Notes and News

An Artificial Eye that Mimics the Human Eye

An international team led by Fan Zhiyong and Dr. Gu Leilei and colleagues at the Hong Kong University of Science and Technology (HKUST) has recently developed the world's first 3D artificial eye with capabilities claimed to be better than existing bionic eyes, and in some cases, even exceed those of the human eyes, bringing vision to humanoid robots and new hope to patients with visual impairment.

The key component of any artificial eye is a sensor that detects light falling on it and turns it into electrical signals. Conventional image sensors used in cameras are flat, but this new device is hemispherical in shape, more like the retina of the eye. This makes the artificial eye, described as a 'biomimetic electrochemical eye', more like the natural eye both in look and performance. Its core component is a high-density array of light-sensitive nanowires that serves as the retina. The nanometre-sized photo-sensors were created directly inside the pores of a hemispherical shell of aluminium oxide (Al2O3) by the researchers (Nature, 10 June 2020; DOI:10.1038/s41586-020-2285-x).

Signals from the nanowire photo-sensors are carried by thin, flexible wires made of a liquid metal (gallium-indium alloy) sealed in thin soft rubber tubes to external circuitry for signal processing. These wires mimic the nerve fibres that connect the human eye to the brain. The artificial retina is held in place by a socket made from a silicone polymer, to ensure proper alignment between the wires and nanowires.

To complete the artificial eye, a lens combined with an artificial iris is placed at the front of the device, as in the human eye. The lens and iris combined with the retina at the back forms a spherical chamber (the 'eyeball'). The chamber is filled with an ionic liquid that mimics the vitreous humour – the gel that fills the space between the lens and the retina in the human eye. ❐

Adapted from the article of Biman Basu in Dream 2047, August 2020, Vol. 22 No. 11

Researchers use Supercomputer to Understand Hepatitis B

Hepatitis B is a serious liver infection caused by the hepatitis B virus that is easily preventable by a vaccine.

Recently, researchers at the University of Delaware (UD) in USA, using supercomputing resources and collaborating with scientists at Indiana University, have gained new understanding of the virus that causes hepatitis B and the "spiky ball" that encloses the virus's genetic blueprint.

Computer simulations performed by the UD scientists investigated the effects of a mutation that impairs the assembly process. Their work provides insights into how the capsid – a protein shell that protects the blueprint and also drives the delivery of it to infect a host cell – assembles itself. The Indiana University (IU) researchers had been studying the dimers, which are two-part, T-shaped molecular structures, and investigating whether a mutation could activate or deactivate a switch to turn on the capsid's assembly mechanism. Together the two teams revealed that the region of the protein that contains the mutation, the spike, can communicate with the region of the protein that links with other subunits to assemble the capsid. They found evidence that a change in the shape of the capsid protein switches it into an "on" state for assembly (ACS Chemical Biology, 13 August 2020 | DOI: 10.1021/acschembio.0c00277).

Jodi A. Hadden-Perilla, assistant professor in UD's Department of Chemistry and Biochemistry and a co-author of the ACS Chemical Biology paper, and the team used the National Science Foundation-supported Blue Waters super - computer at the University of Illinois at Urbana-Champaign, the largest supercomputer on any university campus in the world, to perform what are known as 'all-atom molecular dynamics simulations'. Molecular dynamics simulations allow researchers to study the way molecules move in order to learn how they carry out their functions in nature. Computer simulations are the only method that can reveal the motion of molecular systems down to the atomic level and are sometimes referred to as the "computational microscope". The researchers believe that

the capsid is an important target in developing drugs to treat hepatitis B, a life-threatening and incurable infection that afflicts more than 250 million people worldwide. ❐

Adapted from the article of Biman Basu in Dream 2047, October 2020, Vol. 23 No. 1

A Generator That Works Under Light-and-shade

We all know about photovoltaic cells used to generate electricity from sunlight. Researcher Swee Ching Tan and his team at the National University of Singapore (NUS) have now come up with a new device that exploits the contrast between bright spots and shade to create a current that can power small electronics. The greater the contrast between light and dark, the more energy such generators provide.

Tan and his team created the device, called a 'shadow-effect energy generator' (SEG), which utilises the contrast in illumination between lit and shadowed areas to generate electricity. They made the device by placing a super-thin coating of gold on silicon, which is the main material used to make solar cells. As in a solar cell, light shining on silicon energises its electrons, but with the gold layer, the excited electrons jump from the silicon to the gold. With part of the device shaded, the voltage of the illuminated metal increases relative to the dark area and electrons in the generator flow from high to low voltage. Sending the electrons through an external circuit creates a current that can power a gadget (Energy & Environmental Science, 18 February 2020 | DOI:10.1039/D0EE00825G). Using eight SEGs, the team ran an electronic watch in low light. The devices can also serve as sensors. They further explained that while commercially available solar cells can perform the role of this device in an outdoor environment, their energy harvesting efficiency drops significantly under indoor conditions where shadows are persistent.

