-based drugs targeting liver diseases like ARC-AAT as well as drugs like ARC-520 and ARC-521 which targets the hepatitis B virus (HBV). These therapeutics showed promising results in clinical trials and opens the opportunity for treating diseases other than metabolic one.

RNAi based therapeutics market is growing at a CAGR of 28.4% (2014-2020) and expected to reach \$1.2 billion by the year 2020.

This market constitutes mainly therapeutics for cardiovascular, kidney, oncological diseases, metabolic disorders, infectious diseases and others, mainly dependent upon two technologies i.e. RNAi and RNA antisense technologies. These therapeutics geographically concentrated on North America, Europe, Asia-Pacific and LAMEA.

Key companies for these therapeutics are Alnylam Pharmaceuticals, Inc. (USA), Benitec Biopharma Limited (Australia), CenixBioScience GmbH (Germany), Dicerna Pharmaceuticals, Inc. (USA), Genzyme Corporation (USA), ISIS pharmaceuticals Inc (USA), Quark Pharmaceuticals, Inc. (USA), Silence Therapeutics PLC (UK) and Tekmira Pharmaceuticals Corp. (Canada). ISIS pharmaceuticals, Inc. (USA) has developed two drugs namely Mipomersen (Kynamro) and Fomivirsen (Vitravene) based on antisense technology.

Prior to this, a different class of RNA-based therapy was approved in 2016. This approval is second in the series of RNA-based drug therapy and opened the way to devise RNA molecules against several hereditary and other disease causing genes. Several researchers from the University of Massachusetts working in the area of RNAi based drugs claimed it to be transformational in the field of drug development. James Hamilton of Arrowhead Pharmaceuticals, Inc.(CA, USA) said **“The anticipated first US FDA approval of a siRNA therapeutic will be a major step for the entire field. Beyond that, extrahepatic targeting will be instrumental to realization of the full potential of siRNA as a therapeutic class. Historically, siRNA therapeutics have been limited to hepatocyte gene targets. An ability to address gene targets in cell types other than hepatocytes will be important for siRNA to maximize utility as a new therapeutic modality”**.

This therapy also emphasizes the potential role that human genome sequencing project could play for development of new generation drugs customized at patient level. Targeting of specific genes in specific tissues have also created safety concerns for these drug delivery methods, however with the advancement of molecular biology and emergence of specific gene editing methods like CRISPR-Cas, we can hope the beginning of a new area of drug discovery targeting specific genes.

Comparatively, swift development of basic science research into adoptive clinical technology for treatment of diseases will provide impetus for new era of RNAi based drug development.

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Guest Article

“Blockade of immune checkpoint therapy for advanced cancers”- A topic of 2018 Nobel Laureate in Physiology or Medicine

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Abstract

A big challenge that we have been facing in medical domain is to search a better cure for cancer. Despite several treatment regimens prevailing in cancer treatment such as radiation therapy, a few drugs viz., Vinblastine Sulfate, Vincristine Sulfate, Uridine Triacetate, Tamoxifen Citrate, Methotrexate and several monoclonal antibodies, the cure and consequent longevity are still in dubious. A cancer patient suffering is unending. In this line, 2018 Nobel Laureates contributions have given us the hope. The immune biology underlying the investigations for cancer cure in brief is narrated in this article.

Introduction

Mammalian immune organ system comprises of about 1.0% of the total body weight of an organism. It constitutes bone marrow, thymus, spleen, lymph glands and WBCs. Of the WBCs, leukocytes and lymphocytes belong respectively to myeloid and lymphoid progeny. Embryonically, the yolk sac is the starting point for the genesis of blood cells which include RBCs and WBCs. Gradually in the development of mammalian organ systems, hemocytoblasts in the bone marrow perpetually keep differentiating into adult erythrocytes (RBCs), leukocytes and lymphocytes with the influence of cytokines and activation by the respective antigenic peptides. Each of these leukocytes and lymphocytes has destined roles in the immune modulation of an organism. Therefore, they are collectively called as immune cells. T- (Thymic), B-(Bursa of Fabricius) and NK- (Natural Killer) cells are the lymphocytes. T-cells mature in thymus gland through thymic schooling. B-cells upon priming in the

germinal centres of lymphoid follicles of lymph nodes get differentiated as plasma cells that produce tailored immunoglobulins. NK cells distinguish between self and non-self cells and eradicate the latter (bacteria, etc) or missing-self cells (cancer cells). T-cells are called immune master cells as they regulate the rest of the immune functions such as tissue repair (1), mediation of inflammation (2), attack on non-self cells and missing-self cells (3), secretion of cytokines (4) and initiate the production of antibodies (5). These immune cells are in use for therapeutic purpose to suppress cancer growth. However, the trials relating to the use of immune cells in suppressing cancer growth have been gradually progressing. To begin with, the tumor infiltrated cells (TIC) are harvested and conditioned *in vitro* with IL-2 cytokine to recruit more number of TIC and re-infused at the site of the tumor to initiate regression (6). This reinfusion of conditioned tumor infiltrated cells is not found to be successful at all times. Therefore, the recent unfolding by James P. Allison and Tasuku Honjo, 2018 Nobel laureates in Physiology or Medicine, have revealed vividly how T cytotoxic lymphocytes (Tc) play a prominent role for cancer regression.

Functions of Immune cells

The major function of immune cells is to target foreign (non-self) cells. In this line, each of the immune cells follows its destined in-built protocol. The leukocytes comprises of neutrophils, basophils, eosinophils, dendritic cells, macrophages and monocytes. They are the first sentinels of the immune system. They are characteristically distributed in all ventilated regions of an organism to capture the invading pathogens. Of them, the contribution of dendritic cells to the host innate immune system is noteworthy. Of the leukocytes, neutrophils, dendritic cells, macrophages and monocytes are endowed with toll-like receptors with which they identify and anchor pathogens based on their pathogen associated molecular patterns. These patterns also include cancerous antigens. Though cancerous peptides/proteins are generated from our own organ systems, they are treated as foreign proteins or antigens i.e. non-self primarily because of the reason that they develop quite later to thymic schooling. Primordial T-cells though originate from the bone marrow, get matured in thymus, a primary lymphoid organ. They differentiate into T helper (Th) and Tc cells. Th cells promote adaptive immunity by priming B-cells, whereas Tc kills virus infected cells and/or cancerous cells upon priming through HLA class I transmembrane molecules coupled with antigenic peptides of antigen presenting cells. These Tc lymphocytes have come into limelight in the year 2018 due to the two Nobel Laureates who authenticated and accentuated their function to kill cancer cells.

