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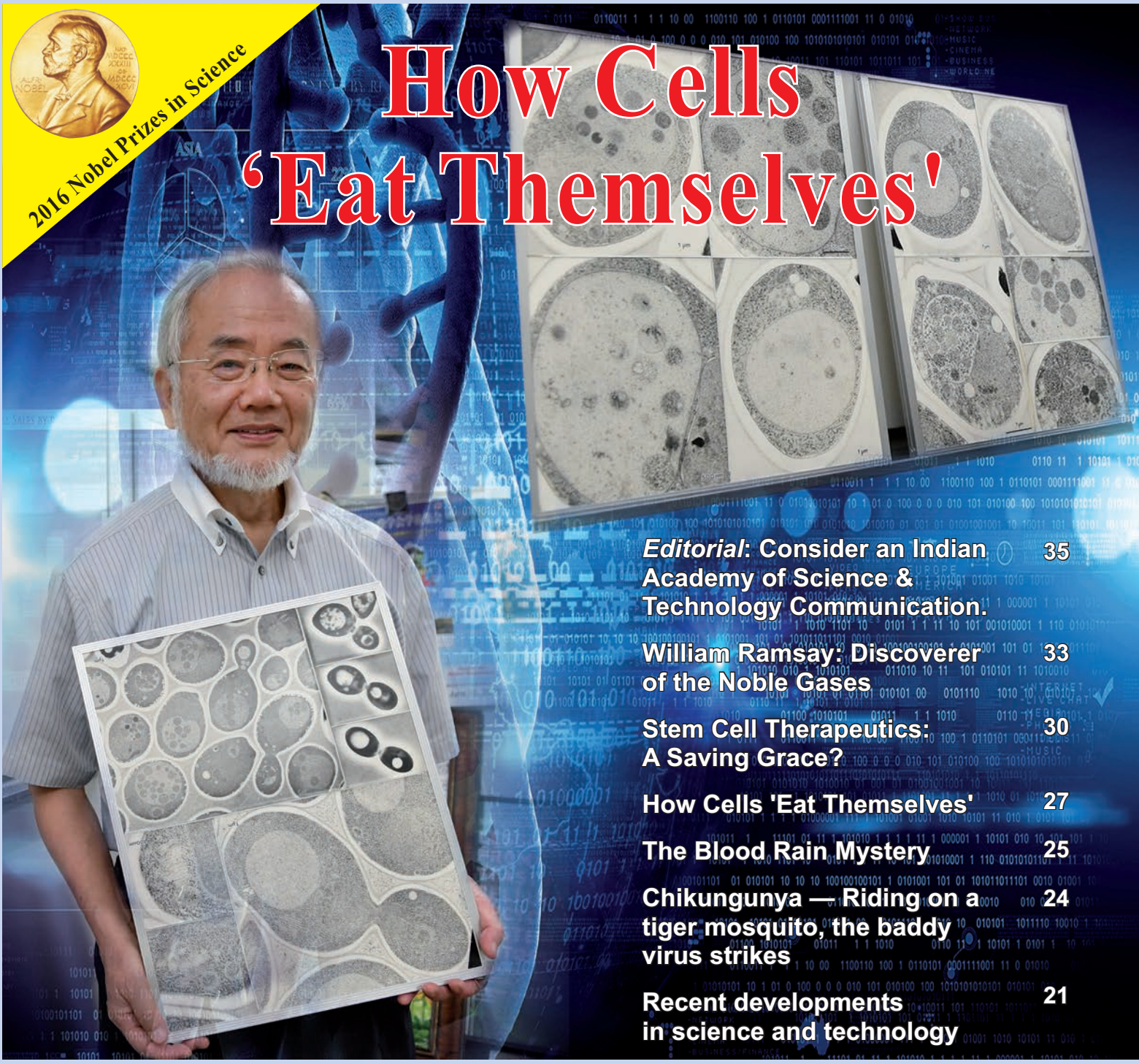




... think scientifically, act scientifically... think scientifically, act scientifically... think scientifically, act...

# Consider an Indian Academy of Science & Technology Communication (IASTC)

Dr. R. Gopichandran

The call for focussed science communication was clear in Article 51 A (h) of our Constitution. National policies on science, technology and innovation also reinforce this call. The Department of Science & Technology, Government of India responded to this call through the activities of its National Council for Science & Technology Communication. DST's autonomous organisation Vigyan Prasar, CSIR's National Institute for Science Communication and Allied Information Resources, and Ministry of Culture's National Council for Science Museums have also delivered consistently through mutually reinforcing approaches, aligned with the communication agenda referred above. Education and communication initiatives of various ministries (say energy, education, health, sanitation, environment, agriculture, etc.) too focus on aspects of science and technology relevant for their thrusts.

In the present-day context of development and significantly enhanced public engagement through missions and other public policy interfaces and/programmes it is important to develop and deliver a much greater quantum of outputs and on a wider variety of topics. This can be achieved by consolidating outputs delivered over the decades and insights that guided them. I propose three important pathways and related outcomes for this purpose.

(1) Create a repository/compendium of the large variety of locally adapted knowledge products developed and successfully used across our country. A well-defined framework of science communication including information support and education attributes can embed these as case examples. It will help highlight skills communicators at the local level are endowed with. Opportunities to further strengthen these skills can be part of integrated human and institutional development mechanisms to sustain action at the local level. It is likely many initiatives are hand held by scientists/communication specialists from the stated institutions to enhance local relevance.

- An immediate focus can be on the support provided to formal curricula through non-formal teach and learn augments. It is well-known that a large number of teachers across the country inspire and help learn through their innovative approaches. It is important to document these unique abilities on high priority.
- Several development oriented community initiatives on water, soil, energy, bio resources management and livelihood options have succeeded through well-defined communication. These are as important as the above stated and have to be documented systematically. These are just two of a large number of thrusts.

(2) Create a robust Community of S & T Communicators (COSMOS), supported by an understanding of the specific skills and heuristics responsible for the success of innovative communication approaches and outputs; delivered by members of such a COSMOS. Two related important public policy benefits will emerge from this consolidation.

- Skills at the local level can be harnessed to deliver mission-specific messages in a timely manner.
- These skills can be used to strengthen strategically important bottom-up reality checks on the forms and functions of IEC (information, education and communication) strategies. These are especially important when awareness and information support are forerunners to enable well informed action; especially pertaining to alternatives.

(3) I take note of the invaluable service already provided by the academies of science in our country; in so far as communication is concerned. A predominant feature of such communication initiatives has been networking; followed by knowledge consolidation amongst and within the community of scientists. Importantly the academies have focussed also on the history of science/scientists and achievements even from a policy perspective. Science popularisation, aimed at communication with and for non-science stakeholders including citizens at large has also been on their agenda; albeit on a much smaller scale compared to the former. Understandably and rightly so. This therefore creates an opportunity to

- Ask if it will be useful to create an academy (the IASTC) that will predominantly acknowledge striking efforts, outputs and outcomes of science and technology communication. All media of communication can be considered within this framework.
- Establish a robust platform dedicated to inspire communication in multiple forms and functions aligned with logical frameworks.
- Acknowledge excellence and confer the halo of recognition on a much larger number of grass-root level high end

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achievers. A well-defined impact analysis framework can be developed to guide the process of identifying and acknowledging achievements.

Five additional reasons inspire the proposal for the IASTC.

i. Communication is often seen as a trivial activity. There is huge tendency to mix apples and oranges as it were; while assessing impacts of communication. The apples are about the process and numbers; while the oranges are about the actual impacts of communication expected to emerge as well informed action. Let us not trivialise communication efforts without understanding the importance of enabling circumstances that can transform the intent of compliance into realities of collective good, through learning.

ii. Communicators fall between the stools of subject specific academic excellence and grass-root level action; including packaging and inspired delivery. The latter is by and large seen as far removed from academic rigour. It is actually not so.

iii. Science of science communication and activities that serve the communication agenda are areas as robust as any other intellectual pursuit. Three thrusts of areas are highlighted recently (February this year) in the deliberations of the National Academies of Science, Engineering and Medicine of the USA as part of a research agenda. One need not know rocket science to appreciate the public policy and applications value, the research agenda presents about the field of science communication.

I am inspired also by the insights presented in the publication "Science Culture: where Canada stands" and the indicators related to public understanding of science presented by the National Science Foundation of the USA. My earlier editorials have cited these references systematically.

We need empirical evidences about our country-specific contexts to derive much needed holistic inferences about

- preparedness of stakeholders to receive and imbibe messages/learnings and use tools to sustain flow of messages;
- robustness of circumstances that help transform learnings into well informed action;
- locally adapted knowledge systems that can enrich and enhance outreach benefits; and
- challenges pertaining to all these.

These are essential to create and strengthen theoretical constructs about processes and impacts of science and technology communication; duly adapted to our country's circumstances.

iv. The missions of the Government of India provide excellent opportunities for us to build on the science and technology communication learnings we have gathered over the decades in our country.

v. Most importantly however, communicators too should be clear about the objective of communication they will be engaged in. It is absolutely important to abide only by the agenda of science and its open-endedness. Communicators cannot impose any other agenda; even inadvertently so. After all; success of communication is determined by credibility at all levels; perceived and notional.

The overarching guiding principle for the activities of the proposed IASTC is inclusiveness. Science and technology communication should be given its rightful value and place as a policy tool to help transform policy intents to reality. The IASTC should work in close association with the other academies; not duplicate their efforts; yet add value to their outputs. Inclusiveness is a hallmark of the human value of common good. In this case it twins the values of clarity and precision science brings along. Excellence demonstrated by communication efforts by people in all spheres of communication can be acknowledged. This will only enrich communication efforts.

A comprehensive note on the logical framework for the IASTC will follow this prime mover. The framework will clearly state the:

A. Opportunity to define and fulfil agendas (and unfinished agendas) of communication across missions and all elements of the landscape of science and technology;

B. Specific goals, approaches, tools and indicators of progress along a road map;

C. Immediate, medium and long term benefits through unique functions and synergies

D. Cross cutting benefits for academics, grass root – level activities and policy applications &

E. Benefits of consolidating India's niche in the field of science and technology communication at the regional and global levels too.

Science and technology communication cannot be over-simplified as child centric alone; notwithstanding the need to be ever more precise and inspiring while communicating with leaders of the future. This editorial draws attention to the fact that science communication pervades all levels and spheres of engagement wherein science and technology led development determines quality of life. Let me hasten to add, I am not proposing a woolly all-embracing worldview of communication. This is to only reinforce the fact we need to act at all levels with equal zeal.