Interestingly, say the researchers, "When the whole shadow-effect energy generator cell is under illumination or in shadow, the amount of electricity generated is low or none at all. But when a part of the SEG cell is illuminated, a significant electrical output is detected". The researchers also found that the optimum surface area for electricity generation is when half of the SEG cell is illuminated and the other half in shadow, as this gives enough area for charge generation and collection respectively. ❐

Adapted from the article of Biman Basu in Dream 2047, August 2020, Vol. 22 No. 11

Astronomers Unveil the Magnetic Field of the Solar Corona

The Sun's corona is the outermost part of the Sun's atmosphere, which expands into interplanetary space. The solar corona is so faint that it is visible only during a total solar eclipse when the bright solar disc is completely blocked by the Moon. The corona releases streams of energised, charged particles, primarily electrons and protons, flowing outward which is called the solar wind. The solar wind, mostly made of plasma, travels through the solar system at speeds as high as 900 km/s and a temperature of 1 million degrees Celsius.

According to astronomers, the properties of the solar corona arise from the Sun's complex magnetic field, which is produced in the solar interior and extends outward. Graduate student Benjamin Boe at the University of Hawaii Institute for Astronomy (IfA) have now succeeded in measuring the shape of the coronal magnetic field with higher spatial resolution by using data of total solar eclipse observations spanning more than 20 years (The Astrophysical Journal, 3 June2020 | DOI: 10.3847/1538-4357/ab8ae6).

Boe says, "The corona has been observed with total solar eclipses for well over a century, but never before had eclipse images been used to quantify its magnetic field structure." For this study, Boe traced the pattern of the distribution of magnetic field lines in the corona, using an automatic tracing method applied to images of the corona taken during 14 eclipses across the past two decades. This data provided the chance to study the changes in the corona over two 11-year magnetic cycles of the Sun.

According to Boe, during periods of minimum solar activity, the corona's field emanated almost straight out of the Sun near the equator and poles, while it came out at a variety of angles at mid-latitudes. During the solar activity maximum, on the other hand, the coronal magnetic field was far less organised and more radial. ❐

Adapted from the article of Biman Basu in Dream 2047, September 2020, Vol. 22 No. 12

Paradise Lost to Paradise Regained - A Long Haul to Know Many Unknowns of COVID-19

The Webinar entitled 'A voyage across COVID-19 pandemic era - physiological, pathological and

psychological fears and facts' was organized by Department of Physiology and IQAC, Sabang Sajanikanta Mahavidyalaya, Paschim Medinipur, WB on September 21-22, 2020. One of two invited talks in this Webinar was delivered by Dr Syamal Roy, Professor and Dean, National Institute of Pharmaceutical Education and Research, Kolkata and formerly Chief Scientist at CSIR-IICB on the afore-mentioned fascinating topic.

Speaking about story of the poem 'Paradise Lost' in relation to COVID-19 ('C'), Dr Roy said that Coronavirus as Satan (Devil) has pushed our lives in some kind of darkness. On basis of Socratic Paradox, he said that regarding 'C', virtually we don't know anything that we can do something to help to solve this problem. Whether it is 1st wave of infection, or deadlier one is waiting in horizon, we don't know. In movie 'The Seventh Seal', infectious disease epidemic was described that happened worldwide; the pulse of anxiety is very much vivid in our mental landscape. In allegorical story 'The Masque of Red Death' (story of Bubonic plague), it was tried to propose that inevitable and unavoidable thing in world is death. Dr Roy discussed successive waves of extraordinary epidemics *viz.*, Bubonic plague, small pox, tuberculosis (poets Sukanto Bhattacharya, John Keats victims of TB), cholera, yellow fever, influenza, now 'C', that impacted human history and civilization and enveloped in darkness from time to time.We have survived every microbe in epidemics owing to well-developed immune system. With no medicines/vaccines, we are facing giant wave of 'C'and don't have any instrument to combat it.

Infectious diseases caused human morbidity and mortality more than guns and swords. Animal-origin pathogens, responsible for about 70% of human infections, got adapted and grew inside us as we came in close proximity to cows and animal kingdom. Dr Roy discussed about June Almeida, discoverer of 1st human Coronavirus in 1963; SARS-CoV-2 spike protein (sp) having affinity for ACE-2 receptor on lung cell; six RBD amino acids critical for ACE-2 binding in host cell with high affinity; unique amino acid sequence present in human SARS-CoV-2 in USA, China, Japan, Wuhan but not in other Coronaviruses and pangolin may be source of it; pathogenic potential of virus is very similar between Pangolin CoV and SARS-CoV-2; cleavage at S1/S2 site by furin essential for spike-driven viral entry into lung cells; early/non-severe (immune protection) and severe (inflammation damaging) stages of this 'novel pneumonia' infection, conditions of lung alveoli; cytokines responsible for 'C' pathology of lung. 'C' can reach to severe stage in 10% people, who are very much susceptible and Glucocorticoid therapy can take care of hyperinflammatory response. In new research, T-cell compartment showed much importance in protection mechanism.