James P Allison

Dr. James P Allison, popularly known in the scientific community as Jim Allison (Fig.1), is holding prestigious positions. A few to mention here are:

- (1) Chair, Department of Immunology, Division of Basic Science Research, The University of Texas MD Anderson Cancer Centre, Houston, TX
- (2) Vivian L Smith Distinguished Chair in Immunology, Department of Immunology, The University of Texas MD Anderson Cancer Centre, Houston, TX
- (3) Executive Director, Immunotherapy Platform, The University of Texas MD Anderson Cancer Centre, Houston, TX
- (4) Deputy Director, David H Koch Centre for Applied Research of Genitourinary Cancers, The University of Texas MD Anderson Cancer Centre, Houston, TX

(5) Director, Parker Institute for Cancer Immunotherapy (PICI), The University of Texas MD Anderson Cancer Centre, Houston, TX

The funding for Allison's attempts in immunotherapy has come from the NIH, particularly the National Cancer Institute, the Cancer Prevention & Research Institute of Texas, Howard Hughes Medical Institute, the Cancer Research Institute, Prostate Cancer Foundation, Stand Up to Cancer and PICI.

Allison began his scientific journey at MD Anderson in 1977, as a researcher in a new basic science research centre located in Smithville, Texas. Later took an assignment in MD Anderson in November 2012 to lead the Immunology Department. He profoundly established an immunotherapy research platform for MD Anderson's Moon Shots Program. This program conducts immune therapeutic monitoring by analyzing tumor samples. This platform did perform more than hundred immunotherapy based clinical trials at MD Anderson. The focus of Jim is on basic biological inventions of the master immune T cells and blockade of its immune checkpoint to accentuate treatment for cancer. In his exploration, he has chosen one of the T-cell transmembrane proteins namely cytotoxic T lymphocyte associated antigen-4 (CTLA-4), which inherently negatively regulates Tc cell function upon binding to B7 and hence acts as a break to restrain from the full and everlasting potential of activation. His aim is to prevent negative regulation of Tc by blocking CTLA-4 so as to make Tc free to attack cancer cell. He is greatly succeeded and rewarded. An antibody (Ipilimumab) against CTLA-4 is developed by Jim to block CTLA-4 from binding to B7 receptor of APC (antigen presenting cell) and free from negative regulation (7). This experimented ipilimumab is approved in a fast-track procedure by U.S. Food and Drug Administration in 2011. Clinical trials using this immune therapy technique are in progress in several other cancer types. Ultimately, Jim's research has led to "life-saving treatment" for ill people who otherwise have had no hope.



Fig.1.James P Allison and his wife Padmanee Sharma.

Source: Google images.

Blockade of Immune Checkpoint therapy for cancer

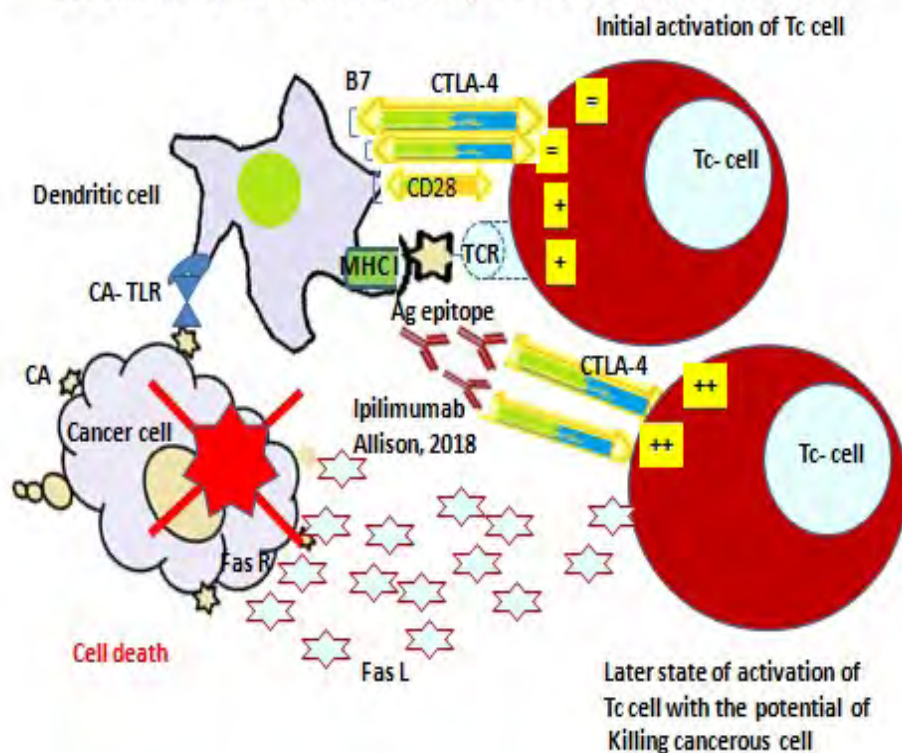


Fig.2. The presentation of cancer antigen to the TLR (Toll-like Receptors) on dendritic cell, and further through MHC I (Major Histocompatibility Complex) to the TCR (T-Cell Receptor) complex of Tc cell, the inhibitory interaction of CTLA-4 upon anchoring to B7 and acceleration of the function of CTLA-4 upon blocking with ipilimumab (promoted by Allison) ultimately leading to the death of cancer cell are shown.

Tasuku Honjo

Tasuku Honjo, a Japanese immunologist, discovered the mechanism and proteins related to the regulation of Tc cell immune responses and the same led to the development of novel immunotherapies against cancers such as melanoma. Honjo (Fig.3) bagged prestigious awards and honours, including the Kyoto Prize (2016) and the Keio Medical Science Prize (2016). Honjo is a medical graduate obtained M.D. from Kyoto University, Japan, in 1966 and recipient of a Ph.D. in medical chemistry (1975) from the same University. He was a foreign associate of the U.S. National Academy of Sciences (2001) and a member of the German National Academy of Sciences (2003) and the Japan Academy (2005). Honjo was recognized by the Assembly of Karolinska Institute in Stockholm for his investigations in immunotherapies against human patients suffering from melanoma in the 2018 Nobel Prize for Physiology or Medicine. Professor Tasuku Honjo shared this award with James P. Allison, who deduced yet another different pathway to kill even advanced cancer cells.

In the early 2000s, Honjo hypothesized that inhibition of PD-1 in laboratory animal models of cancer uniquely restores the immune potential of Tc cells to target and kill cancer cells. In this journey, Tasuku Honjo and his colleagues, from the department of medical chemistry at Kyoto University, Japan, discovered a programmed cell death protein (PD-1) on the surface of Tc cell. In later experiments, he deduced its function as a negative regulator of immune response similar to CTLA-4. Honjo showed that PD-1 of Tc cell binds to its corresponding ligand molecules PD-L1 and PD-L2 produced by cancer cells (8). This binding literally stops Tc-cell function and causes them to self-destruct. Thus, through this strategy, cancer cells cleverly evade the immune surveillance. Honjo focused on blocking PD-1 on Tc cells with an antibody in animal models of cancer and thus disallowed molecules (PD-L-1) from cancer cells to bind. This attempt has shown interestingly that Tc-cells retained their potential to target and kill cancer cells. Honjo's discoveries led to the development of novel anti-PD-1 cancer immunotherapies namely nivolumab and pembrolizumab. Nivolumab, marketed as Opdivo, is a humanized IgG4 anti-PD-1 monoclonal antibody. It is approved for the treatment of melanoma, a skin cancer.