I take this opportunity to say I am indeed grateful to Shri Somesh Jhingan, Shri Kapil Tripathi, Shri Nimish Kapoor, Shri Brinder Tyagi, Dr Bharat Bhushan, Shri Manish Mohan Gore and Shri Inderjit Singh for the interest they evinced on the contents of this editorial. They are colleagues in Vigyan Prasar and have been at the forefront of science and technology communication activities; through trials and tribulations.

This editorial is dedicated to all science and technology communicators whose efforts over the decades have created the context for this call. This includes the ones I have referred to above. Our country has provided excellent real life opportunities for highly motivated communicators and continues to provide an expanding array. Bottom up reality checks as defined above will only enhance the value of these efforts and the esteem of this important public policy tool.

Science communication and communicators cannot be trivialized. It is time we realign our efforts for greater visibility and impacts. The IASTC (as and when it comes into existence) will galvanize these efforts further. Fellows and initiatives of the IASTC will have to also upfront state the limits and limitations of one's own understanding of the dynamics of communication and its impacts to avoid self-aggrandisement. This will be the best expression of scientific temper to start with. We will serve the mandate as called for by India's Constitution in this context; ever more emphatically.

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# William Ramsay
## Discoverer of the Noble Gases

**Dr. Subodh Mahanti**
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"It cannot, of course, be stated with absolute certainty that no element can combine with argon; but it appears at least improbable that any compounds will be formed."
The above statement by William Ramsay in 'Gases of the Atmosphere' (1896) held true for over a century until the first argon compound, , argon fluorohydride, was formed in August 2000; but it is stable only below 40 K or -233°C)

"Progress is made by trial and failure; the failures are generally a hundred times more numerous than the successes; yet they are usually left un-chronicled. The reason is that the investigator feels that even though he has failed in achieving an expected result, some other more fortunate experimenter may succeed, and it is unwise to discourage his attempts. "
William Ramsay in 'Radium and its Products', *Harper's Magazine,* December 1904

"Ramsay was awarded the Nobel Prize for chemistry in 1904. He is the only man to have discovered an entire periodic group of elements. He was much liked, and all his best work was done with a co-worker."
*The Cambridge Dictionary of Scientists* (2nd edition), 2002

William Ramsay was one of the world's leading scientists at the end of the nineteenth century. It may be noted that the final decade of the 19th century was a period that witnessed a number of major discoveries in physical and chemical sciences. In 1869, the Russian chemist Dmitri Ivanovich Mendeleeve (1834-1907) had formulated the Periodic Table; in 1895 the German physicist Wilhelm Conrad Rontgen (1845-1923) discovered X-rays; in 1896 the French chemist Antoine Henri Becquerel (1852-1908) discovered radioactivity; and in 1897 and the British physicist Joseph John Thomson (1856-1940) discovered the electron. Ramsay also did spectacular research between 1894 and 1898. He is known for his pioneering work, which established a whole new group in the Periodic Table. In 1894, he along with the British physicist John William Strutt, better known as Lord Rayleigh (1842-1919), announced the discovery of argon (from the Greek meaning 'inert'). In 1895, he isolated helium. Ramsay was the first person to isolate helium by liberating it from the mineral cleveite. Helium was first observed in the spectrum of the Sun during a solar eclipse by Norman Lockyer and Edward Frankland 30 years earlier. Ramsay also demonstrated that the element helium was continually produced during the radioactive decay of radium.

*William Ramsay*

In 1898, Ramsay jointly with the British chemist Morris William Travers (1872-1961) isolated three elements namely neon (from the Greek meaning 'new'), krypton (from the Greek meaning 'hidden'), and xenon (from the Greek meaning 'stranger') from liquefied air. These elements are called inert, rare or noble gases. Ramsay proposed that the five new gases formed a new group of elements in the Periodic Table.

In 1910, Ramsay detected the presence of the last of the noble gases, radon (then called 'niton') in radioactive emissions. Ramsay jointly with the British chemist Frederick Soddy (1877-1956) discovered that helium was produced during the radioactive decay of radium. This discovery was of crucial importance to a modern understanding of nuclear reactions. It was Frederich Ernst Dorn (1848-1916), a German chemist, who had discovered radon in 1900, but Ramsay produced it in sufficient quantities to show that it belonged to same family as the other noble gases.

Ramsay provided the keystone to our understanding of the electronic structure of atoms and the way electrons bind the atoms together into the nucleus. He was awarded the Nobel Prize in Chemistry in 1904 for 'his services in the discovery of the inert gaseous elements in air, and his determination of their place in the periodic system'. He was the first person from Great Britain to receive a Nobel Prize in Chemistry. It may be noted that in the same year Lord Rayleigh, another scientist from Great Britain and who inspired Ramsay to take up the work that led to the discovery of noble gases, got the Nobel Prize in Physics.

All noble gases are very rare except argon, which makes up less than 1% of the air. Although helium is uncommon on

Earth, it is the second most common element (after hydrogen) in the universe. Noble gases except radon (which is radioactive) are used in discharge and fluorescent tubes and for work requiring inert atmosphere. Helium in liquid form is used as a cryogen, an extreme refrigerant. Liquid helium has the lowest boiling point known (–269°C). Noble gases are chemically the most unreactive elements. Their inertness was important in early theories of chemical bonding, which contributed to the 'octet rule' in the theory of chemical bonding. The electronic configuration of helium is $1s^2$ and the configurations of the others terminate in $ns^2np^6$ with all inner shells fully occupied. The elements thus represent the termination of a period and have closed-shell configuration and associated high ionisation energies and lack of chemical reactivity. It was the American chemist Carl Linus Pauling (1901-1904) who first suggested in 1933 that compounds of the noble gases should be possible. In 1962, Neil Bartlett prepared the first noble gas compound, xenon hexafluoroplatinate ($XePtF_6$). Compounds of most of the noble gases have now been prepared.

*Frederick Soddy*

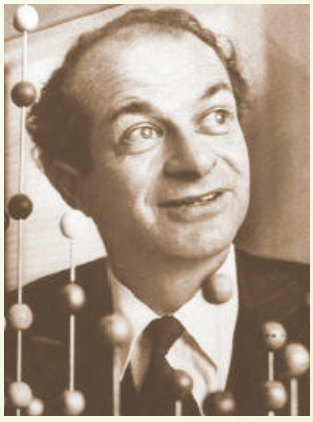
*Lord Rayleigh*

Ramsay's early work was in organic chemistry. He studied physiological action of alkaloids and established their relationship to pyridine, a nitrogen-containing organic compound that closely resembles benzene in chemical structure. Jointly with John Shields he verified Roland Eotvos' law for the constancy of the rate of change of molecular surface energy with temperature.

*Frederich Ernst Dorn*

William Ramsay was born on 2 October 1852 in Glasgow in Scotland. His father, also named William Ramsay, was a civil engineer. His mother was Catherine Ramsay (*nee* Robertson). His paternal grandfather was a chemical manufacturer. He was a nephew of the geologist Andrew Ramsay, who was a Professor of Geology at the University College of London and later became the Director General of the Geological Survey. His maternal grandfather was a physician. Ramsay was proud of his scientific heritage. In his Nobel Lecture he said: "My grandfather on my father's side, William Ramsay, was a chemical manufacturer in Glasgow. He came of a long line of dyers, who carried on their work in Haddington, a small county town in the east of Scotland…My mother's father was a medical man, practising in Edinburgh. He was the author of a series of textbooks for medical students…Hence, I inherited the taste for chemistry from my ancestors on both side of the family."

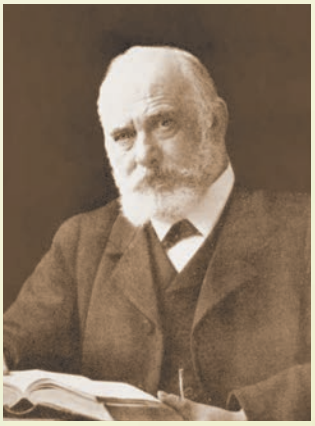
Ramsay completed his secondary education at the Glasgow Academy and in 1866 he entered the University of Glasgow. He developed an interest in chemistry at an early age. At the age of eight while studying in the local preparatory school, he broke a leg playing football and while he was recovering from the injury he was drawn to chemistry. He said: "During my convalescence I read Graham's chemistry, chiefly, I must admit because I wanted to know how to make fireworks. I remember that my father gave small quantities of potassium chlorate, phosphorous, sulphuric acid and some small flasks and beakers and a spirit lamp and with these I amused myself during several months."



*Carl Linus Pauling*

While studying at Glasgow University he worked for some time in the laboratory of the city's analyst Robert Tatlock to gain practical experience in chemistry. He left the Glasgow University in 1870 without taking a degree. His original plan was to work with the famous German chemist Robert Bunsen at the University of Heidelberg. However, he did not stick to his original plan and after six months he started working as a doctoral student in the University of Tubingen under the supervision of the German chemist Rudolf Fittig (1835-1910), particularly known for discovering the pinacol-coupling reaction, a reaction that involves the reductive homo-coupling of a carbonyl compound to provide a symmetrically substituted 1,2 diol. He received his doctoral degree in 1872.

After returning to Scotland in 1872 Ramsay joined the Anderson College in his native town Glasgow as a tutorial assistant in Chemistry Department and after two years he moved to Glasgow University on a similar position. In 1880, he was appointed Principal and Professor of Chemistry at the University College, Bristol. In 1887, Ramsay was appointed as the Chair of Inorganic Chemistry at University College, London. He succeeded the British chemist Alexander William Williamson (1824-1904), who is remembered for what is known as Williamson's synthesis, a method of making ethers by reacting sodium alcoholate with haloalkane. Ramsay remained in this post until retirement in 1913.



*Rudolf Fittig*

After working in organic chemistry for almost a decade (1970-79), Ramsay shifted

his interest to the area of physical chemistry. His contributions in the area of physical chemistry were mostly on stoichiometry and thermodynamics. It was, however, in inorganic chemistry that his most noted discoveries were made.

In 1892, Lord Rayleigh (1842-1919) publicly questioned chemists to explain the difference between the atomic weight of nitrogen found in chemical compounds and the heavier free nitrogen found in the air. Rayleigh had shown that nitrogen isolated from the air was 5% heavier than nitrogen produced chemically. Ramsay took up the challenge to explain the reason. Rayleigh's original view was that synthetic nitrogen was probably contaminated with a lighter gas. He thought this was because of the presence of previously unknown element in the air. To find this out he passed the nitrogen gas over hot magnesium, which slowly absorbed most of the gases (as hot magnesium reacts with nitrogen to form magnesium nitrite) and he was left with a denser, monatomic gas, an inert new element. The gas was later identified as a new element spectroscopically by William Crooks. The discovery of argon was announced by Rayleigh and Ramsay in 1898.