Exploring 'correlates of protection' (what to see in one's serum), in words of immunologists, is important to design effective vaccines but we have no idea about it in 'C'. We don't know which person will be susceptible and be protected to 'C' infection. Cumulative confirmed 'C' death per million people in different countries during 21/1/'20 - 14/9/'20 was explained. Dr Roy continued his talk with 'How we can regain paradise?' Pharmaceutical companies trying to repurpose drugs, but still no specific drug molecule available to combat 'C'. Greek philosopher Thucydides first recognized importance of immune memory as early as 430 BC and proposed concept of herd immunity; mild infection or vaccination can offer it. In 'C' vaccine development, antigen protein able to offer protection is identified first, should be immunogenic without showing any otherwise symptoms in Ph. I trial. Bringing a molecule to market, believed to be as vaccine, is lengthy process. Ebola vaccine first developed showed protection in animal model, people in Africa died of this infection that time but it was not introduced as Ph. II and III human trials weren't done. Dengue vaccine withdrawn from market after it showed untoward effect.

In trials in mouse system, it is all same for a vaccine but wide variety of effects observed in trials in human population. Dr Roy spoke on basic platforms in developing vaccines against 'C', *viz.*, Oxford University vaccine having Adenovirus expression system and sequence of SARS-CoV-2 sp, RNA vaccine technology of Moderna, inactivated SARS-CoV-2 with adjuvant as in Sinovac, sp as DNA vaccine. Pipeline of 'C' vaccine candidates by technology platform, stage of development in exploratory projects and those crossed Ph. I trial, was discussed. Dr Roy said we are trying to develop vaccine and defensive mechanisms against 'C', repurpose drugs with different combinations, as if carrying a rock towards the top of steep hill. Our efforts are monumental, like Sisyphus performing upward task - some day we will succeed. Problem is pathogens have certain antigenic variations, same in amino acid (antigenic) sequences in SARS-CoV-2, it can escape our immune system *via* mutation. Humans evolved defense against limitless pathogens, but not against all as pathogens have their own evolutionary agendas. Despite this pandemic, Dr Roy expressed about seeing hope somewhere.

Highlighting on painting 'Daddy Longlegs in the Evening' (symbol of hope) of artist S. Dali, Dr Roy finally mentioned that public health burden increases as new virus

like SARS-CoV-2 arrives, but opportunity arises for new research, new vaccines and treatments, for new knowledge. We didn't knew how 'C' attacks us, research is conducted worldwide to gain new information. Immunologists should probably develop molecules, ideas, mechanisms, vaccines, all new, to control and combat it. Dr S. Roy's ways of presentation and lucid explanations were enriching, capturing careful attention of listeners. In similar manner, he spoke about scientific journey and taking a road in context with Robert Frost's poem, opportunity to explore more in nature, creativity in science, randomness in mind and source of creativity, Double Helix and Darwinian Natural Selection as paradigm in science, strengthening application-oriented biology in his inaugural address in National Seminar on 'Trends in modern biology: techniques and applications' on 23/3/2019 at Zoology Department, Visva-Bharati. ❐

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Biomolecules from Marine Finfish and Shellfish Waste

A two-days' National-level Online Workshop on 'Tools and Techniques in Biological Research' was organized by Department of Zoology, Vimala College Autonomous, Thrissur, Kerala on October 6-7, 2020. In it, as one of three invited speakers, Dr Binsi P. K., Sr. Scientist, ICAR-Central Institute of Fisheries Technology, Kochi spoke on 'Marine biomolecules: research directions and future dimensions'. She mentioned that in 100kg of edible finfish, 60-65kg is unutilized that comprise head, frame meat, skin, scales, bone, viscera, gills; but these fish processing discard/wastes or 'zero cost raw material' are sources of protein, minerals (fish head, scale, bone), collagen (scale), poly-unsaturated fatty acid (head), chondroitin (bone), industrial enzymes (viscera) and iron (gills). Nutraceuticals from marine sources are 'a golden goose industry'; biomolecules from marine resources have application in pharma, human nutrition, pets and farm animal nutrition, agriculture - with maximum volume and low price involved in agriculture and less volume and maximum price in pharma.