Fig.3. Tasuku Honjo

Source: Google images

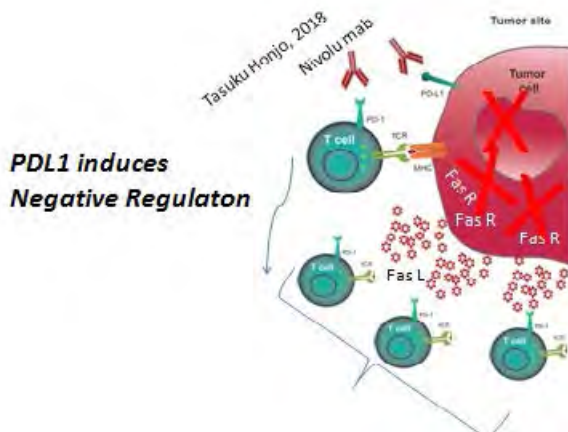


Fig.4. Blocking of PD-1 of Tc cell by nivolumab (invented by Tasuku Honjo) and further acceleration of Tc cells' cytotoxic activity against tumor cell are shown.

Clinical trials

Cancer kills millions of people annually and it is one of the greatest health challenges we are currently facing. To meet this challenge, a hope is given to us by the 2018 Nobel Laureates. By stimulating the inherent ability of our immune system to attack tumor cells, 2018 Nobel Laureates in Physiology or Medicine have established an entirely new principle for cancer therapy. Both the invented products namely ipilimumab and nivolumab do interfere with the ability of tumor cells to proliferate. In clinical trials, the voluntary patients receive nivolumab IV over 30 minutes on days 1, 15, and 29. Whereas, anti CTLA-4 *viz.*, ipilimumab IV is given over 60 minutes on day 1 and repeat for every 42 days till the completion of the surveillance. Thus, to refrain from the cancer growth, the clinical trials enrolled participants belonging to 37 cancer cohorts based on severity at National Cancer Institute, Bethesda. Interested volunteers may browse the website: www.cancer.gov/about-cancer/treatment/clinical-trials/intervention/nivolumab.

Clinical design

1.	Study type	Interventional (Clinical trial)
2	Estimated enrolment	707 participants
3	Intervention model	Single group assignment
4	Primary purpose	Treatment
5	Official title	DART: Dural Anti-CTLA-4 and Anti-PD1 Blockade in Rare Tumors
6	Actual Study Start date	January 13, 2017
7	Estimated Primary Completion date	August 31, 2020

Conclusion

The Nobel Prize in Physiology or Medicine has been awarded to 214 Nobel Laureates between the years 1901 and 2017. The 2018 Nobel Prize in Physiology or Medicine was bestowed on Allison and Honjo, who independently established and unravelled how the two different strategies for blocking the checkpoints on the immune system particularly Tc cells are used in the treatment of patients suffering from cancer illness. Their seminal discoveries showcased a new principle for cancer therapy and a landmark in the fight against cancer.

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Press Release

Start-up Podium®

The first edition of the Start-up Podium, a platform to engage in a dialogue on innovation and start-up was launched at the Hitex City in Hyderabad from 3rd to 5th May at Mediko 2019.



An initiative to bring together individuals and start-ups at the forefront of healthcare innovation across industries and functions. The event was one of its kind that offered product demos, innovation showcase, expert talks along with B2B networking to explore synergy and develop partnerships with industry players.

The three ways of engagement at the Start-up Podium was through Innovation Talks where the experts and decision makers shared the insights and learnings; Networking platform for the start-ups to showcase their innovation and connect with innovation leaders of the industry and Innovation

Showcase where the start-ups showcased their ingenious solutions to the MedTech stakeholders and players from academia and industry.

Over the three days there were several discussions, presentations and conversations with key industry and academia players on incubation, innovation, commercialisation and technology translation in the area of healthcare. Some of the speakers and panellists were heads of incubators, faculty, mentors and entrepreneurs from University of Hyderabad, IKP Knowledge Park, LV Prasad Eye Institute, CCMB Atal incubation Centre, IIT Hyderabad, IIIT Hyderabad (OJAS)etc. The discussions and conversations revolved around thenuances of mentoring, difference between Consulting Vs Mentoring, stating that the former delivers outcomes while the later shows results, difference between healthcare and life sciences start-ups from the other high-tech start-ups, women participation in the MedTech space, investment interest and challenges in the MedTech space and hospital and start-up collaboration. The candid conversations and discussions provided valuable insights to the start-ups and viewers. It also provided a good platform for the entrepreneurs to connect and interact with the decisions makers as the program was very focussed.

On the third day of the program a start-up competition was organized. 10 teams were shortlisted for the live pitch at the start-up podium, the pitches were very diverse addressingdifferent areas in the healthcare space like rehabilitation and assistive technology, surgical simulation, neonatal care, neuromotor disorder diagnosis etc. The jury comprised of incubation heads, successful entrepreneurs, healthcare consultants and investors who asked very pertinent questions focussed on business and technology alignment. Three start-ups won the competition and were awarded a small cash prize as an encouragement.

Overall, it was great kick off to the first edition of the Start-up Podium. Multiple shows are curated and designed by start-up podium for the exhibitions and trade show, the next upcoming show is in Thailand.We would be excited to partner potential partners to organize the start-up podium.
<http://startup-podium.com/>

NEWS: Govt & Industry

Indian scientists develop colored varieties of wheat

Agricultural biotechnologists' team led by Monika Garg at the National Agri-Food Biotechnology Institute or NABI located in Mohali have not just developed these coloured wheat varieties, but they have also transferred the technology to different companies. Few firms with whom this Department of Biotechnology lab has signed accords are already cultivating them.

Garg who has been working on these varieties since a decade said, "We have not released them for individual growers as they may find it hard to sell them, at least for the time being".

Garg said the coloured varieties offer many health benefits. Black wheat, for example helps in preventing fat deposition, improves insulin tolerance, controls glucose levels and lower blood cholesterol, as said by mouse studies at NABI. In addition to anthocyanins, the varieties have relatively high levels of proteins & vital micronutrients like zinc. The antioxidants may also help protect against ageing, obesity & diabetes. The varieties have been developed with the use of classic biotechnology tools that are usually used by plant breeders.

When the scientists found that it has adjusted well with the local climatic conditions and has produced adequate yield levels, they transferred the technology to few companies. Garg told that the in-



stitute has inked MoUs with 10 companies from various States like Bihar, Gujarat and Maharashtra etc.

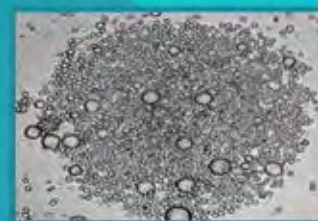
She added that "We want to make bakery products as well as atta from these unconventional varieties of wheat popular among customers, so that the benefits of antioxidants could reach the population through their favourite cereal".