*Robert Bunsen*

Ramsay was the first to write chemistry textbooks based on the periodic classification of elements, namely *A System of Inorganic Chemistry* and *Elementary Systematic Chemistry for the Use of Schools and Colleges* (both the books were published in 1891). Other books written by him include: *The Gases of the Atmosphere* (1896), *Modern Chemistry*, 2 vols. (1900), *Introduction to the Study of Physical Chemistry* (1904), *Essays Biographical and Chemical* (1908), and *Elements and Electrons* (1913).

After his formal retirement from the University College, London Ramsay moved to Buckinghamshire and continued to work in a private laboratory. Upon the outbreak of the First World War in 1914 he made effort to ensure the participation of scientists in the creation of the government science policy. Ramsay was a talented linguist and he loved travelling.

Ramsay acted as an adviser in setting up the Indian Institute of Science in Bengaluru by Jamsetji Nusserwanji Tata (1839-1904), a pioneer in industry and a rare visionary. He reached India on 7 December 1900 for the purpose and spent two-and-a-half months. He visited fourteen educational centres located in different cities of the country namely Mumbai, Pune, Bengaluru, Chennai, Kolkata, Patna, Varanasi, Allahabad, Kanpur, Roorkee, Lucknow, Agra, Delhi, and Vadodara. He also visited some industries. He made a presentation titled "Report on an Institution to be named the Indian Institute of Research." It was Ramsay who had suggested Bengaluru as the most appropriate location for the proposed institute.

Ramsay was elected a Fellow of the Royal Society of London in 1888 and knighted in 1902. He served as the President of the Chemical Society of London (1907-09) and the British Association for the Advancement of Science (1911). He was made KCB (Knight Commander of the Order of Bath) in 1902 and was also Knight of the Prussian Order, 'Pour le merite', Commander of the Crown of Italy and Officer of the Legion d'Honueur of France. He received Davy Medal of the Royal Society of London and Longstaff Medal of the Royal Society Chemistry of London, the Barnardo Medal and a prize of 5,000 US dollars from the Smithsonian Institution, and the A. W. von Hoffmann Gold Medal (Berlin, 1903).

*Morris William Travers*

Ramsay died on 23 July 1916 in Buckinghamshire, England. He was 63 years old. The University of Glasgow created the Ramsay Chair in Chemistry in honour of William Ramsay, who studied and taught at the university. Ramsay Memorial Medal was founded by the University College of London in 1923. A school named after Ramsay (Sir William Ramsay School) was established in Buckinghamshire in 1976. A lunar impact crater has been named after Ramsay.

It is worthwhile to end this brief write-up on Ramsay by quoting him: "The noblest exercise of the mind within doors, and most befitting a person of quality, is study."

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*(This article is a popular presentation of the important points on the life and work of William Ramsay available in the existing literature. The idea is to inspire the younger generation to know more about Ramsay. The author has given the sources consulted for writing this article. However, the sources on the Internet are numerous and so they have not been individually listed. The author is grateful to all those authors whose works have contributed to this article.)*

**Dr. Subodh Mahanti** worked in Vigyan Prasar (1994-2014) and co-ordinated several science popularisation projects. He has written extensively. He writes both in Hindi and English.

# Stem Cell Therapeutics: A Saving Grace?

**Ms. Aisha Saldanha** **Dr. N. K. Joshi**

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Stem cells are the most basic and fundamental cells one can find in a human body. They are unspecialised cells and hence can develop into any kind of cell. This property is due to the fact that the specific genes have not been expressed or activated to perform specific tasks yet. Stem cells occur in many organs and are required for normal organ development and maintenance of its structure and function. Stem cells have two unique attributes: high self-renewal capacity and multi-lineage differentiation potential. The presence of both characteristics in one cell makes them attractive for therapeutic purposes to treat diseases where organ structure and function is lost and needs to be restored.

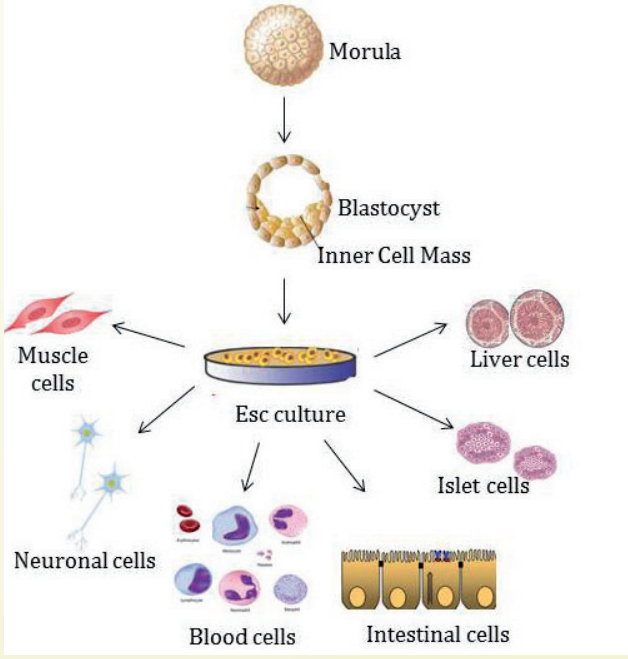
## Stem cells - Whereabouts

There are two types of stem cells depending on their origin – embryonic stem cells (ESCs) and adult stem cells (ASCs). Embryonic stem cells, as the name suggests, come from embryos. They can mature virtually into any cell type in the body as they have not reached the stage of specialisation into specific cells, which leads to the development of foetal organs. They are thus called "totipotent". They can grow rapidly and are therefore very useful in repair of various tissues that are damaged as a consequence of diseases. There are several human clinical trials ongoing using embryonic stem cells merely due to their excellent totipotency.

However, there are ethical considerations related to using embryonic stem cells. First, there is a fear that in order to obtain stem cells, one would have to kill the embryo. Although the ESCs are derived largely from IVF procedures where excess eggs are used, there is yet a big controversy, especially in religions where people believe that embryo is a person or contains a soul. Secondly, making the embryos in a lab ("test-tube babies") is considered unethical and society condemns it, even when science is progressing and the need for these embryos is high. Their beliefs are justified as these embryos would be someone's baby, even if the person didn't care. Even the use of animal embryos is frowned upon.

Additionally, there are other risks associated with using these stem cells. Firstly, embryonic stem cells have a vast growth potential and can divide and grow rapidly. Therefore, they could also develop into tumours or can have adverse effects on the patient. Secondly, there is a chance of their rejection if the existing body cells recognise them as foreign cells. This could happen by the immune system attacking these cells and again, putting the patient in danger.

Fig 1 - Totipotent Embryonic Stem Cells




Adult stem cells, also known as Mesenchymal Stem cells (MSCs) are found in several human organs/body fluids and can be directly obtained from such tissues. They can be derived from umbilical cord blood (CBSCs), bone marrow (BMSCs), adipose tissue (ADMSCs), peripheral blood (PBMSCs), and several other regions. They cannot mature into as diverse cell types as the ESCs and hence called pluripotent or multi-potent.

Some of them are present in small numbers and deep into tissues, therefore not easy to obtain. However, it is now widely recognised that adipose tissue (body tissue containing stored fat that serves as a source of energy) is an abundant source of adult stem cells. The lipoaspirate from liposuction procedures (in which excess fatty tissue is removed from under the skin by suction), which was long considered as a medical waste, is 10 times richer source of stem cells compared to bone marrow. Such ADSCs also show phenotypic and functional similarities to bone marrow derived stem cells BMDSCs. Interest in ADSCs is growing in the scientific and medical community, as evidenced by the ever-growing number of research journal publications and over 100s of clinical trials taking place around the world. Finally, cord blood stem cells come from umbilical cord that attaches the mother to the foetus in the womb. They are easy to obtain but only a limited quantity of cells can be obtained. They also cannot differentiate into any cell possible – usually just blood cells.

Adult stem cells or MSCs are also present in the brain and called neural stem cells. Scientists presume that these cells are responsible for plasticity and tissue regeneration in the brain. They would presumably be helpful in curing degenerative brain diseases. Adult stem cells are relatively safer to use as they come from the recipient's body and have the least chance of rejection.

## Stem cells – *Ex vivo* culturing and expansion

The MSCs may be intended for autologous (the patient's own stem cells are used), syngenic (meaning genetically identical – the cells come from an identical twin or

triplet), or allogeneic use (the stem cells come from a matched donor – even outside the family). Cells are generally characterised using various physical, phenotypic, and functional properties. Large scale *ex vivo* (outside human body) cultivation of MSCs is being extensively researched to meet an objective of low cost, rapid clinical scale expansion to produce quality cells. Once manufactured, they may be administered into patient's blood via intravenous route or other local routes such as intra-articular or intra-parenchymal injection depending on the disease location.

MSC products are currently expensive and need hospital chains for distribution unlike other medicines that are available at pharmacies. Their production needs to be compliant with good manufacturing practice protocols (GMP) to ensure that cell preparations are collected, processed, quality controlled, stored and labelled under controlled environment to ensure a final product with expected quality. All these processes must receive approval and certification from the appropriate national regulatory body such as USFDA (US food and drug administration), EMA (European Medical Agency) or CDSCO (Central Drugs Standard Control Organisation – India)

## Stem cells – Promising therapeutics or mere text book science?

Therapeutic benefits of stem cells are documented in many animal studies and even in human patients. As a result, stem cells seem to be promising and novel treatment options for difficult to treat diseases of bone, heart, brain and cancers. Stem cell therapy is being explored in many medical branches due to their ability to suppress function of various immune cells that get over-activated during inflammatory diseases and due to their ability to regenerate lost tissues or provide the host tissue with growth factors.

One of the most widely known and oldest uses of stem cells is to treat blood cancers. It is known that cancer is a disease caused by the body itself and so to treat this disease, stem cell transplants are used to replace the blood-cell-producing stem cells that are killed during chemotherapy. The cells then regenerate to produce healthy blood cells. This is especially useful to cure lymphoma, leukaemia, and certain myelomas. Globally there are over 150 stem cell trials (therapies still being tested in humans) underway to treat miscellaneous blood cancers. Most are autologous stem cell trials as they are most promising due to the fact that these cells have lowest rejection rate.

