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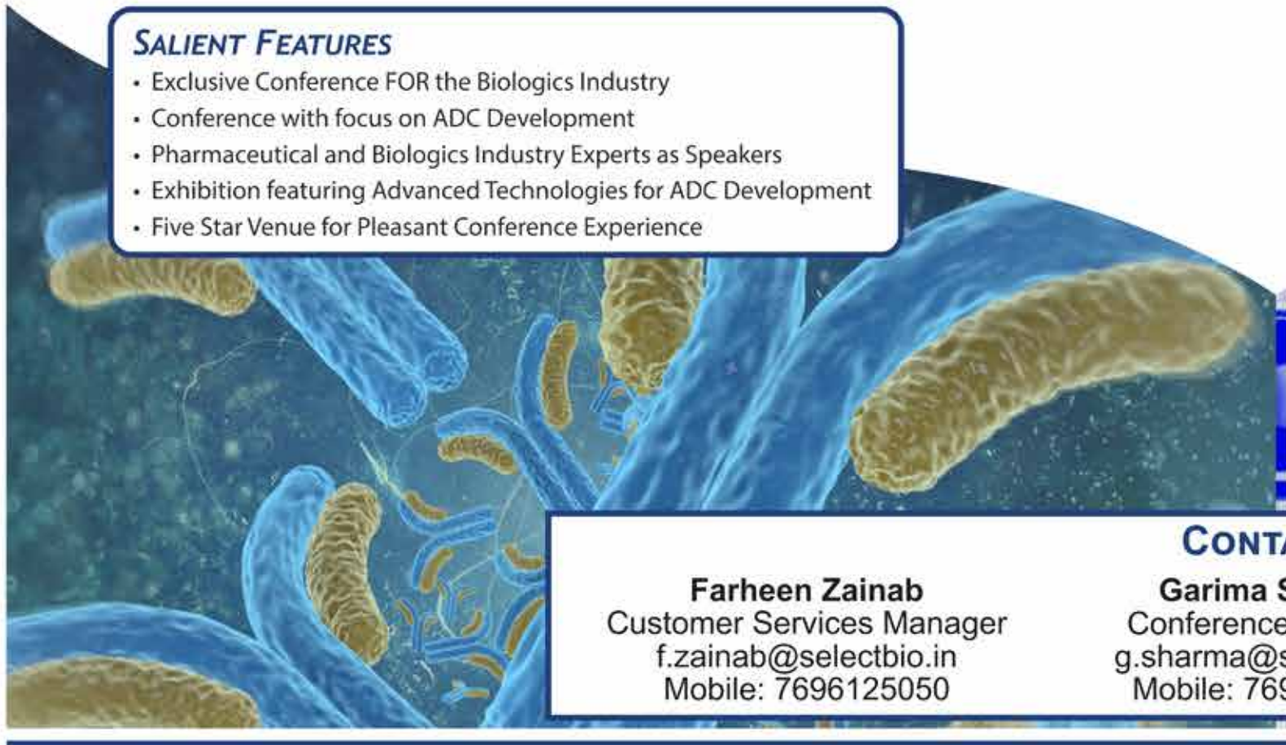

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NOT ALL STEM CELLS ARE CREATED EQUAL!

What is so unique about SanoStem's Stem cells

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Editorial

Stem Cell Drugs and not therapy would be subjected to regulations, according to health ministry India

by Kamal Pratap Singh

The Union health ministry earlier in this month has proposed to amend Drugs and Cosmetics Act that may finally bring stem cells and cell-based products under the ambit of the law. In a notification issued on April 4, the ministry defined the category of stem cells and their derivatives that would be termed a drug, and would thereby have to follow the protocols mandated for any drug development.

Drug Controller General of India S Eswara Reddy said the Union Health Ministry has proposed amendments in the Drugs and Cosmetics Rules, 1945 to regulate the Stem Cell-based drugs. Reddy was speaking at the 4th international conference SCSICON 2018 organised by the Stem Cell Society of India on 28-29th April 2018.