PRIMARY HUMAN DERIVED STEM CELLS FOR PREDICTIVE PLATFORMS

Trans-MSC is Human derived primary pluripotent stem cell aggregate model that can predict test chemical's safety and preclinical prognosis



Trans-HSC is Human derived primary hematopoietic stem cell aggregate model that can predict test chemical's safety and preclinical prognosis



Stem Cells for Real Time Safety & Efficacy studies of Chemical Entity

- ▶ Our Stem cell aggregates are either stromal or hematopoietic in nature
- ▶ Test readouts are 100% relevant to humans
- ▶ Tests performed can be robust, specific, sensitive, and reproducible
- ▶ Suitable for both low throughput and high throughput screening
- ▶ Suitable for cell based modelling
- ▶ Primary in nature; Not transformed; Not genetically modified
- ▶ Customized units
- ▶ Ready to use; Can be maintained at -80° C till use

Stem Cells for Real Time End Points Test in Oncology

- ▶ Cancer and it's type specific primary tissue architecture
- ▶ Tumor tissue derived primary cancer cells exhibiting native characteristics
- ▶ Suitable to develop Patient Derived Xenografts
- ▶ Tissue and Cancer cell based *ex-vivo* models for conducting assays
- ▶ Suitable for cryopreserved and re-use
- ▶ Suitable to develop Organoid models for regulatory or R&D testings
- ▶ Devoid of any bioburden

* Our products are human derived adult stem/cell based primary platforms that can be predictive real time human/patient relevant tools in your discovery, development, test compound's toxicity related testings, test compound's efficacy

Gagandeep Kang becomes first Indian woman scientist to receive UK Royal Society

April 19, 2019



Gagandeep Kang, the executive director of Translational Health Science and Technology Institute, has become the first Indian woman scientist to be selected as a fellow of the prestigious Royal Society, London.

Kang —known for her interdisciplinary research, development and prevention of enteric infections and their sequelae in children in

India — has built national rotavirus and typhoid surveillance networks, established laboratories to support vaccine trials and conducted phase 1-3 clinical trials of the vaccine.

Yusuf Hamied, scientist and chairman of Indian pharmaceutical major Cipla, has also been awarded an honorary fellowship of the Royal Society.

Other Indians elected fellows in the 2019 intake are: Prof Gurdyal Besra, Bardrick Professor of Microbial Physiology and Chemistry, Institute of Microbiology and Infection, School of Biosciences, University of Birmingham; Prof Manjul Bhargava, R Brandon Fradd Professor of Mathematics, Department of Mathematics, Princeton University; Prof Anant Parekh, Professor of Physiology, Department of Physiology, Anatomy and Genetics, University of Oxford; and Prof Akashay Venkatesh, Professor, School of Mathematics, Institute for Advanced Study.

Kang and four other Indians join the honorary ranks of Sir Issac Newton (1672), Charles Darwin (1839), Michael Faraday (1824), Albert Einstein (1921) and Alan Turing (1951).

The Royal Society is an independent scientific academy of the UK and the Commonwealth, dedicated to promoting excellence in science.

World's first Malaria vaccine pilot launched in Malawi

April 23, 2019

WHO welcomes the Government of Malawi's launch of the world's first malaria vaccine today in a landmark pilot programme. The country is the first of three in Africa in which the vaccine, known as RTS,S, will be made available to children up to 2 years of age; Ghana and Kenya will introduce the vaccine in the coming weeks.

Thirty years in the making, RTS,S is the first, and to date the only, vaccine that has demonstrated it can significantly reduce malaria in children. In clinical trials, the vaccine was found to prevent approximately 4 in 10 malaria cases, including 3 in 10 cases of life-threatening severe malaria.

The pilot programme is designed to generate evidence and experience to inform WHO policy recommendations on the broader use of the RTS,S malaria vaccine. It will look at reductions in child deaths; vaccine uptake, including whether parents bring their children on time for the four required doses; and vaccine safety in the context of routine use.

The vaccine is a complementary malaria control tool – to be added to the core package of WHO-recommended measures for malaria prevention, including the routine use of insecticide-treated bed nets, indoor spraying with insecticides, and the timely use of malaria testing and treatment.

The WHO-coordinated pilot programme is a collaborative effort with ministries of health in Ghana, Kenya and Malawi and a range of in-country and international partners, including PATH, a non-profit organization, and GSK, the vaccine developer and manufacturer, which is donating up to 10 million vaccine doses for this pilot.

Gilead Sciences announced to donate 2.4 million doses of its HIV treatment Truvada annually

May 10, 2019

As part of a national effort from the federal government to combat HIV and prevent future infections, Gilead Sciences announced it will annually donate 2.4 million doses of its HIV treatment Truvada for PrEP to the U.S. Centers for Disease Control and Prevention

(CDC) to provide treatment for uninsured Americans.

Foster City, Calif.-based Gilead said the donation is among the largest seen in the United States and is part of the company's ongoing initiative to help ensure that all patients who can benefit from Truvada for PrEP can have access to it. PrEP, which has a list price of \$20,000, is used to reduce the risk of HIV infection in individuals who are at higher risk for HIV. It has been shown to reduce the risk of new infection by up to 97 percent when taken consistently.

Truvada is indicated in combination with safer sex practices for HIV PrEP to reduce the risk of sexually acquired HIV in at-risk individuals who are HIV-negative. Descovy is already approved as an HIV treatment, but not for PrEP.

Greg Alton, chief patient officer at Gilead, said the company is proud to partner with the CDC in order to expand the use of the company's medication in order to prevent new infections.

It is estimated that about 200,000 of the 1.1 million people who are at risk for HIV in the United States already receive Truvada for PrEP. However, broader use among at-risk populations is hampered by a number of barriers, including limited awareness of PrEP among providers and patients, as well as a lack of access to healthcare.

While Gilead is donating these doses, the company has been un-

der fire from some HIV/AIDS activists over its HIV drug patents. The company has been accused of withholding safer formulations of its HIV drugs in order to maximize profits on those medications that had already been approved, such as Truvada. Both Truvada and Descovy have boxed warnings regarding the risk of post-treatment acute exacerbation of hepatitis B. Truvada also carries a Boxed Warning for the risk of drug resistance with PrEP in undiagnosed early HIV infection.

Roche launches Hemophilia A drug Hemlibra in India

May 9, 2019

Drug firm Roche has launched Emicizumab under the brand name Hemlibra in India for preventive treatment of Hemophilia A.

Lara Bezerra, Chief Purpose Officer, Roche Pharma was reported as saying, "The introduction of Emicizumab (Hemlibra) is a significant milestone in the treatment of Hemophilia A in India and reaffirms our commitment to bring Roche's ground breaking medicines to patients in India as early as possible."

Bezerra added, "This breakthrough medicine represents a completely new way to manage Hemophilia A

and redefines the standard of care.”

According to Roche Pharma, Hemlibra is approved by multiple regulatory authorities across the world and is now also approved and available in India.

Glenmark Appoints Dr. Yasir Rawjee as CEO of Glenmark Life Sciences its Subsidiary

Glenmark Pharmaceuticals Ltd., a research-led global integrated pharmaceutical company, today announced that it has appointed Dr. Yasir Rawjee as the Chief Executive Officer of Glenmark Life Sciences Ltd., its subsidiary for the API (Active Pharmaceuticals Ingredients) business.