Apart from cancer, stem cells are found to be effective in various joint diseases such as osteoarthritis and rheumatoid arthritis where body's defence system attacks body's own tissues. MSCs are shown to correct cartilage defects and rebuild cartilage in animal models and osteoarthritis patients (Dimitris Reissis *et al. Expert Opinion on Biological Therapy* 2016, volume 16(4), p 535-557). Further, stem cells have been extensively used for bone and cartilage tissue engineering research purposes. Other uses are in cardiovascular disease, spinal cord injury and eye diseases. Several stem cell products have been approved for human use in Europe, Canada and New Zealand. Many other products are progressing in clinical trials, with some showing early benefits to patients and likely to be available as marketed therapeutics in near future. Table 1 shows a snapshot of miscellaneous stem cells based products under human clinical trials (Alan Trounson and Courtney McDonald, *Cell Stem Cell*, 2015, volume 17(1), p 11–22). Majority of trials are with allogenic MSCs and happening all around the world with highest activity in US, Europe and China.

**Table 1. Miscellaneous stem cells based products under human clinical trials**

| Total number of ongoing trials | Disease | Human Clinical Development Stage |
|---|---|---|
| **MSC Trials** | | |
| ~315 | Bone / Cartilage / Neuro / Autoimmune/ Diabetes / Kidney / Lung / Liver / Gastrointestinal diseases | Phase I through IV |
| **ESC Trials** | | |
| 8 | macular degeneration / Dystrophy / type I diabetes mellitus/heart failure/Parkinson's disease / spinal cord injury | phase I/II |
| **Neural Stem Cell Trials** | | |
| 6 | Recurrent high grade gliomas/ALS/spinal cord injury/stroke/lower limb ischemia/neuronal ceroid lipofuscinosis/macular degeneration/Pelizaeus-Merzbacher disease / Parkinson's disease | phase I/II |
| **Placental Stem Cell Trials** | | |
| 4 | Chrohn's Disease/Multiple Sclerosis/peripheral artery disease/rheumatoid arthritis/Graft Vs Host Disease/haemorrhagic cystitis/idiopathic pulmonary fibrosis/immune disorders | phase I |

## What are the current challenges with stem cell based therapeutics?

Certain challenges in the path of proving their consistent and robust therapeutic use are inadequate knowledge of the optimal stage of the disease to start treatment. Secondly, the therapy is often given to advanced-stage patients who have no other therapy available and such patients have other disease burdens that often result in clinical ineffectiveness thus masking its true medical potential. There is also no clear cut understanding of the minimal or optimal number of cells to be transplanted. Besides, stem cell therapy will only be useful if the cells can be manufactured at sufficient quantity and quality to treat large numbers of patients.

Long-term safety of stem cell products was also debated considering their survival in patients for several years and possibility of causing uncontrolled tissue growth or tumours or other irreversible side effects. Few recent studies do describe their safety in patients (Daniel Weiss *et al.*, *Chest*, 2013, volume 143, p 1590-98). On the whole,

**Table 2. Institutes offering stem cell courses in India**

| | |
|---|---|
| *Indian Institute of Science* | Bengaluru |
| *National Centre for Biological Science (NCBS)* | Bengaluru |
| *National Centre for Cell Science (NCCS)* | Pune |
| *National Institute for Research in Reproductive Health, Mumbai* | Mumbai |
| *Manipal Institute of Regenerative Medicine (MIRM)* | Bengaluru |
| *Centre for Cellular and Molecular Biology (CCMB)* | Hyderabad |
| *Indian Institute of Technology* | Chennai |
| *National Institute of Nutrition and National Institute of Immunology Centre for Stem Cells Sciences* | Hyderabad |
| *Centre for Stem Cell Research* | Vellore |

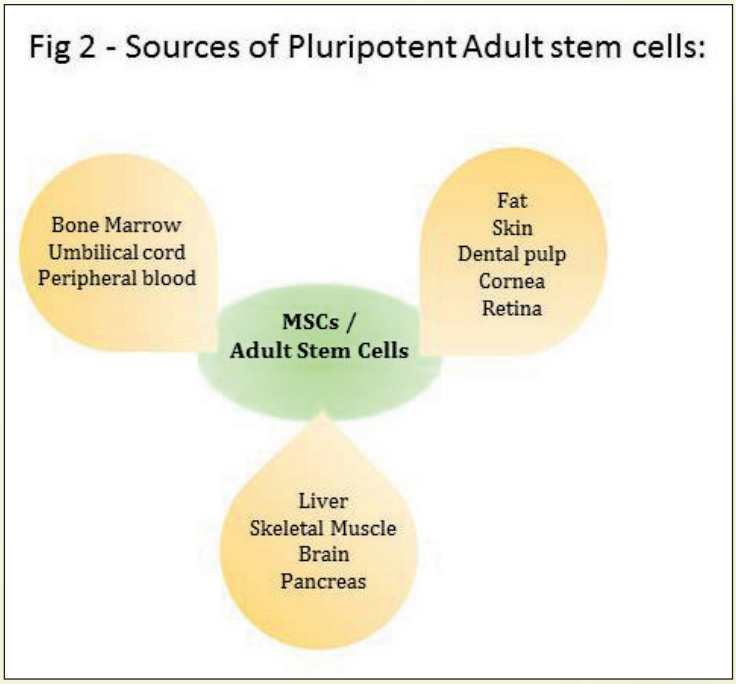
their risks are neither clearly demonstrated nor ruled out.

Despite all these challenges, large number of clinical trials are ongoing currently. As the clinical research continues to evolve and address the challenges, it is likely that MSCs may become valuable therapeutics in clinical practice in the near future to provide potential treatment opportunity for hopeless patients suffering from incurable diseases. Hence, overall, stem cell science, which was a textbook science decades ago, is rapidly evolving into saleable medical commodities.

## Stem cell research and products: Where does India stand?

In India too, stem cell research is popular and pacing up rapidly. Several research institutions and, hospitals are engaged in stem cell-based research. Government of India provides support to conduct basic and translational research, to establish training centres to handle stem cells and facilities in medical schools and few MSc, and PhD programs in stem cells across the country. Some of the institutions that offer stem cell courses in India are listed in Table 2.

The Indian government supports small and large biotech companies through a SBIRI scheme (Small Business Innovative Initiative). Several research institutes and biotech companies are equipped with good manufacturing practices (GMP)-compliant facility for stem cell products and also conduct large scale expansion of MSCs (Sanjay Gottipamula *et al.*, *J Tissue Eng and Reg Medicine,* 2013, volume 10 (2), p 108-19). In 2013, stem cell clinical trials were legalised and brought under regulatory governance. The DCGI (Drugs Controller General of India) /CDSCO have laid down a rule that stem cells therapy cannot be offered directly as a treatment for diseases (except hematopoietic disorders; that is, disorders pertaining to the formation of blood or blood cells), the patient must be part of clinical trials (www.cdsco.nic.in) and all such trials must be listed on the Indian clinical trial registry. All activities related to their usage, i.e., manufacture/isolation/ collection, storage and transplantation into patients must be done only under a license or permission that would be granted by the DCGI/CDSCO. It addresses both autologous and allogeneic stem cell products. Failure to comply with the conditions of this document or using stem cell products without a CDSCO/DCGI license shall lead to penalties as per the provision of the Drugs and Cosmetics Act. The hope is that with these regulations in place now, the patients will not receive treatment under false pretences. Stem cell banking, that was unheard of a few years back, has become popular in the recent past as an alternative to treat genetic or difficult-to-cure diseases. On the whole, the stem cell therapy in India is poised to shape up at a fast speed. In near future, India is expected to be one of the important players in stem cell research and therapy in a non-fraudulent, legal fashion complying with regulatory rules.




## Summary

Stem cells have unlimited potential to help science to find causes of diseases as well as offering solutions to cure diseases. Their high proliferation and immune-modulatory capacity make them promising candidates for future clinical applications in various diseases – importantly the diseases for which there is currently no satisfactory cure. Stem cells offer a unique disease-modifying potential so as to rebuild or regenerate lost tissue structure and function which no other therapeutic platform has achieved so far. In particular, the MSCs show great potential for the replacement of damaged tissues such as bone, cartilage, tendon, and ligament. Stem cell research and medical applications will continue to expand under close cooperation and interaction among scientists, clinicians and pharmaceutical companies. Although it cannot be claimed today that stem cell therapy will be uniformly effective and fool-proof, but it is clearly a saving grace for patients who seem to be benefiting from it.

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# How Cells 'Eat Themselves'

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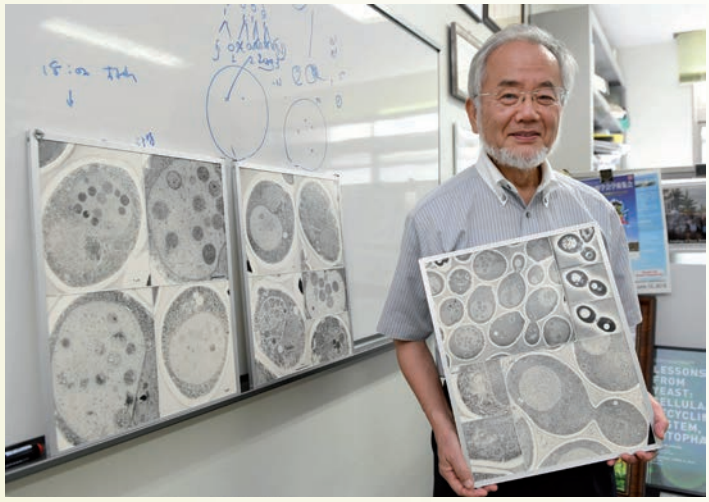
Cells in our body do not live forever, but keep dying and the body recycles the components to make new cells. Autophagy is a normal physiological process that deals with destruction of cells in the body. It works more like a cellular garbage collection and recycling service providing a physiological method for detoxification where the body's cells recycle and remove their internal waste products. It maintains homeostasis or normal functioning by protein degradation and turnover of the destroyed cell organelles for new cell formation. When the body is under stress such as during fasting the process of autophagy speeds up to rapidly provide fuel for energy and building blocks for renewal of cellular components. The concept of autophagy emerged during the 1960s, when researchers first observed that the cell could destroy its own contents by enclosing it in membranes, forming sack-like vesicles that were transported to a recycling compartment, called the lysosome, for degradation.