Dr Binsi discussed about waste generation profile in seafood processing sector; bioactive hydrolysates *viz.*, tuna red meat hydrolysate, tuna discard hydrolysate, bioactive peptides that have prospects in functional food and sports, infant and clinical nutritions. It has growing market, sold @ USD 10-50/kg. Waste hydrolysate showed higher antioxidant properties compared to fish meat hydrolysate. Chocolate-flavoured fish protein hydrolysate (drink mix) is abundant in lysine and glutamine. Collagen (MW: 300kD), convertible to gelatin and collagen hydrolysate (MW: 3kD), has rare amino acids proline, hydroxyproline and used in cosmetics, pharmaceutical industry. Sagging of human skin in old age occurs due to collagen and elastin degradation, collagen can relieve osteoarthritis and osteoporosis. ICAR-CIFT has developed pure collagen peptide from fish scales, no fishy smell, can be mixed with cornflakes as breakfast food. It also goes to nutraceutical industry. Collagen constitutes 20% of fish skin (wet wt.), 30-40% of fish scales and 40-45% of fish bones. Gelatin is made from fish skin and bones.

Fish scales contain collagen, hydroxyapatite (HAP; 40-45%) and moisture. According to Dr Binsi, HAP can be substitute for human bone regeneration/implant. In addition to simulating human bone, HAP is applied in dentistry for dentin fracture, filling of teeth, as enamel cap and is found maximum in fish bones (50-60%). This institute generated HAP from fish scales, calcium capsules (in form of $Ca_3(PO_4)_2/CaHPO_4$, better than $CaCO_3$) for adults and elderly women from scales and fish bones, melanin gel from cuttlefish having anti-inflammatory and UV protective properties.

Fish bone oil can be extracted from big marine finfishes like tuna. Fish oil encapsulated fish oil powder is produced by ICAR-CIFT. Dr Binsi discussed about major steps in chitin and chitin-calcium preparation (demineralization, deproteinization) from shrimp exoskeleton waste, chitin converted to chitosan for industrial use and carboxy-methyl chitosan with chemical modification. ICAR-CIFT developed health products *viz.*, succinyl chitosan-based hydroalcohol hand sanitizers, wound healing gel from chitosan, chitosan soapand toothpaste, chitosan sponge, chitosan 'Chitone' for obesity management. Chitone has high fat-binding property from foods, chitosan aids in fruit ripening and agriculture production. Dr Binsi informed about glucosamine hydrochloride plant set up at ICAR-CIFT, which is formed from crustacean shells by hydrolyzing chitin, used for treating osteoarthritis. Polyunsaturated hydrocarbon squalene, having strong anti-oxidative effect, is obtained from deep-sea shark liver. She considered roe of freshwater fishes (major carps) as 'hero' of fish nutrition. ICAR-CIFT developed Fish Caviar substitute from fish roe, nitrogen-rich tonic from fish silage (liquefied whole fish or its non-edible parts), fish silage-based foliar spray facilitating growth of agricultural crops,

which can be added with fertilizer and used.

In the end, DrBinsi highlighted on Pilot Plant facility and Product Development Centre at ICAR-CIFT and emphasized on need of proper infrastructure and cold chain management system for production of fish- and shellfish-based nutraceuticals and other products for human consumption, as animal nutrient and of pharmaceutical importance. ❐

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Promotion of Science in area of Genetic Scissors (CRISPR-Cas9)

The DST PURSE-II programme and ENVIS Biotechnology, Kalyani University, WB jointly with NASI and INSA organized a Webinar 'Promotion of Science in area of Genetic Scissors (CRISPR-Cas9): Nobel Prize (NP) in 2020' on 15/10/2020. Hon'ble VC Dr Sankar Kr. Ghosh expressed need to develop ourselves more in promotion of science. Documentary was shown on 'Clusters of Regularly Interspaced Short Palindromic Repeats: Hallmark of acquired immunity in bacteria'. Bacteria can fight viral infection; lots of them have repeat sequences in chromosome interspaced with sequences derived from viruses. After an infection, pieces of viral DNA sequences allowed to be integrated into CRISPR locus and used later by bacteria to protect itself from same virus infection. CRISPR sequences are transcribed in cell into RNA pieces and used together with Cas (CRISPR-associated) genes-encoded proteins to form interfering complexes; they induce information in form of those RNA to search and base pair with matching sequences in viral DNA. Detected viral DNA in bacterial genome cut off by Cas proteins.

Dr Hemanta Kr. Majumdar, Former Scientist 'G' at CSIR-IICB, Kolkata said Prof. M. N. Saha, founder of NASI, felt about real dearth of knowledge in post-World War India and it has to be propagated to entire nation. INSA was established to educate people, science and technology must reach to mostly the underprivileged. Dr Majumdar used CRISPR-Cas technology for some *Leishmania* sp genes. Speaking on genetic/molecular scissors or genome editing, Dr Swapan Kr. Datta, Former DDG (Crop Science), ICAR, New Delhi said that with new discoveries made, we are learning new science and interpreting it differently. In poems, Rabindranath Tagore continuously used 'scissors' to remove a word, insert new word, developed new creation and expression out of his poems and corrections. In today's science of molecular breeding, insertion of targeted gene cassette done in predictable manner to develop a trait. Removing or changing a particular gene (for a desirable trait and improvement), inserting certain DNA pieces, genetic changes occurring, shuffling certain amino acids - aiming for better expression of particular genes. Such techniques have tremendous beneficial application in plants, animals and humans.