Stem Cell Society of India President Dr Alok Sharma said the cells or tissues taken from the patient's body and merely subjected to cleaning and separation for administering immediately without its manipulation outside the body is termed as 'minimally manipulated stem cells.' On the other hand, the cells or tissues taken out from the body and multiplied or subjected to genetic manipulation in the laboratory and subsequently stored for administering it to the same or another patient are termed 'more than minimally manipulated stem cells.' More than minimally manipulated and substantially manipulated stem cells' would be considered as 'drug' under the amended Drugs and Cosmetics Rule, 1945, whereas 'minimally manipulated stem cells' would form part of the 'stem cell therapy' and fall under the purview of surgeons or clinicians as opposed to 'stem cell drugs' which would be a product or a drug.

The proposed amendments would demarcate 'stem cell- based drugs' from the 'stem cell therapy' and ensure that the physicians using the latest medical technique in treatment is not legally inconvenienced.

The ICMR has objected to amendments to the Drugs and Cosmetics Rules, 1945 on the regulation of stem cells procedures on 9th May i.e. much before the deadline of raising any objection. The amendments seek to exclude certain kinds of processed stem cells, called minimally manipulated stem cells, from being defined as new drugs. Such an exclusion will man that these cells will not have to be tested in clinical trials for efficacy and safety before they receive market approval. If passed, these amendments may legitimise the use of unproven stem cell therapies in India.

The role of the Central Drugs Standard Control Organisation (CDSCO), under the health ministry, will be central in this case. It is the national regulatory body for Indian pharmaceuticals and medical devices, and serves parallel function to the European Medicines Agency of the European Union, the PMDA of Japan, the Food and Drug Administration (FDA) of the United States and the Medicines and Healthcare products Regulatory Agency of the United Kingdom.

Earlier, In a move to curb "rampant malpractice", India has banned commercial use of stem cells "as elements of therapy" and warned of punishments to erring clinicians claiming stem cell cures for diseases through direct-to-consumer marketing. "No stem cell administration to humans is permissible outside the purview of clinical trials," according to the revised National Guidelines for Stem Cell Research, jointly prepared by the Department of Biotechnology (DBT) and the Indian Council of Medical Research (ICMR) and announced on 11 October 2017.

ICMR NOT CONSULTED

- Union health ministry says **stem cells and their derivatives will have to follow the protocols** mandated for any new drug development
- Stem cells and products which are **substantially altered will now need drug regulatory authority's clearance**
- **Doctors welcome move,** say it will curb unethical exploitation of the therapy in India

But any stem cell use in patients, other than that for treating approved blood (hematopoietic) disorders is "investigational at present" and can be conducted only in the form of a clinical trial after obtaining regulatory approvals from Central Drugs Standard Control Organization (CDSCO). Genome modification – including gene editing of stem cells, germ-line stem cells or gamete and human embryos – is restricted only to in vitro studies. Only spare embryos or gametes can be used and genome modified human embryos "should not be cultured beyond 14 days of fertilization".

The existing guidelines prohibit research related to human germ line gene therapy, reproductive cloning, and clinical trials involving "xenogeneic" cells – those derived from different species. "Breeding of animals in which any type of human stem cells have been introduced is prohibited."

According to National Guidelines For Stem Cell Research 2017 , Stem cells and their derivatives fall under definition of 'Drug' as per the Drugs and Cosmetics Act 1940, and are categorized as 'Investigational New Drug (IND)' or 'Investigational New Entity (INE)' when used for clinical application. Hence the principles of bioethics and regulation must be followed accordingly before initiating clinical trials. Adequate safeguards must be in place so that recipients of these cells in clinical trials are fully protected. Societal concerns regarding compensation for research related injuries and unforeseen adverse effects are additional concerns that need to be adequately addressed.

Need of Stem Cell based therapies in India

Stem-cell therapy is the use of stem cells to treat or prevent a disease or condition. Bone marrow transplant is the most widely used stem-cell therapy, but some therapies derived from umbilical cord blood are also in use. Research is underway to develop various sources for stem cells, and to apply stem-cell treatments for neurodegenerative diseases and conditions such as diabetes, heart disease, and other conditions.