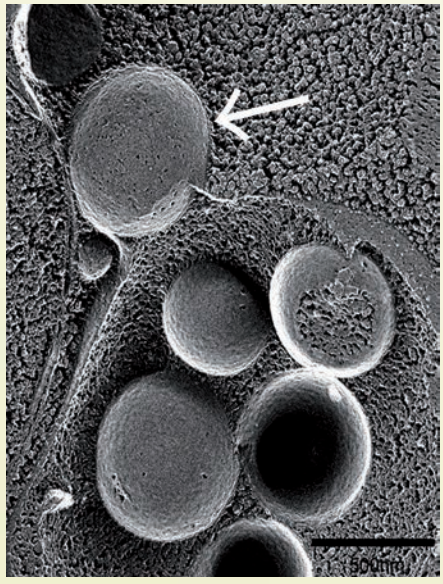


*Yoshinori Ohsumi in his lab*

Although autophagy was recognised in the 1960's, the mechanism and physiological relevance remained poorly understood for decades till Yoshinori Ohsumi of Tokyo Institute of Technology in Japan used baker's yeast to identify genes essential for autophagy. He then went on to elucidate the underlying mechanisms for autophagy in yeast and showed that similar sophisticated machinery is used in human cells to recycle components. The Nobel Prize for 2016 in Physiology or Medicine has been awarded to Oshumi for his discoveries of mechanisms for autophagy.

The story began in the mid-1950s when scientists observed a new specialised cellular compartment, called an organelle, containing enzymes that digest proteins, carbohydrates and lipids. This specialised compartment is referred to as a "lysosome" and functions as a workstation for degradation of cellular constituents.

Soon after the discovery of the lysosome, researchers found that portions of the cytoplasm are sequestered into membranous structures during normal kidney development in the mouse. Similar structures containing a small amount of cytoplasm and mitochondria were observed in cells of rat kidney during hydronephrosis (a condition that typically occurs when the kidney swells due to the failure of normal drainage of urine from the kidney to the bladder). Membrane structures containing degenerating cytoplasm were also present in normal rat liver cells and their abundance increased dramatically following exposure to toxic agents. Recognising that the structures had the capacity to digest parts of the intracellular content, Belgian cytologist and Nobel laureate Christian de Duve coined the term 'autophagy' in 1963. He also extensively discussed this concept in a review article published in 1966 in *Annual Review of Physiology*. It was speculated that autophagy might be a mechanism for coping with metabolic stress in response to starvation and that it might have roles in the pathogenesis of disease.

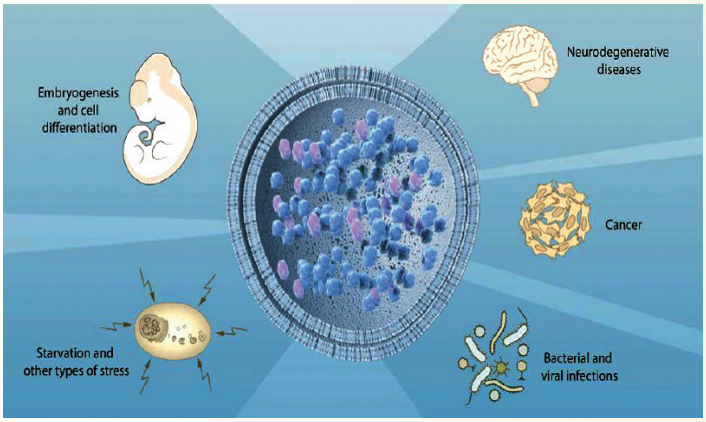


*A microscopic image of a cell shows how proteins in a membrane-bound sack (indicated by arrow) merges with another sack containing enzymes in autophagy (Credit: Yoshinori Ohsumi)*

Despite many indications that autophagy could be an important cellular process, its mechanism and regulation were not understood, probably because only a handful of laboratories were working on the problem. As a result, till 1990's, almost 30 years after de Duve coined the term autophagy, the process remained a biological enigma. It was then that Yoshinori Ohsumi, then an Assistant Professor at Tokyo University, decided to study autophagy using the budding yeast *Saccharomyces cerevisae* as a model system. The first question he addressed was whether autophagy exists in this unicellular organism. Ohsumi had been active in various research areas, but upon starting his own lab in 1988, he focussed his efforts on protein degradation in the '*vacuole*', an organelle that corresponds to the lysosome in human cells. Yeast cells are relatively easy to study and consequently they are often used as a model for human cells. They are particularly useful for the identification of genes that are important in complex cellular pathways.

The yeast vacuole is the functional equivalent of the mammalian lysosome. Ohsumi reasoned that, if autophagy existed in yeast, then inhibition of enzymes found in the vacuoles would lead to the accumulation of engulfed cytoplasmic components in the

vacuole. To test this hypothesis, he developed yeast strains that lacked the vacuolar enzymes proteinase A, proteinase B and carboxy-peptidase. He found that autophagic bodies accumulated in the vacuole when the engineered yeast was grown in nutrient-deprived medium, producing an abnormal vacuole that was visible under a light microscope. Using the mutants, Ohsumi identified as many as 15 genes that are essential for the activation of autophagy in eukaryotic cells. As new autophagy genes were identified in yeast and other species, a unified system of gene nomenclature using the ATG (denoting "autophagy-related") abbreviation was adopted. During the following years, Ohsumi cloned several ATG genes and characterised the function of their protein products.




*Autophagy in health and disease. Autophagy is linked to physiological processes including embryogenesis and cell differentiation, adaptation to starvation and other types of stress, as well as pathological conditions including neurodegenerative diseases, cancer and infections. (Credit: nobelprize.org)*

Ohsumi and colleagues were the first to identify mammalian homologues of the yeast ATG genes, which allowed studies on the function of autophagy in higher eukaryote (organisms with membrane-bound nuclei in cells). The pioneering studies by Ohsumi generated an enormous interest in autophagy. The field has become one of the most intensely studied areas of biomedical research, with a remarkable increase in the number of publications since the early 2000s.

Insights provided by Ohsumi's work have been instrumental in advancing the understanding of autophagy and its involvement in cell physiology and a variety of pathological states. It is now known that the system operates continuously at basal levels. Unlike some enzymes that preferentially degrades short-lived proteins, autophagy removes long-lived proteins and is the only process capable of destroying whole organelles, such as mitochondria, peroxisomes and the endoplasmic reticulum. Thus, autophagy plays an essential role in the maintenance of cellular homeostasis. Autophagy also kills the cells under certain conditions. These are form of programmed cell death (PCD) and are called autophagic cell death. Programmed cell death is commonly termed apoptosis.

The discovery of autophagy genes and the elucidation of the molecular machinery for autophagy by Yoshinori Ohsumi have led to a new paradigm in the understanding of how the cell recycles its contents. It is mainly because of Ohsumi's work that we now know that autophagy controls important physiological functions where cellular components need to be degraded and recycled. Autophagy can rapidly provide fuel for energy and building blocks for renewal of cellular components, which is essential for the cellular response to starvation and other types of stress. After infection, autophagy can eliminate invading intracellular bacteria and viruses. Autophagy enables cells to survive stress from the external environment like nutrient deprivation and also allows them to withstand internal stresses like accumulation of damaged organelles and pathogen or infective organism invasion. Autophagy also contributes to embryo development and cell differentiation. Autophagy is today recognised as a fundamental process in cell physiology with major implications for human health and disease. According to experts, autophagy may one day be central to therapies for longer, healthier living.

Yoshinori Ohsumi was born on 9 February 1945 in Fukuoka, Japan and received a PhD from the University of Tokyo in 1974. He started out in chemistry but decided it was too established a field with few opportunities. So he switched to molecular biology. But his PhD thesis was unimpressive, and he could not find a job. His adviser suggested a postdoctoral position at Rockefeller University in New York, USA, where he was to study *in-vitro* fertilisation in mice. But there he grew very frustrated and switched to studying yeast. He became an associate professor and established his research lab in 1988. There, at age 43, he made the discoveries that won him this year's Nobel.

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# The Blood Rain Mystery

**Felix Bast**
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Blood rain is a weird, but natural, phenomenon in which raindrops appear red, sometimes dark red, resembling the human blood. Spells of this extraordinary phenomenon had been reported since ancient times. Mention of blood rain can be found even in the *Iliad*–an ancient Greek epic set during Trojan war believed to have been authored by Homer around 700 BC. This phenomenon has been reported almost every year from South India – especially from the state of Kerala, and Sri Lanka; with the latest episode reported during December 2013. According to witnesses, rain droplets were so red that the sun-dried white laundry turned dark-red after drenching in the rain.

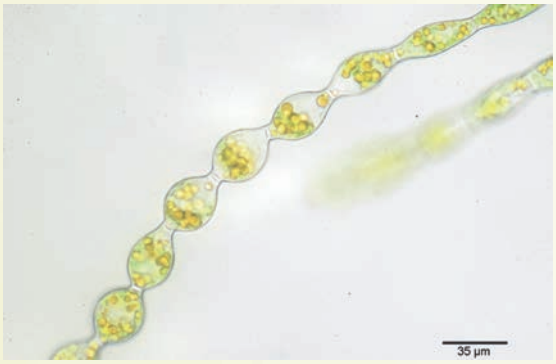


*Fig. 1 Microscopic morphology*

Since then some purported causes for this mysterious phenomenon have been circulating, including divine spell (god and goddesses from the heavens caused it) and alien involvement (extra-terrestrial aliens caused it). For example, an American newspaper *The Huffington Post* reported in 2012 that the blood rain was caused by extraterrestrial life (aliens). Our group at the Central University of Punjab was interested in this phenomenon and decided in 2013 to work on it, using evidence-based scientific methodology. This write-up presents an overview of 'behind the scene' works done by our team that ultimately lead to the resolution of this mystery. First, we needed the sample of blood rain, for which we collaborated with scientists from Kerala, Dr. Nataraja Panikkar and Dr. Jakson Achankunju. Under the optical microscope, it was confirmed that samples contained beautiful beaded-necklace-like organisms, mostly green but sometimes red (Fig 1). It did look like microscopic algae, but we needed a reliable confirmation, so we decided to sequence its DNA.

Deoxyribonucleic Acid (DNA) is a double-helical molecule found in the nucleus of cells in which genetic information is coded in the form of unique letters called nucleotides. For reading the DNA letters or its so-called "sequence", we rely on chemical reactions, followed by an analysis of products of those reactions by spectroscopy. In a typical DNA sequencing, DNA molecules are multiplied by a technique called polymerase chain reaction (PCR) in which enzyme DNA polymerase 'reads' the parent DNA and makes an exact copy of it, the daughter DNA, like a Photostat copy (Fig. 2). This process is repeated 30 or 40 times, each 'cycle' resulting in the doubling of DNA molecules. For example, one molecule to 2 molecules by the end of the 1st cycle; 2 to 4 by the end of the 2nd cycle; and so on. By the end of the 40th cycle, we will have 34 billion molecules, all looking exactly the same. Typically we start not with just one molecule, but millions of it, so you can imagine the number of molecules we get after 40 cycles!