Yasir joins Glenmark Life Sciences from Mylan Inc., where most recently, he was the Head of Global API Operations. He has held positions of increasing responsibility at Mylan including Senior Vice President of API Technical Operations and Senior Vice President and Head for Sales and Marketing for the API Business. Yasir started his career with SmithKline Beecham Pharmaceuticals based in the USA and has been associated with GlaxoSmithKline and Matrix Lab-

oratories Ltd. previously. He has over 25 years of experience in the pharmaceutical industry. He has a Ph.D. in Chemistry from Texas A&M University, USA and holds a degree in B.Sc.(Tech.) from UDCT Mumbai, India.

Glenmark's API business has witnessed robust growth rate of 15% CAGR over the last 5 years while maintaining its leadership position globally across several molecules. To provide a strategic focus to this business, Glenmark had earlier this year transferred the API business to a wholly-owned subsidiary Glenmark Life Sciences.

“We see significant growth potential in our API business given the increasing demand for good quality and sustained supply of APIs globally. With this view, we housed our API business into a separate subsidiary, which will be run independently. We are happy that Dr. Yasir Rawjee will now spearhead the API unit and take it to greater heights with his rich experience both in the technical and marketing aspects of the business,” said Glenn Saldanha, Chairman and Managing Director, Glenmark Pharmaceuticals.

“Glenmark Life Sciences has built strong partnerships across the globe and has a very focused approach to further expand the API business. I am pleased to join the organization at a time when I believe I am getting an opportunity to contribute meaningfully in scaling up and shaping the next leg of growth for the API unit,” said Dr. Yasir Rawjee.

About Glenmark Pharmaceuticals

Glenmark Pharmaceuticals Ltd. (GPL) is a research-driven, global, integrated pharmaceutical organization. It is ranked among the top 75 Pharma & Biotech companies of the world in terms of revenue (SCRIP 100 Rankings published in the year 2018). Glenmark is a leading player in the discovery of new molecules both NCEs (new chemical entity) and NBEs (new biological entity). Glenmark has several molecules in various stages of clinical development and is focused in the areas of oncology, dermatology and respiratory.

May 09, 2019

Merck & Company is planning a \$1 billion expansion

Merck & Company is planning a \$1 billion expansion to its manufacturing facility in Elkton, Over the course of the next three years that will include the addition of approximately 100 new jobs,

Merck will add 120,000 square feet to its existing 1.1 million-square-foot operation in Elkton in order to increase the production of its Human Papillomavirus (HPV) vaccines.

For Merck, the expanded focus

on the HPV vaccine comes about a month after the company announced a collaboration with Tessa Therapeutics. The companies will pair Tessa's armored human papillomavirus-specific T cell (HPVST) therapy with Merck's vaunted checkpoint inhibitor, Keytruda as a potential treatment for patients with recurrent or metastatic HPV 16 and 18-positive cervical cancer.

Merck has operated its Elkton manufacturing plant in Rockingham County for over 75 years and currently employs approximately 900 workers at the site. This the latest expansion for the Merck site. In 2016, the company invested \$170 million into an expansion of the facility.

Merck's expansion of the manufacturing facility is supported, in part, by state-funded grants that will support stormwater and infrastructure upgrades that are necessary to support the expansion of the facility. The company is also eligible to receive Sales and Use tax exemptions on manufacturing equipment, as well as a Major Business Facility Job Tax Credit for new, full-time jobs created, the office of the governor said.

Gov. Ralph Northam said the billion dollar investment in Rockingham County is a symbol of the global pharma giant's commitment to the region and will support further economic growth in the area.

"Merck has long been a valued employer and important corporate steward in Virginia that continues to play a vital role in advancing the

21st-century manufacturing sector in our commonwealth," Northam said.

Sanat Chattopadhyay, president of Merck Manufacturing Division, said the company is grateful for its partnership with the local and commonwealth governments. That partnership will help Merck sustain its commitment to the area's economic growth, Chattopadhyay said in a brief statement.

In addition to the expansion of the facility, Merck will also form a partnership with Blue Ridge Community College and James Madison University to groom potential future employees for the company. The partnership is aimed at addressing short- and long-term employment needs at the company. BRCC and JMU will establish a pipeline of biotechnology engineering and computer science talent that will allow the Shenandoah Valley to accommodate the future growth of Merck and other life science industries and manufacturers in the region. Northam said the collaboration between Merck and the academic programs will ensure we have a pipeline of skilled talent in the Shenandoah Valley for decades to come.

Pfizer announced it intends to buy Therachon, a

rare disease biotech company based in Basel, Switzerland for \$810 Million

On March 25,

Under the terms of the deal, Pfizer will pay \$340 million upfront with another \$470 million in payments contingent on milestones for the development and commercialization of TA-46 for the treatment of achondroplasia. Achondroplasia is a genetic condition that is the most common form of short-limbed dwarfism. The disorder can also cause serious cardiovascular, neurological and metabolic problems for about 250,000 people worldwide. There are currently no approved treatments for achondroplasia.

TA-46 is a soluble recombinant human fibroblast growth factor receptor 3 (FGFR3) decoy. It is believed it can normalize the overactive FGFR3 signaling pathway that is implicated in bone development abnormalities linked to achondroplasia. Therachon is developing it as a weekly subcutaneous injection for children and adolescents with the disorder.

The drug has finished Phase I trials. The European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA)

have both granted the drug Orphan Drug Designation.

In addition to headquarters in Switzerland, Therachon has research laboratories in Nice, France and business operations in the New York area.

On March 25, Therachon presented data from the Phase I trial of apraglutide in short bowel syndrome at the ASPEN 2019 Nutrition Science & Practice Conference organized by the American Society for Parenteral and Enteral Nutrition in Phoenix, Ariz. Short bowel syndrome (SBS) is caused by extensive intestinal resection as the result of chronic inflammatory bowel disease (IBD), acute events such as mesenteric infarction or congenital abnormalities. Symptoms include diarrhea, dehydration, malnutrition and weight loss.

Apraglutide is designed to increase the intestine's ability to absorb nutrients and decrease the need for parenteral support (PS), which is the intravenous delivery of essential nutrients, calories and fluids. The drug is currently being studied in two Phase II clinical trials in SBS patients in Denmark.

For its part, Pfizer's acquisition of the achondroplasia will set them on a path to compete with BioMarin Pharmaceutical, which is developing vosoritide for the disorder. In 2015, BioMarin announced positive Phase II proof-of-concept data for the drug, with data from 26 children in the trial showing a favorable safety profile and effica-

cy at the 15 micrograms/kilogram/daily dose.

In June 2018, BioMarin dosed the first patient in a global Phase II trial of the drug. The drug has also been granted Orphan Drug Designation in the U.S. and Europe. The trial will study the drug in about 70 infants and young children with achondroplasia in newborns and children less than 5 years old for 52 weeks. There will then be an open-label extension. The primary objectives of the study are safety, tolerability, and the effect of vosoritide on height Z-scores. It also plans to augment that score with data on proportionality, functionality, quality of life, sleep apnea, and foramen magnum dimension in addition to the beginning of major illnesses and surgeries.