With around 26 million births a year, India is set to be one of the largest hubs for the harvest of umbilical cord blood. This lucrative opportunity explains the growing interest of the leading stem cell banking companies in India. Several associated companies, backed by quality foreign investments have set-up shop in the Indian subcontinent. The major driver for stem cell banking in India is undoubtedly government initiatives such as "Make in India". The fact that India is also one of the most sought-after destinations for medical tourism, along with its favorable regulatory environment, have further elevated the country as the next preferred destination for stem cell banking. Furthermore, private players like Lifecell International, cord blood banks like Jeevan Stem Cell Blood Bank, Transcell Biologics Pvt Ltd and public

and private stem cell banking companies like Reliance Life Sciences among few others have completely reinvented this budding industry in India. Thoughtful inserts like EMI payments, make it a lot more easier and practical for prospective clients to access stem cell facilities for a myriad of treatments. It is not sure yet that how amendment will bring benefit to existing players but allowing stem cell therapy will definitely provide an alternative to generic, branded and biotech drugs or may even lower the cost of treatment.

Stem Cells Regulations in other major countries

In the United States, FDA's Center for Biologics Evaluation and Research regulates human cells, tissues, and cellular and tissue-based products intended for implantation, transplantation, infusion or transfer into a human recipient, including hematopoietic stem cells. A National Library of Medicine report says that China has one of the most unrestrictive stem cell policies in the world. In Japan, while the government allows scientists to conduct stem cell research for therapeutic purposes, there are no formal guidelines. South Korea's reputation as a leader in stem cell research suffered a blow in 2006 when it was discovered that the country's leading biomedical researcher, Dr Hwang Woo-suk, falsely claimed that he was the first scientist to clone human embryonic stem cells for the purpose of clinical trials, a Pew Research Centre report stated.

Global Stem cell companies

Sangamo Therapeutics: The company has 12 drug candidates in its pipeline, all involved in different stages of trials and research. Some collaborations in the pipeline are with big pharma companies, including Shire, Bioverativ and Pfizer. In February, Sangamo announced the regulatory agency in the UK granted the company permission to begin a new phase ½ clinical trial for SB-FIX. Also in February, the company announced a new collaboration to develop a next-generation cell therapy for cancer with Kite Pharma, a subsidiary of Gilead.

Athersys: Athersys is a biopharmaceutical focused on its MultiStem programs, which is a stem cell product developed to treat multiple diseases and conditions such as inflammatory bowel disease, congestive heart failure, ischemic stroke and more. The company recently announced a new collaboration intent in March with private Japanese company Healios to expand MultiStem further.

Pluristem Therapeutics: This clinical-stage biotherapy product develops cell therapy to treat inflammation, ischemia, radiation damage and more. Pluristem develops placenta-derived off-the-shelf products. Pluristem produces its cells in a one-of-a-kind 3D bioreactor that resembles the environment of the human body, which can generate the cells on a mass scale.

Cellular Biomedicine Group: This company has its eyes set on China as it hopes to become a leader in the specialty pharmaceutical market for cell therapeutics. Late 2017, Cellular Biomedicine opened a new Shanghai-based joint laboratory and manufacturing facility. Earlier this year, the company additionally announced a new cell therapy manufacturing agreement with GE Healthcare.

Vericel: Vericel bases its treatment in tissue collection from the patient. Its two lead products, Carticel and Epicel, are seeking to treat cartilage defects in the knee and patients with burns greater than or equal to 30 percent of total body surface area respectively. The company initiated a collaboration with the private company Innovative Cellular Therapeutics. Vericel has the intention to use the collaboration to bring its cell therapy products to patients in Asia.

Indian Stem cell companies

In India, stem cell industry still move around stem cell banking, because the guidelines to regulate stem cell based therapies need to be formulated. This has hindered the growth of many stem cell companies of India which are just at the verge of making breakthrough in stem cell based therapies of some major devastating disorders. The companies like –Reliance Life Sciences, Stempeutics, Regrow and APAC Biotech have shown positive results in research for indications such as limb ischemia, Type 1 Diabetes Mellitus, bone and-cartilage defects, Graft Vs Host disease and dendritic vaccines in last few years.

Apart from only stem cell banking, some of the stem cell based medical research companies of India are – AdvanceCells, CelluGen Biotech Pvt. Ltd., International Stem Cell Services Ltd. (iCREST), ReeLabs Pvt. Ltd., Revita Life Sciences, Transcell Biologics Pvt Ltd., Stem Plus Cryopreservation Pvt. Ltd., Stemcyte India Therapeutics (SCITPL) and Stemcell care India. Government of India is also running a stem cell dedicated research lab "inSTEM" through the Department of Biotechnology.