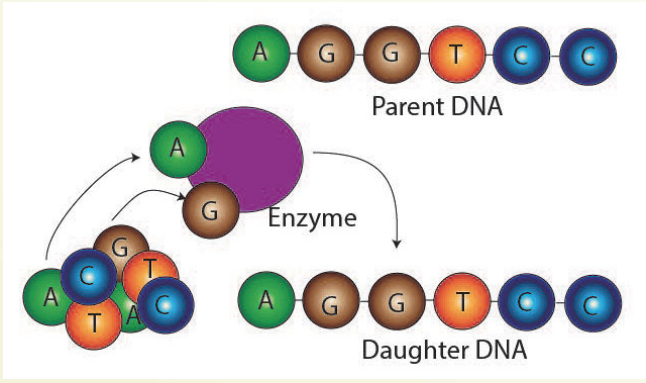


*Fig. 2 Amplification of DNA by DNA Polymerase enzyme (purple) in Polymerase Chain Reaction*

In DNA sequencing, "sequencing PCR" is performed in which normal nucleotides are mixed with fluorescently labelled nucleotides, such that when these fluorescently 'capped' nucleotides incorporate, amplification terminates. This results in products with different lengths, each bearing a cap of four different types, depending on the sequence at particular positions (Fig. 3).

The molecules are then separated by a technique called 'capillary gel electrophoresis' and analysed using spectroscopy. We used a genome sequencing machine in our lab to sequence a section of the genome of the mysterious organism found in red-coloured rain. The DNA sequence was found to be around 1,000-letters long. To confirm the identity, we made use of a database called GenBank, offered by the Government of USA, and is accessible via the internet free of charge. GenBank informed us that the organism in the blood rain was the microscopic green algae, *Trentepohlia annulata*. Our initial suspicion that it was a microalgae got confirmed, but we were surprised to know about this particular alga, as it had never been reported from the Indian subcontinent earlier. In fact,

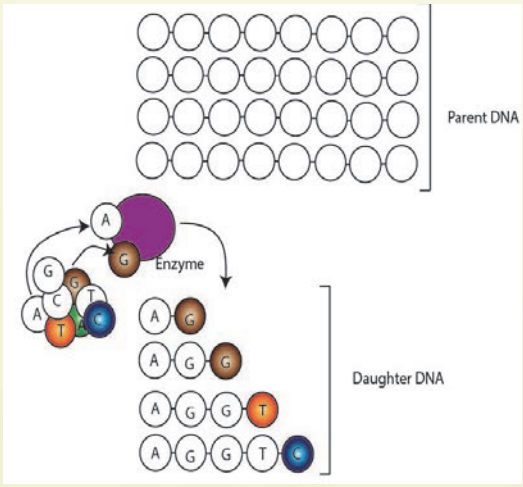


*Fig. 3. DNA sequencing reaction (Sequencing PCR).*

*Continued on page 22*

# Chikungunya — Riding on a tiger mosquito, the baddy virus strikes

**Dr. Yatish Agarwal**
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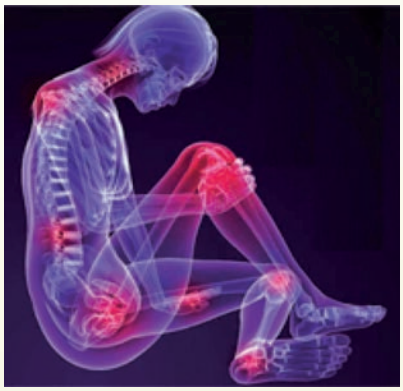
With large parts of the country having suffered a chikungunya outbreak, the waning of the disease has brought a big sigh of relief. Still, the big outbreak has left many people maimed, with painful swollen joints, and shivering at the thought that their loved ones might someday be forced to live the nightmare of the terrible virus which piggybacks the tiger mosquitoes (*Aedes albopictus*) to enter the human system.

## The story behind its name

A mosquito-borne viral disease, which first struck the natives of southern Tanzania in 1952, chikungunya is an illness caused by a RNA virus. It derives its name from the Kimakonde lingo, a tongue spoken by the Makonde, an ethnic group in southeast Tanzania. When translated into English, 'Chikungunya' simply means 'to become contorted', literally describing the temporary bodily disfigurement and the tell-tale incapacitating joint pains associated with the disease.



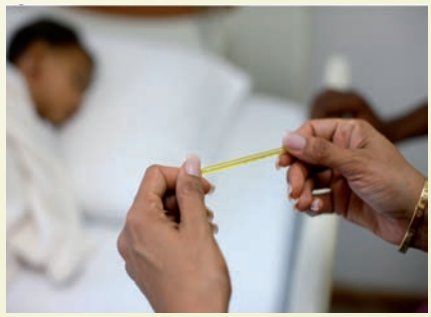
Until the dawn of the present millennium, the human chikungunya infections were mostly limited to small numbers in Africa. The first large outbreak occurred in 1999–2000, affecting the Congolese people. The virus has since spread to many other parts of the world, travelling across man-made geographic boundaries and several continents. Today, its footprints extend over large parts of the world, most of all in Africa, Asia and the Indian subcontinent, but it has also breached into Europe and the Americas.

A major epidemic hit the islands of the Indian Ocean in early 2005. This outbreak peaked in 2006, and the same year, a large outbreak affected India, which ran on till 2007. Several other countries in South-East Asia were also hit. Since these years, India, Indonesia, Maldives, Myanmar and Thailand have reported millions of cases.

The first transmission was reported in Europe in 2007, when a localised outbreak occurred in north-eastern Italy. This established that *Aedes albopictus* mosquitoes could lead to chikungunya outbreaks in Europe. Since late 2013, when France confirmed two home sprung cases in the French part of the Caribbean island of St Martin, some 43 countries and territories in the Americas have suffered local spread of the disease. Till April 2015, close to 1.4 million people in the Caribbean islands, Latin American countries, and the United States of America had likely suffered chikungunya. During the same period, 191 deaths were also attributed to the disease. The United States of America, Canada, and Mexico have also had chikungunya patients who contracted the disease in other countries. Montpellier, a city in southern France, recorded a few cases of locally-acquired chikungunya infection in October 2014, and later the same year, outbreaks occurred in the Pacific islands. The Cook Islands, Marshall Islands, American Samoa, French Polynesia, Kiribati and Samoa continue to suffer outbreaks of chikungunya, but the outbreak that hit a number of states across India this year, was perhaps one of the largest recorded in recent times. The current information with the World Health Organization records the presence of chikungunya virus in over 60 countries in Asia, Africa, Europe and the Americas.

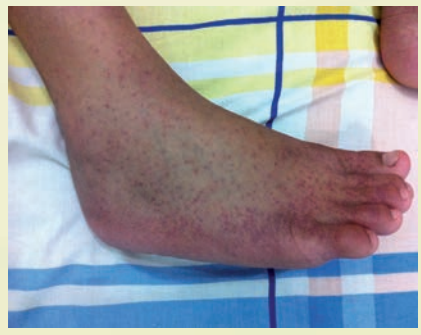
## Signs and symptoms

The majority of people infected with chikungunya virus develop symptoms. Characteristically, the disease presents with a moderate-to-high grade fever (typically temp. higher than 39°C [102°F]), which begins abruptly. The patient may also commonly complain of muscle pain, headache, nausea, and fatigue. These symptoms usually begin 3–7 days after being bitten by an infected mosquito. The fever usually recedes within a week and often, by the third or the fourth day, but the patient may develop joint pains, joint swelling, and a peculiar rash. At this time, clinical laboratory tests may demonstrate low lymphocyte and platelet counts, higher numbers for hepatic enzymes and deranged kidney function.



In some people, the symptoms are so mild that the infection may go unrecognised. The acute symptoms typically resolve within 7–10 days. Most patients recover fully, but in some cases joint swelling and pain may persist for several months, or even years.

Serious complications are uncommon, but newborns exposed during pregnancy, older adults (above 65 years), and people with pre-existing medical conditions such as high blood pressure, diabetes, or heart disease may be at a more serious risk.



The disease may also turn nasty in others. Some patients may suffer from gastrointestinal complaints, while others may rarely develop eye, heart or nervous system related complications. These rare complications include uveitis, retinitis, myocarditis, hepatitis,

nephritis, bullous skin lesions, haemorrhage, meningoencephalitis, myelitis, Guillain-Barré syndrome, and cranial nerve palsies. A few patients may also develop fluid around the lungs (pleural effusion) or in the tummy (ascitis).

Some patients might have relapse of joint and muscle symptoms (e.g., polyarthralgia, polyarthritis, tenosynovitis) in the months following acute illness. Studies report variable proportions of patients with persistent joint pains for months to years.

The good news is: once a person has had chikungunya, he or she is likely to be protected from the disease for all times to come, with the infection lighting up the body's natural defence system.

## Spread of the virus

The chikungunya virus is transmitted from one infected human to another by the bites of infected female Aedes mosquitoes. The proximity of mosquito breeding sites to human habitation, therefore, is a major risk factor.

### *The notorious carriers*

Two species of the Aedes family, namely, *Aedes albopictus* and *Aedes aegypti*, are notorious for transmitting the virus. Incidentally, these very mosquitoes also carry the dengue and Zika virus. Characterised by their black-and-white-striped legs, and small black-and-white-striped body, about 2 to 10-mm in length, the *Aedes albopictus* mosquito looks much like a tiger, and being a native of the tropical and subtropical areas of Southeast Asia is called the Asian tiger mosquito.

While *Aedes aegypti* is confined to the tropics and sub-tropics, *Aedes albopictus* also thrives in temperate and cold temperate regions. In the recent years, *Aedes albopictus* has spread from Asia to find new haven in areas of Africa, Europe and the Americas.

The species *Aedes albopictus* multiplies in a wide range of water-filled breeding sites, including coconut husks, cocoa pods, bamboo stumps, tree holes and rock pools, besides artificial containers such as vehicle tyres and saucers beneath plant pots. This diversity of habitats allows *Aedes albopictus* to survive both in the rural as well as periurban areas and shady city parks.

*Aedes aegypti* is more closely associated with human habitation and uses indoor breeding sites, including flower vases, water storage vessels and concrete water tanks. However, it is not averse to the artificial outdoor habitats that *Aedes albopictus* enjoys.

Besides *Aedes aegypti* and *Aedes albopictus*, several other members of the Aedes family, including *Aedes furcifer*-taylori and *Aedes luteocephalus*, also act as carriers of chikungunya in Africa. Curiously, good evidence exists that some animals, including non-primates, rodents, birds and small mammals, may also act as reservoirs of the disease.

### *The biting habits of the mosquito*

The *Aedes aegypti* and *Aedes albopictus* mosquitoes bite throughout the daylight hours, but early mornings and late afternoons are their favourite hunting hours. Both species may bite a person outdoors, but *Aedes aegypti* also readily feeds indoors.