Dr Dutta spoke about 'Genome safe harbour' technology. He developed 'Golden rice', three genes driven by endosperm-specific promoter (gene cassette) inserted in rice, it made gene expression and carotenoid pathway (cp) in seed/endosperm. Selectable marker gene could be removed and gene expressing cp introduced. Golden rice can be developed by CRISPR-Cas9 based genome editing (marker-free golden rice); it will accelerate molecular breeding for crop development, make it simpler, precise and more predictive.

Dr Anindya Bandyopadhyay, Vice President, Reliance Industries Ltd (Synthetic Biology-Genome Editing Lab), Mumbai spoke on 'Genetic Scissors (CRISPR-Cas9) Nobel Prize 2020: Science, Application and Future Perspectives'. He discussed about chronology of CRISPR genome editing, observation of special area with repetitive sequences in bacterial genome by Y. Ishino in 1987. During 2012-13, this year's Chemistry NP winners showed these genome editing elements/CRISPR elements could be taken into eppendorf tube, be modified and used back into plant or animal cell for editing/changing particular genome area. While explaining 'Paradigm shift: targeted editing by CRISPR', he said previously gene transfer or modification done in some part of genome, was random, specific area couldn't be targeted. In CRISPR-Cas genome editing, single protein (Cas) fused with designed gRNA targets particular region of genome; gRNA goes to this region and do necessary changes.

CRISPR is bacterial adaptive/memory dependant immune system. Dr Bandyopadhyay stated that people, who ate yoghurt from shops, consumed good amount of CRISPR-Cas9. Cheese producers use bacterial strains for yogurt production and found some bacterial strains resistant to phage viruses, which are used by big yoghurt-producing companies. He explained how bacteria use CRISPR-Cas tool to resist invading virus attack. Class-2 CRISPR system in bacterial world used for genome editing. During repair at double strand break caused by protein-gRNA complex, mutation arises and gene region edited,

its activation stopped. Alternatively at this break region, artificial gene from outside can get in by homology directed repair. In CRISPR-Cas9 modifications, scientists showed gRNA can be changed and attached with fluorescent molecule; facilitating microscopic observation of certain area of genome. With this system, activities like gene repression, activation and knock-out, purification of genomic loci, tagging certain area of genome, imaging genomic loci attaching fluorescent molecule with Cas9, single strand cutting characteristics (Nick), genome-wide screening, are possible. Advances made during 2013-2017 in CRISPR-Cas9 include SNP (replacement of one base), CRISPR-X generating targeted point mutations, Retron RT-mediated CRISPR system, EvolvR Technology for different kinds of mutations, Agrobacterium Vir gene aided HDR in plants, RNA-guided DNA insertions by CRISPR-associated transposes, use of pegRNA instead of gRNA.

Dr Bandyopadhyay elaborated on delivery of CRISPR system into cell in algae, human beings and plants; applications in human disease research, CRISPR-aided drug discovery, gene and cancer therapies (Esophageal cancer PD-1 gene knocked out and cell turned non-cancerous), treatment of fertility, genetic and infectious diseases, in pets and livestock disease prevention, production of healthier fish, faster horse breed, edited mosquito against malaria. CRISPR-based methods of genome editing helped in faster viral disease diagnosis. CRISPR-engineered bacteria (enriched cell lines) developed for pharmaceuticals; yeast, algae, fungi changed so that they produce better; microalgae modified for quality biofuel, pigments, bulk chemicals. Cross-breeding and mutation breeding in agriculture takes 8-10 years but by genome editing, product with novel traits can be developed in 1-2 years and given to farmers in 2-6 years. He also spoke about alignment of CRISPR editing in designer crop product pipeline, regulatory status of CRISPR crops globally and rice with improved drought tolerance developed *via* CRISPR-Cas9.

Dr Amit Ghosh, Former Director, CSIR-IMTECH, Chandigarh shared his thoughts and perceptions on how science is done; how CRISPR-Cas9 technology unfolded; contributions of Lithuanian scientist Virginijus Siksnys (was close contender for NP 2020) in CRISPR-Cas9, Spanish biologist Francisco Mojica (found repeats in halophilic bacteria genome separated by spacers) and Arso Nakuta (found similar sequences in *E. coli*). Dr Ghosh explained that in context of science, distinction exists between 3 terms, *i.e.*, discovery, invention and innovation; spoke about 22-year story of CRISPR unfolded across 12 cities in 9 countries, importance of dedication and intense work in researching a problem in lab. Finally VC Sir said research students worldwide must get some kind of motivation and interest in their research to give some impact to society, must respect science and society. ❐

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Marsquakes Measured for the First Time

Mars is one of the most explored planets of our solar system. Till date, 26 successful missions have been sent to Mars to better understand it. But all the probes sent to Mars till date primarily investigated the surface history of the Red Planet by examining features like canyons, volcanoes, rocks and soil. None of them was designed to explore the inner structure of the planet. However, according to planetary scientists, signatures of the planet's formation can only be found by sensing and studying its "vital signs" far below the surface.