Tafamidis Approved in First for Rare Heart Disease

Pfizer won approval for two formulations of tafamidis-based drugs, including a first for the treatment of the cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM).

The U.S. Food and Drug Administration (FDA) approved the new drug known as Vyndaqel (tafamidis meglumine) for ATTR-CM,

which makes this the first drug in the U.S. approved to treat this rare heart disease. In addition to Vyndaqel, the FDA also approved another formulation of tafamidis. The FDA approved also Vyndamax (tafamidis). The two drugs are approved for ATTR-CM in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization

Approval of Vyndaqel was based on Phase III results that showed the therapy reduced the risk of death in patients by 30 percent. In addition to the reduced risk of death, Pfizer said use of tafamidis also reduced the rate of cardiovascular-related hospitalizations by 32 percent for this patient population, compared to placebo.

Paul Levesque, global president of rare disease at Pfizer, said the approvals of Vyndaqel and Vyndamax deliver on the company's promise to develop life-changing medications. The two tafamidis drugs do that for patients with ATTR-CM, he said.

"This milestone is a game changer for patients, who until today had no approved medicines for this rare, debilitating and fatal disease. We will continue to focus efforts on working with the physician community to increase awareness and ultimately detection and diagnosis of this disease," Levesque said in a statement.

According to Reuters, Pfizer has set a list price of \$225,000 a year for the medicine. Analysts have al-

ready pegged the drug as a potential blockbuster, with annual sales expected to exceed \$1 billion in 2024, Reuters said.

Pfizer's price for the ATTR-CM drugs comes in about \$200,000 lower than treatments for hereditary TTR amyloidosis, which also caused by a buildup of transthyretin protein in the body. Drugs developed by Alnylam Pharmaceuticals and Ionis Pharmaceuticals for that disease have a price of about \$450,000 a year, Reuters noted.

Researchers find high-risk genes for schizophrenia

April 23, 2019

Using a unique computational "framework" they developed, a team of scientist cyber-sleuths in the Vanderbilt University Department of Molecular Physiology and Biophysics and the Vanderbilt Genetics Institute (VGI) has identified 104 high-risk genes for schizophrenia.

Their discovery, which was reported in the journal *Nature Neuroscience*, supports the view that schizophrenia is a developmental disease, one which potentially can be detected and treated even before the onset of symptoms.

"This framework opens the door

for several (research) directions," said the paper's senior author, Bingshan Li, PhD, associate professor of Molecular Physiology and Biophysics and an investigator in the Vanderbilt Genetics Institute (VGI).

One direction is to determine whether drugs already approved for other, unrelated diseases could be "repurposed" to improve the treatment of schizophrenia. Another is to find in which cell types in the brain these genes are active along the development trajectory.

To solve the problem Li, with first authors Rui Chen, PhD, research instructor in Molecular Physiology and Biophysics, and postdoctoral research fellow Quan Wang, PhD, developed a computational "framework" they called the Integrative Risk Genes Selector.

The framework pulled the top genes from previously reported loci based on their cumulative supporting evidence from multi-dimensional genomics data, as well as gene networks.

Which genes have high rates of mutation? Which are expressed in prenatally? These are the kind of questions a genetic "detective" might ask to identify and narrow the list of "suspects."

The result was a list of 104 high-risk genes, some of which encode proteins targeted in other diseases by drugs already on the market. One gene is suspected in the development of autism spectrum disorder. "Schizophrenia and autism

have shared genetics," Chen said.

A Bayesian framework that integrates multi-omics data and gene networks predicts risk genes from schizophrenia GWAS data. *Nature Neuroscience*, 2019; DOI: 10.1038/s41593-019-0382-7

Stem cell scientists step closer to create transplant arteries

Scientists at the Morgridge Institute for Research are working toward a dream of creating artery banks -- similar to blood banks common today -- with readily-available material to replace diseased arteries during surgery.

The latest work in the lab of Morgridge regenerative biologist James Thomson puts the science one step closer to that goal.

In a paper published online in *Stem Cell Reports* on May 9, 2019, the Thomson Lab highlights a better way to grow smooth muscle cells, one of the two cellular building blocks of arteries, from pluripotent stem cells. The work also identifies a potential drug for reducing post-surgical risks in patients who undergo bypass surgery.

"We decided to focus on blood vessels because cardiovascular

disease is a major cause of death worldwide,” Thomson says. “In the U.S. for example, heart disease and stroke are the No. 1 and No. 3 killers, respectively. And this work also has implications beyond making vessels for transplantation; it’s sort of a stepping stone to more advanced tissue engineering.”

Producing arteries in the lab requires two essential cell types: endothelial cells and smooth muscle cells. In 2017, the lab demonstrated methods to generate and characterize endothelial cells, while the new research focuses on the smooth muscle cells.

Jue Zhang, lead author and a Morgridge associate scientist, says widely used growth factors for producing smooth muscle cells from stem cells can also cause intimal hyperplasia, one of the most common reasons a bypass graft fails.

In intimal hyperplasia, a portion of the arterial wall thickens -- due to proliferation and migration of smooth muscle cells -- and causes a narrowing of the blood vessel.

“We wanted to have a protocol that can reduce the risk of intimal hyperplasia,” Zhang says. “It’s a common problem in smooth muscle cell differentiation, and if you want to make a useful artery, you don’t want that risk.”

Healthy smooth muscle cells need the ability to contract, which helps them distribute blood throughout the body and regulate blood pressure. Using a high throughput screen, the team identified a small

molecule, known as RepSox, that had the best potential to produce cells with contractile properties.

RepSox was identified out of a screen of 4,804 small molecules. In contrast to current widely used growth factors, RepSox inhibits intimal hyperplasia. It’s more stable than these growth factors and is also a cheaper alternative.

The characteristics that make RepSox good for differentiating smooth muscle cells also make it a desirable drug candidate to reduce risk of post-surgery complications, like intimal hyperplasia. Thus, this stem cell based high throughput screen can be used as a novel strategy for identifying drugs to restrict narrowing of blood vessels.

“Even after you have a bypass surgery, you can have some problems with your artery, like restenosis (narrowing arteries) due to intimal hyperplasia,” Zhang says. “Currently there are only two FDA-approved drugs on the market [to address these problems], and they’re not cell-type specific, meaning they have side effects. We found that RepSox inhibits intimal hyperplasia and has fewer side effects.”

RepSox is cell-type specific, so it inhibits smooth muscle cells and prevents the development of intimal hyperplasia without affecting neighboring cell types like endothelial cells.

While this finding brings scientists closer to improving treatments for cardiovascular disease, Zhang says

there’s still another challenge to address: cell maturity.

“Basically this cell type is better than previous efforts, but it’s still not mature yet,” Zhang says. “We need to induce these cells to become more mature, to be more similar to our native artery, to make it more functional.”