### *The bite to fever time*

Once a person has been bitten by an infected mosquito, and the virus burden is severe enough to cause chikungunya, the illness usually surfaces between the fourth and eighth day of the bite. The bite to fever time, called the incubation period, however, can range from 2 to 12 days.

### *Other modes of transmission*

The chikungunya virus is primarily passed on to humans through the bites of infected *Aedes* mosquitoes. However, during an epidemic, the disease may also be conveyed through other means; for instance, through blood-borne transmission. Cases have occurred among laboratory personnel handling infected blood, a health care worker drawing blood from an infected patient, or a patient receiving contaminated blood at the time of transfusion.

Rare *in utero* transmission has been recognised mostly during the second trimester. During childbirth, when a mother is viraemic (prone to entry of virus particles in the bloodstream) around the time of delivery, the virus may infect the newborn. However, the virus has not been found in breast milk and breast feeding does not lead to chikungunya infection in infants of mothers affected with chikungunya virus.

### *The risky period*

The risk of a person transmitting the virus to a biting mosquito or through blood is highest when the patient is viraemic during the first week of illness.

## The diagnosis

The symptoms of chikungunya are similar to those of dengue and Zika, diseases spread by the same mosquitoes that transmit chikungunya. Your doctor may therefore order specific blood tests to determine the diagnosis.

Several methods can be used. The virus may be isolated from the blood during the first few days of infection. Various reverse transcriptase–polymerase chain reaction (RT–PCR) methods are available, but are of variable sensitivity. Some are suited to clinical diagnosis. RT–PCR products from clinical samples may also be used for genotyping of the virus, allowing comparisons with virus samples from various geographical sources.

Serological tests, such as enzyme-linked immunosorbent assays (ELISA), may confirm the presence of IgM and IgG anti-chikungunya antibodies. IgM antibody levels are highest 3 to 5 weeks after the onset of illness and persist for about 2 months. Samples collected during the first week after the onset of symptoms should be tested by both serological and virological methods (RT-PCR).

## The treatment

### *General rules*

There is no specific antiviral therapy for chikungunya virus infection. The treatment focusses on relieving the symptoms. Get plenty of rest. Drink a lot of fluids to prevent dehydration. Take medicine such as paracetamol or acetaminophen to reduce fever and pain. Do not take aspirin and other non-steroidal anti-inflammatory drugs (NSAIDS) until dengue can be ruled out to reduce the risk of bleeding.

### Joint pains

If you develop persistent joint pain, you may benefit from use of NSAIDs, corticosteroids, or physiotherapy.

### Protect yourself from mosquito bites

If you have chikungunya, prevent mosquito bites for the first week of your illness. During the first week of infection, chikungunya virus can be found in the blood and can be passed from an infected person to a mosquito at the time a mosquito bites. An infected mosquito can then spread the virus to other people.

## The preventive drill

No vaccine or preventive drug is available. The best way to prevent chikungunya virus infection is to avoid mosquito bites.

### Avoid travel

Travellers at increased risk for more severe disease, including travellers with underlying medical conditions and women in their late pregnancy, may consider avoiding travel to geographic areas which prone to a chikungunya outbreak. If travel is unavoidable, adequate protective measures against mosquito bites must be taken.

### Protective clothing and nets

Basic precautions should be taken by people travelling to risk areas and these include use of wearing long sleeves and pants and ensuring rooms are fitted with screens to prevent mosquitoes from entering. For those who sleep during the daytime, particularly young children, or sick or older people, insecticide-treated mosquito nets afford good protection.

### Mosquito repellents, coils and insecticide vaporisers

Repellents can be applied to exposed skin or to clothing. Repellents should contain DEET (N, N-diethyl-3-methylbenzamide), IR3535 (3-[N-acetyl-N-butyl]-aminopropionic acid ethyl ester), or icaridin (1-piperidinecarboxylic acid, 2-(2-hydroxyethyl)-1-methylpropylester). Mosquito coils or other insecticide vaporisers may also reduce indoor biting.

### Community prevention and control

The proximity of mosquito vector breeding sites to human habitation is a significant risk factor for chikungunya. Prevention and control relies heavily on reducing the number of natural and artificial water-filled container habitats that support breeding of the mosquitoes. This requires enlistment of affected communities in effecting adequate steps by all concerned. During outbreaks, insecticides may be sprayed to kill flying mosquitoes, to treat water in containers to kill the immature larvae, and applied to surfaces in and around containers where the mosquitoes land.

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## The Blood Rain Mystery (continued from page 25)

*Trentepohlia annulata* is a European species, reported previously only from Austria.

The next step in our investigation was to compare the microscopic morphology of our isolate with that from Austria, for which we collaborated with Prof. Stocker-Wörgötte and Dr. Christina Hemetner from Salzburg University in Austria. Both of the isolates had similar, indistinguishable morphological features, with exact taxonomically pertinent characters, thereby confirming the identity. Our study sought a scientific explanation for blood rain and confirmed that the blood rain is nothing but a mechanism employed by this alga to disperse its spores (similar to plant seeds) to a very large area, so that it can quickly colonise a large area. The red colour of the algal spores is due to the pigment beta-carotene – the same pigment that gives colour to carrots. *T. annulata* is harmless, and the "blood" rainwater is perfectly potable (suitable for human consumption) even for vegetarians! The study was published in February 2015 issue of the journal *Phylogenetics and Evolutionary Biology* (DOI: 10.4172/2329-9002.1000144)

We used molecular phylogenetics to compare the evolution of our sample with that of *T. annulata* from Austria. Our results suggest that the isolate from Kerala is, in fact, a recently introduced species from Austria. How could an alga come all the way from Austria to India? Our research confirmed the likelihood that the introduction happened through clouds over the ocean – a phenomenon of intercontinental species dispersal previously reported for bacteria and fungi, but first time for algae. Clouds-over-ocean dispersal is analogous to the intercontinental flights; spores of this alga from Europe get transported to India *via* clouds that drift across the Arabian Sea. The spores might have got carried first to the clouds for its dispersal. How exactly these lower stratospheric clouds containing algal spores got to Kerala remains unknown. It might be related to the South-West monsoon, as Kerala is the first state the South-West monsoon strikes. Again, trade winds (SE and NE) converge at a region called Inter-Tropical Convergence Zone (ITCZ), which is located close to Kerala and Sri Lanka, which might be another clue for this puzzle. Our next steps would be the analysis of intercontinental clouds using high-efficiency particulate air filters, using the similar DNA sequence-based technique called "metagenomics", which would reveal the entire microbial diversity of these clouds. Who knows what other kinds of microbes the clouds are being transported! It could, for example, transport potent human or plant pathogens, no one has investigated in these lines yet.

Felix Bast holds a Ph.D. in Molecular Phylogenetics from MEXT, Japan and works as Assistant Professor at the Central University of Punjab. He is a regular writer for Indian popular science magazines including *Resonance* and *Science Reporter* and has published a well-received book on Indian animals, *Creatures of India*.

# Recent Developments in Science and Technology

**Biman Basu**
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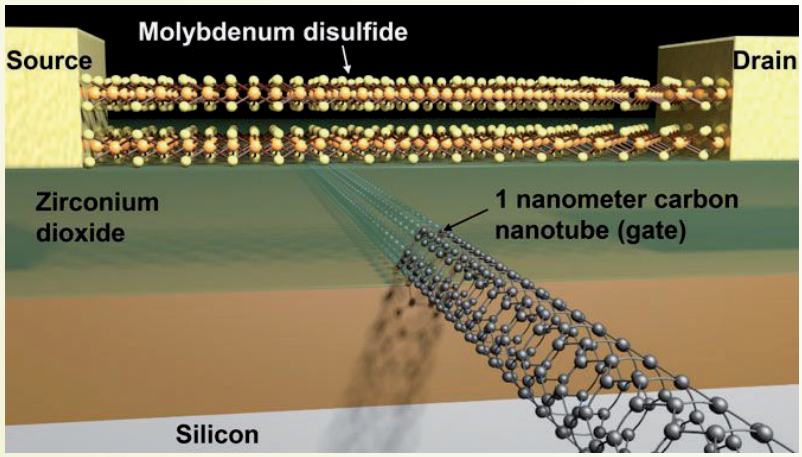
## World's smallest transistor created

A research team at the US Department of Energy's Lawrence Berkeley National Laboratory has created the world's smallest transistor with a working one-nanometre gate. For comparison, a strand of human hair is between 80,000 and 100,000 nanometres thick. The researchers achieved this feat by using a class of semiconductor materials called transition metal dichalcogenides, or TMDs, instead of silicon conventionally used in making chips (*Science*, 7 Oct 2016 | DOI: 10.1126/science.aah4698).

Field-effect transistors consist of three terminals: a source, a drain, and a gate. Current flows from the source to the drain, and that flow is controlled by the gate, which switches on and off in response to the voltage applied. In an integrated circuit (IC), the transistor gate length is the minimum feature size of a transistor on which the flow of current through the junction depends. If the minimum feature size can be reduced, it would mean the transistor gate length can be reduced effectively making the transistor smaller with the same electrical properties. This would allow for lower current flow for the same purpose and lesser heat dissipation.

An integrated circuit is a set of electronic circuits created on one small wafer of silicon, often containing several billion transistors and other electronic components packed in an area the size of a human fingernail. In conventional silicon-based ICs, the minimum gate length hitherto achieved was around 5 nanometres. One reason why 5-nanometre transistors were considered to be the theoretical limit was because, with silicon, if size is reduced further, a phenomenon called quantum 'tunnelling effect' comes into play, making electrons start leaping from one transistor to another and signals going haywire and the circuit breaks down.

The Berkeley researchers, led by Ali Javey, graduate student Sujay B. Desai and their colleagues succeeded in overcoming the size barrier by replacing silicon with a combination of carbon nanotubes and molybdenum disulphide ($MoS_2$), which is sometimes used as an engine lubricant. $MoS_2$ belongs to a family of materials with immense potential for applications in LEDs, lasers, nanoscale transistors, solar cells, and more.




*$MoS_2$ transistor with 1-nanometre carbon nanotube gate. (Credit: Sujay Desai)*

According to the researchers, because electrons flowing through $MoS_2$ face higher resistance, their flow can be controlled with smaller gate lengths. $MoS_2$ can also be scaled down to atomically thin sheets, about 0.65 nanometres thick, with a lower dielectric constant, a measure reflecting the ability of a material to store energy in an electric field. Both of these properties help improve the control of the flow of current inside the transistor when the gate length is reduced to 1 nanometre. In testing, the researchers' prototype device – which combines $MoS_2$ with a 1-nanometre-wide carbon nanotube – showed that the transistor effectively controlled the flow of electrons without being diverted due to tunnelling effect.