Despite decades of exploration by spacecraft, there still remains a lot about the Red Planet that we don't know. We know it has a core, but scientists are unsure how big it is or what it is made of. Mars is often referred to as a dead planet, but it is actually pretty active. Past missions have shown that it had active volcanoes just 50-100 million years ago, relatively recently in geologic terms, and researchers would like to know more about how they were formed and why they stopped erupting. All this is what NASA's latest Mars probe In Sight, which landed on the planet on 26 November 2018, was designed to find out. InSight, short for 'Interior exploration using Seismic Investigations, Geodesy and Heat Transport', is a Mars lander designed to give the Red Planet its "first thorough check-up since it formed some 4.5 billion years ago". It is the first outer space robotic explorer to study in-depth the "inner space" of Mars – its crust, mantle and core.

The InSight lander deployed its seismometer on the Martian surface on 19 December 2018 and it has just sent back the first reports of seismic activity and ground vibrations on Mars. According to NASA scientists, the Red Planet has a moderate level of seismic activity, intermediate between that of Earth and the Moon. Data from the mission's Seismic Experiment for Interior Structure (SEIS) provided the first direct seismic measurements of the Martian subsurface and upper crust – the rocky outermost layer of the planet (Nature Geoscience, 24 February 2020 | DOI: 10.1038/s41561-020-0544-y).

According to the scientists, the seismic data acquired over 235 Martian days showed 174 seismic events or marsquakes. Of those, 150 were high-frequency events that produce ground shaking similar to that recorded on the Moon by the Apollo program. Further, the data showed that the seismic waves bounce around as they travel through the heterogeneous and fractured Martian crust. The other 24 quakes observed by SEIS were predominantly low-frequency events. "Three showed two distinct wave patterns similar to quakes on Earth caused by the movement of tectonic plates." According to the scientists, "Based on how the different waves propagate through the crust, we can identify geologic layers within the planet and determine the distance and location to the source of the quakes."

In addition, the seismometer provided important information about Martian weather. Low-pressure systems and swirling columns of wind and dust called dust devils lift the ground enough for the seismometer to register a tilt in the ground. High winds flowing across the surface of the ground also create a distinct seismic signature. Combined with data from meteorological instruments, SEIS data help paint a picture of the daily cycles of surface activity near the InSight lander.

"This is the first mission focussed on taking direct geophysical measurements of any planet besides Earth, and it's given us our first real understanding of Mars' interior structure and geological processes," said Nicholas Schmerr, an assistant professor of geology at the University of Maryland (UMD) and a co-author of the study. "These data are helping us understand how the planet works, its rate of seismicity, how active it is and where it's active." ❐

Adapted from the article of Biman Basu in Dream 2047, April 2020, Vol. 22 No. 7

Role of Genetics in Medicine

Department of Zoology, Padmavani Arts and Science College for Women, Salem, Tamil Nadu organized the Webinar entitled 'Role of Genetics in Medicine' on 28/10/2020. Dr R. Sivasamy, Asst. Professor and Head, Molecular Genetics & Cancer Biology Lab, Dept of Human Genetics and Molecular Biology, Bharathiar University, Coimbatore discussed on genetically-associated human diseases, genetic disorders, techniques in genetic disease study and associated aspects.

Dr Sivasamy discussed about different stages of Genetics Research Cycle, *viz.*, patients and families, description of phenotype, identification of underlying genes, characterizing mechanism from cause to phenotype, diagnostics, management and therapy; identification of particular mutation by modern genetics and also physiological changes due to germline mutation or environmental mutation by modern genetic testing; gold standard method in genetic testing in connection with disease diagnosis. He highlighted experimental studies and contributions of renowned geneticists G. Mendel, W. Bateson, T. H. Morgan, F. Griffith, O. Avery, C. Macleod and M. McCarty, A. Hershey and M. Chase, J. D. Watson and F. Crick; explained DNA, genes, nucleotides and 1.8mt length of human DNA when stretched out; hierarchical structure of DNA through to the chromosome. Young listeners/participants in Webinar were informed on 'how genes get mutated'; hereditary and acquired mutations, insertion and deletion mutations, frameshift and repeat expansion mutations. Dr Sivasamy explained Trisomy-13 (Patau's syndrome), -18 (Edwards' syndrome), -21 (Down's syndrome) and the resulting associated bodily, intellectual and mental disorders in babies; Turner's syndrome in females, Klinefelter syndrome; X-linked and Y-linked dominant and recessive inheritance(s); diseases transmitted from mitochondrial inheritance.