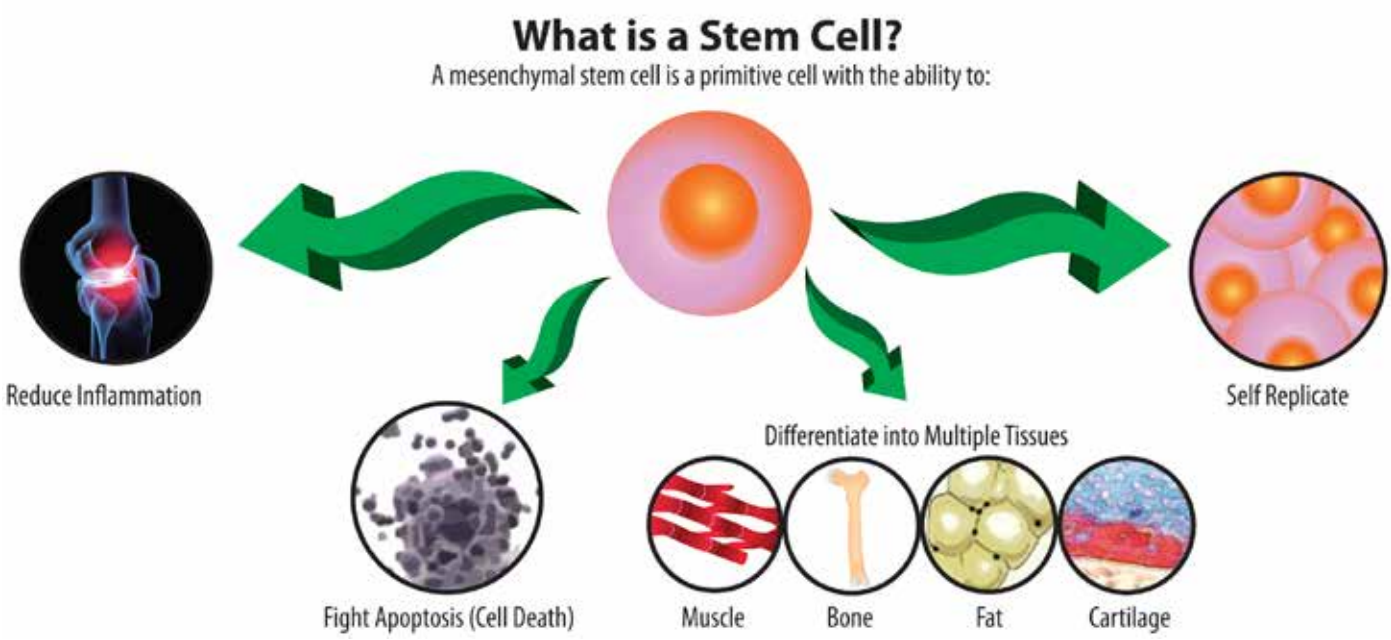
"On hearing news, Transcell Biologics – Stem cell technology investing Company's Founder and Chief Executive Officer S Dravida said, "I am being bullish here as the way NCEs and Biologics are in pipeline and being developed for the treatment of diseases, stem cell based products are the other available options to integrate in managing diseases; sometimes to cure. While there are stand alone cord blood/stem cell banks and regenerative medicine companies, Transcell group of units are built on in-house research spun proprietary stem cell technologies/platforms addressing both drug discovery and therapeutic applications revolving around the story of processing and creating repositories personalizing medicine. Our group has embraced guidelines as regulatory enactment in this space and continue to abide by the rule of the land" .

According to Meghnad G Joshi, CMD Stem Plus Cryopreservation Pvt. Ltd., a DCGI approved cord blood bank in Sangli District of Maharashtra and a R&D company (www.stemplusbiotech.com), "What I think is, in India, this industry should be regulated and at the same time one must also facilitate the newer inventions. India, should promote stem cells as innovative science in medical field. Majority of the time, some niche companies never get exposed and inventions or technologies we develop never gets a chance to come in clinical reality. Researchers, Clinicians and Industrialists should work hand in hand so that some of the technologies can be implemented with sufficient scientific evidence".