According to the researchers, the development could be key to keeping alive Intel co-founder Gordon Moore's prediction that the density of transistors on integrated circuits would double every two years, enabling the increased performance of our laptops, mobile phones, televisions, and other electronics. However, the researchers caution, "It's only a proof of concept. It may take some time to develop large-scale fabrication techniques for commercial manufacture and applications of the new device to become practical."

## Microplastic pollution is devastating our oceans

The harmful impact of plastics on environment is well known. Plastic pollution involves the accumulation of plastic products in the environment that adversely affects wildlife, wildlife habitat, and humans. The

*Toothpaste containing microbeads. Small plastic particles such as these are used in many cosmetic products. (Credit: Georg Mayer/Greenpeace)*

main problem with plastics is that they are non-biodegradable; that is, they are not decomposed easily and remain intact for years (see *Dream 2047*, June 2016). Till recently it was presumed that damage due to plastic waste was limited to only rivers, water bodies, and coastal waters. But now it appears that no environment on Earth has escaped plastic pollution. Recent studies by researchers from the universities of Bristol and Oxford in UK, working on the Royal Research Ship (RRS) *James Cook* at two sites have revealed that plastic waste in the form of microplastics is already threatening deep oceanic life.

Microplastics are defined as small particles that are less than five millimetres long, and include both microfibres and microbeads found in many cosmetic and cleaning products. According to the scientists, microplastics including polyester, nylon and acrylic waste can enter the sea via the washing of clothes made from synthetic fabrics. In studies at two sites in the mid-Atlantic and south-west Indian Ocean, the researchers found plastic microfibres inside a wide range of deep-sea creatures, including hermit crabs, lobsters, and sea cucumbers at depths of 300-1,800 metres (*Scientific Reports*, 30 September 2016 | doi:10.1038/srep33997). The animals were collected using a remotely operated underwater vehicle. The finding marks the first evidence of ingestion of microplastics by animals at such depths. According to Michelle Taylor, lead author of the study, "What's particularly alarming is that these microplastics were found in the deep ocean, thousands of miles away from land-based sources of pollution."

Microplastics are roughly the same size as 'marine snow' – the shower of organic material that falls from upper layers of water to the deep ocean and which many deep-sea creatures feed on. A recent study by scientists of Plymouth University in UK has shown that more than 7,00,000 microscopic fibres could be released into waste water during each use of a domestic washing machine, many of which are likely to pass through sewage treatment and into the environment (*Marine Pollution Bulletin*, September 2016 | DOI: 10.1016/j.marpolbul. 2016.09.025). Their studies showed that plastic waste could find its way deep into the ocean through the faeces of plankton. Studies have shown that laundering an average washing load of 6 kilograms could release an estimated 1,37,951 fibres from polyester-cotton blend fabric, 4,96,030 fibres from polyester and 7,28,789 from acrylic.

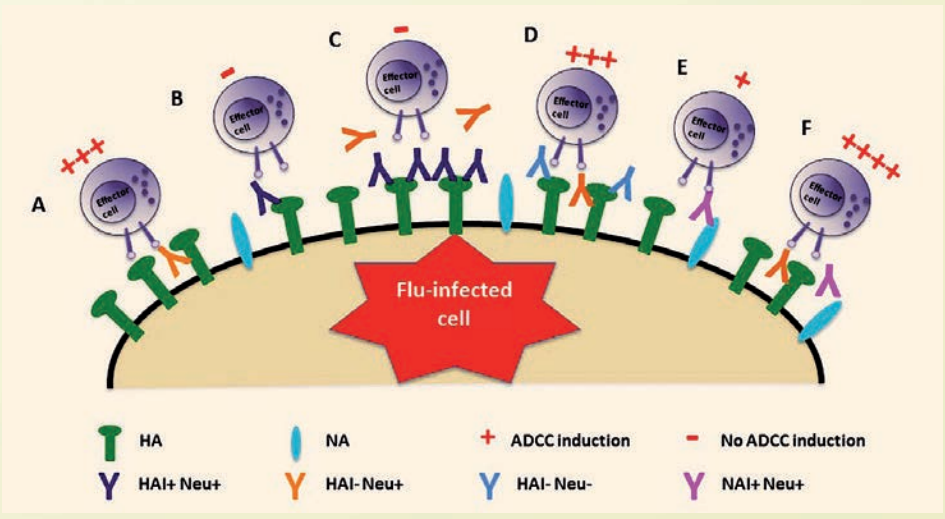
Plastics are enormously beneficial materials, but if marine plastic pollution, especially microplastic pollution in deep sea waters continues to increase, its impact on marine life could be grave. It is important that the accumulation of plastic and microplastic debris in marine habitats is prevented through better waste-handling practices and smarter choices in the materials we use.

The UK Government has recently announced that it would ban plastic microbeads, found in many cosmetic and cleaning products, by the end of 2017. The move followed reports by the House of Commons Environmental Audit Committee about the environmental damage caused by plastics. Late last year US president Barack Obama signed a bill outlawing the sale and distribution of toothpaste and exfoliating or cleansing products containing plastic microbeads. It is time that the Indian Government takes notice of the problem and brings in suitable legislation to counter the growing menace.

## Towards a universal flu vaccine

Influenza, commonly known as flu, is a respiratory illness caused by influenza viruses. The disease is estimated to cause between 3-5 million cases of severe illness worldwide and between 2,50,000-5,00,000 deaths every year, according to the World Health Organisation (WHO). Till recently, the best way to protect against the virus was through flu 'shots', but according to the Centers for Disease Control and Prevention (CDC) n the US, how well a flu vaccine works each year depends on the health and age of the person being vaccinated, the similarity between seasonal vaccine viruses and circulating viruses, and whether a live or inactivated vaccine was used. The main reason for this is that the flu virus often undergoes slight genetic changes during replication, resulting in a virus with different antigenic properties, making the vaccine ineffective. Researchers have been trying to develop a universal flu vaccine that could effectively protect against all flu strains and prevent the occurrence of flu pandemics. An international team of scientists at McMaster University in Canada and two American universities have now moved a step closer to developing an effective, "one-shot" universal flu vaccine to protect against future global pandemics that could kill millions.

Seasonal flu vaccines, which usually protect against three or four influenza virus strains, work by causing antibodies to develop in the body about two weeks after vaccination. These antibodies bind to the virus and prevent it from infecting cells. Universal vaccines work in the same way, but they also involve white blood cells to destroy infected cells. While certain antibodies work together to recruit the helpful white blood cells, other antibodies block their recruitment. The researchers found that where the antibodies bind on the virus




*The universal flu vaccine is designed to produce antibodies that can recognise a part of the virus that remains unchanged each year and hence remains effective for a long time. (Credit: McMaster University)*

makes a significant difference (*Proceedings of the National Academy of Science*, 3 October 2016 | DOI: 10.1073/pnas.1609316113).

The new research was conducted by researchers at McMaster University in Canada, the Icahn School of Medicine at Mount Sinai in New York, and the University of Chicago, USA to build upon their earlier study that uncovered a new class of antibodies capable of neutralising the most dangerous types of influenza viruses. According to the researchers, the newly discovered antibodies can train the immune system to detect a part of the virus that remains unchanged each year, which could pave the way toward a universal flu vaccine that requires one injection with lifelong protective effects. This is because part of the virus is always recognisable – even as the virus changes and mutates – which means that the body can recognise it and safeguard against flu.

According to Matthew Miller, the senior author of the study, while certain antibodies work well together to recruit these helpful white blood cells, others block their recruitment – and where they bind on the virus makes all the difference. "Now that we know the places where antibodies have to bind, we can modify our vaccines so that they generate those antibodies in higher numbers. Using this knowledge, what we can now do is specifically design our universal vaccine to generate the most desirable types of antibodies and avoid antibodies that block the functions that we want. In doing that, we can make sure that the vaccine will work in the most effective way possible," he says.

## The limit to human longevity

How long can a human being live? Till recently scientists did not have any definite answer to this question, although it was known that longevity is linked to the genes and many other factors. People living in certain remote locations on Earth were known live much longer than people elsewhere, but there was no way to determine the limit of human longevity. Now a team of scientists of Albert Einstein College of Medicine, New York, USA have come up with a figure; according to them, "Humans will never get older than 115" (*Nature*, 5 October 2016; DOI: 10.1038/nature19793).

This figure may appear baffling because individuals have been known to live beyond this limit. Jeanne Louise Calment of France is known to be the longest living human

*Jeanne Calment, who lived beyond the age of 122, was the longest lived human on record.*

that has ever lived. Her fully authenticated age was 122 years 164 days when she died on 4 August 1997. There are more than 40 individuals around the world who are known to have lived beyond the age of 115 years. So the question arises: How did the scientists arrive at that figure?

Human life expectancy has steadily increased since the nineteenth century thanks to improvements in public health, nutrition, the environment and other areas. On average, for example, babies born in India today can expect to live nearly until age of 65 years compared with an average life expectancy of only 32 years at the time of independence in 1947. Japan's average life expectancy at birth has risen the most of any country so far – to 83 years. Demographic evidence has shown that old-age mortality has been going down and the maximum age at death has been rising, which may gradually extend human longevity. As a result, since the 1970s, the maximum age to which the oldest people live has been rising. But according to the Albert Einstein College researchers, this upward graph for maximal lifespan has a ceiling – and we may have already touched it.

The study was carried out by Jan Vijg, an expert on aging at Albert Einstein College of Medicine, and his graduate students. Using the Human Mortality Database, which spans 38 countries and is jointly run by US and German demographers, they charted how many people of varying ages were alive in a given year. Then they compared the figures from year to year, in order to calculate how fast the population grew at each age and found that the fastest-growing section of society has been old people. When Vijg and his students looked at data from 40 countries, they found the same overall trend. According to them, the shift toward growth in ever-older populations started slowing in the 1980s and then, about a decade ago, it stopped. According to the researchers, this might have occurred because humans finally have hit an upper limit to their longevity.

To further test this possibility, the researchers analysed the International Database on Longevity, which contains detailed reports on 534 people who have lived to extremely old age. Vijg and his colleagues combed through the data, noting the year that each person in the database died, and charted the greatest age that someone had reached in each year since the 1960s. There finding was revealing. In 1968, the oldest age attained was 111; by the 1990s, that figure had increased to around 115. But then this trend stopped, too. With rare exceptions like Mrs. Calment, no one has lived beyond 115 years.