He spoke about his studies on mitochondria-linked medicine; described available seven genetic testing approaches, *viz.*, pre-implantation, carrier (for autosomal recessive genes), prenatal (trisomy, monosomy), new born (phenylketonuria, hypothyroidism), diagnostic (breast cancer BRCA-1), predictive and pre-symptomatic (Alzheimers' disease) and forensic (paternity) testings; mutation detection methods; cytogenetics and molecular groups of tests done. Features of molecular cytogenetic techniques; FISH tool in early diagnosis of bladder cancer, melanoma; karyotyping in disease diagnosis; karyotype map of Down's, Turner's and Klinefelter syndrome(s); comparative genomic hybridization to determine DNA copy number changes and alteration of genome in cancer; old and new ways of molecular diagnosis and assessment of genetic make-up of human being; molecular diagnostics for known mutations; PCR in diagnosis of meningococcal and other diseases; possible testing of multiple mutations by DNA microarray technique; Sanger's and Max Gilbert's DNA sequencing techniques for analysis of genes at nucleotide level; multiplex ligation-dependant probe amplification for detecting exon deletions; single strand conformational polymorphism for diagnosing unknown mutations; use of denaturing gradient gel electrophoresis; heteroduplex analysis; RFLP to detect mutation at

restriction sites; Next Generation Sequencing (to detect infantile mitochondrial disease) helping genome sequencing projects to complete in few days and obtain qualitative and quantitative sequence data; whole exome, whole genome and transcriptome sequencing techniques - all of these techniques and their application in human disease diagnosis (detecting disorders, defects and others in human system) were explained individually by Dr Sivasamy with support of published research papers in journals on each technique.

He finally spoke about close association of genomics and proteomics in disease diagnosis field, and that understanding genetic basis of human diseases and identifying disease association genes & their products will facilitate us to know about their functions, and will pave way towards effective diagnostic, therapeutic and preventive measures. ❐

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Inside Story of Making Medicines

The International Webinar entitled 'From Bench to Bedside: The Inside Story of How Medicines are Made' was organized by Department of Microbiology and Biochemistry, St. Berchmans College (Autonomous), Dist. Kottayam, Kerala on 7/11/2020. In this programme, Dr Robin Mathew, Global Clinical Strategy Lead, Johnson and Johnson Inc., USA spoke on the subject. While elaborating on drug discovery 'From the cell to the pill: how do we design molecules against cell targets' and differentiating between naturals and synthetic, Dr Mathew mentioned that people want to go for natural alternatives instead of conceiving chemicals, but in fact all of the lots of chemical molecules (medicines) isolated come from plants and implicated in different diseases. Over 28,000 medicines are derived from plants, that include the important drug Paclitaxel that treats cancer. Plants like foxglove (for medicine Digoxin), willow (wonder drug Aspirin), poppy (for Morphine), mayapple (cancer drug Etopside) play important roles in drug discovery. Everything in this universe is a chemical in some fashion and details about the plant and the molecules it consist must be known.

Dr Mathew explained steps in succession for preparing medicines from plants (ethnobotanical information and historic texts, botanical identification, preparation of extracts, biological assays, bioassay-guided fractionation, active compound identification from crude drug extract, medicinal chemistry QSAR and modification of functional groups, toxicology and pharmacology, ADME and formulation, clinical studies); important processes to get valuable pure compounds (liquid-liquid partitions from complex extract, flash chromatography, analytical chemistry, preparative chromatography, mass spectrometry, NMR, X-ray crystallography, structure identification); highlighted Taxol (microtubule binding drug) from tree *Taxus brevifolia* or Pacific Yew) as most important medicine for cancer therapy; described means to improve function of the molecule manipulating groups/subgroups in its 3D structure; Taxol QSAR and functional groups playing important roles in its activity; explained steps of isolation, purification, functional and structural characterization of some of plant-derived medicinal compounds.

While speaking on means of designing more powerful medications on topic 'Playing around with pain: how to make drugs safer', Dr Mathew spoke about QSAR optimizations to reduce hepatotoxicity of Acetaminophen (in pain medication Tylenol); making slight modification in its structure to eliminate liver toxicity. Hindered rotation of rings in isomeric forms in compound Acetaminophen, referred as Atropisomeric forms, have been developed as improved drug for pain relief. He also spoke about manipulating pain sensing Nav1.7 gene in humans by using certain Atropisomerics; introduction of isomerism in Acetaminophen in specific disease condition; cost of drug development worldwide during 2009-2018 in different types of diseases (oncology, ailment, nervous system, anti-infectives, dermatologics); various steps that we go through in developing a drug for humans (disease pathology, identifying molecular mechanisms, synthesis/purification of target compounds, efficacy determination *in vitro*, preclinical *in vivo*, first-in-human trial *in vivo*, Phase I, II and III *in vivo*, Phase IV post-marketing); drug regulatory agencies in different countries; number of drugs that starts with Phase I actually comes to market and that only 3.4% of cancer drugs that goes into Phase I eventually gets approved; briefly spoke about examples of drugs, despite showing safety and efficacy in all Phase trials, can still have problems and had to be withdrawn during 2001-2005.