Reference: A Human Pluripotent Stem Cell-Based Screen for Smooth Muscle Cell Differentiation and Maturation Identifies Inhibitors of Intimal Hyperplasia. *Stem Cell Reports*, 2019; DOI: 10.1016/j.stemcr.2019.04.013

Bioengineer Scientists creates a cellular speedometer

Researchers have discovered that *Pseudomonas* bacteria can detect the speed (shear rate) of flow regardless of the force. By linking the flow-detecting gene to one responsible for illumination, they have bioengineered a real-time visual speedometer: The faster the flow, the brighter the glow.

Many kinds of cells can sense flow, just as our skin cells can feel the difference between a gentle breeze and a strong wind. But we depend on feeling the force involved, the push-back from the air against us. Without that push, we can’t distinguish speed; when the windows are

closed, our skin can't feel any difference in air force whether we are sitting in an office, a speeding car or a cruising airplane. But now, a team of Princeton researchers has now discovered that some bacteria can in fact detect the speed of flow regardless of the force. Their paper appears in the online journal *Nature Microbiology*.

"We have engineered bacteria to be speedometers," said Zemer Gitai, Princeton's Edwin Grant Conklin Professor of Biology and the senior author on the paper. "There's an application here: We can actually use these bacteria as flow sensors. If you wanted to know the speed of something in real time, we can tell you."

The bacterium with the built-in speedometer, *Pseudomonas aeruginosa*, is a ubiquitous pathogen, found in and on bodies, in streams of water, in soil, and throughout hospitals. The Center for Disease Control and Prevention classifies *Pseudomonas* as a "serious threat," responsible for more than 50,000 healthcare-associated infections per year, of which 6,700 are antibiotic resistant and 440 are fatal.

"That's old news," said Gitai. "What we found is that not only do *Pseudomonas* encounter flow, but that they actually can sense and respond to that flow. That's a big deal. If they're in flow, they can change their 'behavior,' if you will, based on feeling they're in flow."

Joseph Sanfilippo, a postdoctoral research associate in Gitai's lab, and Alexander Lorestani, a 2017

graduate alumnus, are the lead authors on the paper. Together, they determined that bacteria can detect and even measure the flow speed of nearby fluids to turn on a set of genes. They called those genes "fro," for "flow-regulated operon."

"Fro's response is not just an on-off switch; it's actually tuned to the speed," said Sanfilippo. "It's more like a dimmer switch than a light switch."

They then bioengineered a connection between fro and a gene that causes *Pseudomonas* to glow, so that fro's genetic response could be seen under a microscope, thereby creating a real-time visual speedometer. The faster the flow, the brighter the glow.

Using that tool, Sanfilippo was able to determine the range of speeds that *Pseudomonas* responds to, with a surprising result: "They turn out to perfectly coincide with the range of speeds of fluids that are known in the blood stream and the urinary tract," said Gitai.

Given the microscopic scale of the bacteria and the strand-of-hair-sized flow chambers in which they tested fro (50 microns tall by 500 microns wide), the researchers did not measure speed in traditional miles per hour (or meters per second) units, but instead measured "shear rate," the rate at which adjacent layers of fluid pass one another. That is measured in distance-less "per-second" units.

They found that fro did not re-

spond to shear rates below 8 per-second -- slower than most fluids found in the human body -- but that it did tune its response to shear rates between 40 and 400 per-second, then plateaued above that. For reference, the shear rate in average-sized human veins is about 100 per-second.

"The speeds that fro responds to are the speeds that are going through your body right now," said Sanfilippo.

"The authors combine their expertise in bioengineering and biophysics (to fabricate these nifty flow chambers) with cutting-edge biology (RNA sequencing) to understand some fundamental questions in microbiology," said Joanne Engel, chief of infectious disease and a professor of microbiology and immunology at the University of California-San Francisco, who was not involved in this research.

"The ability to bring investigators together from diverse fields helps to push research forward in new and creative ways," she said. "As this sensing mechanism is likely to be found throughout biology, it may have broad applications and may even be useful for developing new drugs (antibiotics) to treat bacterial infections, especially blood infections (like sepsis)."

A force-independent response

Sanfilippo and his colleagues had initially assumed that *Pseudomonas*'s sensitivity to flow must depend on its ability to sense force, just as we all intuitively understand that a hand out a car window will

feel more force when we're driving at higher speeds. That intuitive link between flow and force has led to a universal blind spot in the field, said Gitai.

"Other researchers have found that different bacteria can respond to fluid flow, and they've effectively assumed that it was the force," Gitai said. "The intuition was so strong that it should be force, that in fact people didn't bother to explicitly test this."

A way to test that assumption came from Howard Stone, the Donald R. Dixon '69 and Elizabeth W. Dixon Professor of Mechanical and Aerospace Engineering and a co-author on the paper. Stone proposed an experiment that would show whether or not the bacteria was responding to force: submit it to materials of different viscosities, or thicknesses, that are flowing at the same speed.

If you pour water over your hand, then pour honey over it at the same speed, the more viscous honey will push harder against your skin, so your hand will feel more force. Sanfilippo ran experiments with fluids up to 10 times more viscous than the default medium and found that it responded only to the shear rate -- the speed -- not the force of the thicker fluids.

"Doing that one additional experiment -- we call it Howard's experiment -- really was key," said Sanfilippo. That enabled the researchers to say conclusively that *Pseudomonas* was tuning its responses purely to the speed of the

flowing materials, something that has never before been documented. To distinguish this from other kinds of mechanical sensing that have been documented in bacteria, the team coined the term "rheosensing," or flow-sensing, to describe the phenomenon.

"We are launching a mini-field here," said Gitai. "Thinking about how bacteria live in flow is a completely under-explored area. We'd love for people to look at this with other bacteria. And as we said, there's been a huge assumption in mammalian studies that everything is force-dependent -- we'd love for people to read our paper and then go back and revisit some of those assumptions and change the viscosity in their systems."

It's still not clear how *Pseudomonas* benefits from knowing the speed of its surrounding fluids, said Gitai, but it's probably linked to the pathogen's versatility; he calls it the Swiss Army knife of bacteria.

"*Pseudomonas* has a huge arsenal of different ways that it can attack," Gitai said. "One idea is that it wants to know when it's appropriate to use which tool in its arsenal. If you have a burn, and it's just sitting on your skin, maybe the genes that it can use to hurt you are different than the genes that it would use to hurt you in your urinary tract or in your blood. And that's the big idea here, that -- to anthropomorphize it -- it can know if there's flow around, and that may help it tune its response to its environment."

The all-Princeton research team

also included Matthias Koch, a postdoctoral research associate in the Lewis-Sigler Institute for Integrative Genomics; Benjamin Bratton, an associate research scholar in molecular biology; and Albert Siryaporn, a former postdoctoral researcher in Gitai's lab who is now an assistant professor at the University of California-Irvine.

Reference: Microfluidic-based transcriptomics reveal force-independent bacterial rheosensing. *Nature Microbiology*, 2019 DOI: 10.1038/s41564-019-0455-0

Shigella Vaccine Technology is now licensed by ICMR to Hilleman

A new tech developed by ICMR-National Institute of Cholera and Enteric Diseases (NICED) is now licensed by the Indian Council of Medical Research. The tech was executed by the Biotech Consortium India Limited (BCIL). It did this on behalf of ICMR and Hilleman Labs. Now coming to the disease it focuses on which is called Shigellosis, this is an infectious disease that is marked by bloody diarrhoea. It may come with or without a fever. Mainly caused due to the *Shigella* species that is carrying the disease along with them and has affected around 125 million patients in which there have been

160,00 deaths. The main affected ratio is around five years old.

So now the management on this disease is done through the improvement of antibiotic therapy, rehydration therapy and sanitation. Decision makers from WHO themselves say that there is a need for the Shigella vaccine and has rated this as the top priority. Furthermore, the World Health Organization feels this is the need of the hour and is considered to be a major breakthrough. With this in mind, this new step is most certainly said to change the lives of many who are undergoing this problem.

Takeda Divests Eye Drug to Novartis for \$5.3 Billion

In January, Takeda Pharmaceutical announced plans to sell about \$10 billion worth of assets to offset some of the debt the company garnered in its \$62 billion acquisition of Shire. On Wednesday, the Osaka, Japan company announced divestitures worth about \$5.7 billion.

Takeda entered into agreements with Swiss pharma giant Novartis and Ethicon. Novartis agreed to acquire Xiidra (lifitegrast ophthalmic solution) 5% product for \$3.4 billion up front in cash and up to an additional \$1.9 billion in potential milestone payments. Also, Take-

da sold its TachoSil Fibrin Sealant Patch to Ethicon, Inc. for \$400 million in cash. Takeda plans to take the proceeds from these sales and reduce its debt, the company said.

Not only will the sale of the assets help drive down some of the \$30 billion debt load the company has, but the reduction of the assets will allow the company to focus business areas core to its long-term growth. The acquisition of Shire gave Takeda a significant focus on rare diseases, as well as a much larger footprint in the U.S. drug market.

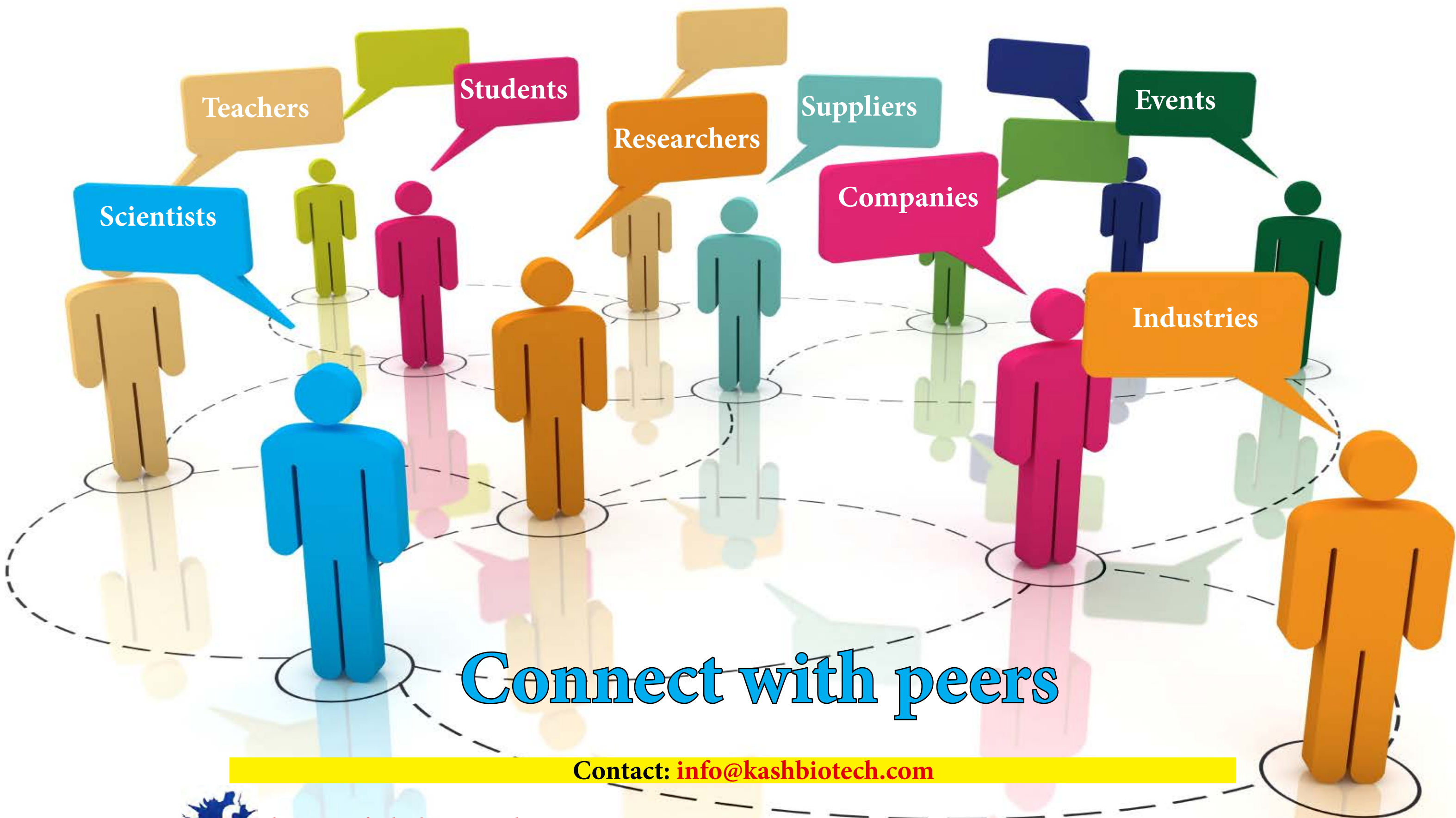
“These initial divestitures represent important steps in advancing the growth strategy Takeda outlined following our transformational acquisition of Shire earlier this year,” Christophe Weber, Takeda’s president and chief executive officer said in a statement. “We are working to strategically simplify and optimize our portfolio, while also rapidly deleveraging and continuing to invest in our growth drivers as a global, values-based, R&D-driven biopharmaceutical leader.”

Following the acquisition of Shire, Takeda will focus on its key business areas – Gastroenterology, Rare Diseases, Plasma-Derived Therapies, Oncology and Neuroscience. This focus enables Takeda to continue to deliver highly-innovative medicines and transformative care to patients around the world, creating long-term value for Takeda shareholders, the company said.

When the Xiidra deal with Novartis closes, about 400 Takeda em-

ployees based in the United States and Canada will become Novartis employees, according to the terms of the deal. The agreement is expected to close in the second half of calendar year 2019. Xiidra is the first and only prescription treatment approved by the U.S. Food and Drug Administration for both signs and symptoms of dry eye disease, with a mechanism of action that targets inflammation. Net sales for Xiidra in 2018 were \$388 million. Xiidra, which Takeda gained from its deal with Shire, was approved in 2016 and seen as a potential competitor to Allergan’s blockbuster dry-eye treatment, Restasis.

Novartis recently spun its eye care business Alcon off into a stand-alone entity, but maintained its prescription eye treatments as part of its core pharmaceutical unit.



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(Last date for submission extended till 25th May, 2019)

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