Dr Mathew begun his speech describing his scientific conversation with Nobel Laureate (NL) scientist (Physiology/Medicine; 2019) Gregg Semenza back in 2010, who studied clone of erythropoietin gene (EPO), Haemophilia factor VIII and other genetic diseases. Dr Semenza introduced human EPO gene into mice, which

expressed EPO and produced RBCs at times of hypoxia and studied how EPO expression was regulated by Hif-1α protein (oxygen control mechanism). Dr Semenza knocked out Hif-1α in mouse and subsequently embryo found not viable; he concluded that Hif-1α plays important role before and after birth supporting blood flow and oxygen distribution, studied on results when it was turned on and turned off. Dr Mathew in this way explained how a molecule can impact overall health of an individual. Based on the results/findings of Gregg Semenza's research in 1998 and that of same year's NLs William Kaelin and Peter Ratcliffe, renowned companies Daiichi Sankyo-Astra Zeneca and Roche came up with medicines namely Enhertu or modified Trastuzumab in 2019 and Herceptin or Trastuzumab in 1998respectively that changed the landscape of successful cancer treatment.

With the help of Hif-1α story, Dr Mathew nicely explained how a molecule is identified that plays a key factor in creating a disease and molecular tools used to create changes in genome to modulate those pathways. He stated that hypoxia induces expression of Hif-1α, which has to be blocked directly or indirectly for cancer treatment. He cited Hif-1α as an example of a target discovery leading to a drug discovery. Digoxin (potent inhibitor of Hif-1α) medicine also came out of Dr Semenza's research. Speaking about achievements of NL scientists (Chemistry; 2020) Jennifer Doudna and Emmanuelle Charpentier, Dr Mathew explained new ways to edit genome of an animal/plant and development of bacterial system CRISPR-Cas, *i.e.*, genetic scissors, and how introduction of tiny precise mutation in one gene (to precisely manipulate its expression) can convert a black coloured mouse into white, can turn right-handed snail into left-handed (change in orientation/direction of shell coiling) and controlled mutation of controller genes of certain phenotypes. ❐

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New Hope for Millions at Risk from Antibiotic-Resistant Infections

Antibiotics are medicines used to prevent and treat bacterial infections. But if misused or overused, antibiotics often become ineffective against bacteria that become resistant to them. When antibiotic-resistant bacteria infect humans and animals, the infections they cause are harder to treat than those caused by non-resistant bacteria. Thus, antibiotic resistance leads to higher medical costs, prolonged hospital stays, and increased mortality.

Today, antibiotic resistance has beco - me one of the biggest threats to global health, food security, and development. A growing number of infections – such as pneumonia, tuberculosis, gonorrhoea, and salmonellosis – are becoming harder to treat as the antibiotics used to treat them become less effective. The good news is, researchers of the University of Queensland in Australia have discovered how bacteria share antibiotic-resistance genes and looking for ways to prevent the sharing, thereby bringing new hope for more than 700,000 people who die each year from antibiotic resistant infections.

Professor Mark Schembri of the University of Queensland says, "The diminishing pool of effective antibiotics makes these infections a major threat to human health, so it's critical we understand the exact mechanics of how antibiotic resistance spreads between different bacteria." According to him, antibiotic resistant-bacteria, in particular emerging 'superbugs', could lead to around 10 million deaths globally by 2050.

In this study, the researchers examined plasmids – self-replicating DNA molecules – which are one of the major drivers for the rapid spread of antibiotic resistance genes between bacteria. They used a powerful genetic screening system to identify all of the components required for the transfer of an important type of antibiotic resistance plasmid from one bacterial cell to another. According to Professor Schembri, many plasmids carry 10 to 15 antibiotic resistance-causing genes, and when they transfer from one bacterial cell to another, two important things happen. Firstly, the plasmid is copied so that it is retained by both the donor and recipient cell, and secondly all antibiotic resistance genes are transferred together, meaning that resistance to multiple antibiotics can be transferred and acquired simultaneously.

The researchers claimed to have discovered genes encoding the 'syringe' component – the mechanism through which plasmid DNA is mobilised, as well as a novel controlling element essential for regulation of the transfer process. They also investigated the crystal structure of this controlling element and revealed how it binds to DNA and activates transcription of other genes involved in the transfer. ❐

Adapted from the article of Biman Basu in Dream 2047, October 2020, Vol. 23 No. 1