Article Invited

Stem cells & their status in India

Source: www.tour2india4health.com



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What are Stem Cells?

Stem cells are cells that have the potential to develop into some or many different cell types in the body, depending on whether they are multipotent or pluripotent. Serving as a sort of repair system, they can theoretically divide without limit to replenish other cells for as long as the person or animal is still alive. When a stem cell divides, each "daughter" cell has the potential to either remain a stem cell or become another type of cell with a more specialized function, such as a muscle cell, a red blood cell, or a brain cell.

What are the Various Classes of Stem Cells?

There are three classes of stem cells i.e totipotent, pluripotent and multipotent (also known as unipotent).
A totipotent cell has potential that is total, meaning that an entire organism can be derived from it. Totipotency is a stem cell's ability to divide and transform itself into any cell required for proper fetal development. Egg fertilization is the starting point of totipotent cells.

A pluripotent cell is derived from a totipotent cell. A pluripotent cell has the capacity to divide and specialize into any of the three main types of body tissue: ectoderm (nervous system and skin tissues), mesoderm (bone, muscle, blood) and endoderm (interior gut lining).

The further specialization of a pluripotent cell results in a multipotent cell, which is a stem cell that is limited in the types of cells it can become. In effect, it becomes too specialized to be used as other bodily tissues.

What are the Different Types of Stem Cells?

Many different terms are used to describe various types of stem cells, often based on where in the body or what stage in development they come from.

Adult Stem Cells or Tissue-specific Stem Cells: Adult stem cells are tissue-specific, meaning they are found in a given tissue in our bodies and generate the mature cell types within that particular tissue or organ. It is not clear whether all organs, such as the heart, contain stem cells. The term 'adult stem cells' is often used very broadly and may include fetal and cord blood stem cells.

Fetal Stem Cells: As their name suggests, fetal stem cells are taken from the fetus. The developing baby is referred to as a fetus from approximately 10 weeks of gestation. Most tissues in a fetus contain stem cells that drive the rapid growth and development of the organs. Like adult stem cells, fetal stem cells are generally tissue-specific, and generate the mature cell types within the particular tissue or organ in which they are found.

Cord Blood Stem Cells: At birth the blood in the umbilical cord is rich in blood-forming stem cells. The applications of cord blood are similar to those of adult bone marrow and are currently used to treat diseases and conditions of the blood or to restore the blood system after treatment for specific cancers. Like the stem cells in adult bone marrow, cord blood stem cells are tissue-specific.

Embryonic Stem Cells: Embryonic stem cells are derived from very early embryos and can in theory give rise to all cell types in the body. While these cells are already helping us to better understand diseases and hold enormous promise for future therapies, there are currently no treatments using embryonic stem cells accepted by the medical community.

Induced Pluripotent Stem Cells (IPS cells): In 2006, scientists discovered how to "reprogram" cells with a specialized function (for example, skin cells) in the laboratory, so that they behave like an embryonic stem cell. These cells, called induced pluripotent cells or IPS cells, are created by inducing the specialized cells to express genes that are normally made in embryonic stem cells and that control how the cell functions.

Where do Stem Cells Come From?

Embryonic stem cells are derived from the inner cell mass of a blastocyst: the fertilized egg, called the zygote, divides and forms two cells; each of these cells divides again, and so on. Soon there is a hollow ball of about 150 cells called the blastocyst that contains two types of cells, the trophoblast and the inner cell mass. Embryonic stem cells are obtained from the inner cell mass.

Stem cells can also be found in small numbers in various tissues in the fetal and adult body. For example, blood stem cells are found in the bone marrow that give rise to all specialized blood cell types. Such tissue-specific stem cells have not yet been identified in all vital organs, and in some tissues like the brain, although stem cells exist, they are not very active, and thus do not readily respond to cell injury or damage.

Stem cells can also be obtained from other sources, for example, the umbilical cord of a newborn baby is a source of blood stem cells. Recently, scientists have also discovered the existence of cells in baby teeth and in amniotic fluid that may also have the potential to form multiple cell types.

What is Stem Cell Therapy?

Stem cell therapy is the use of stem cells to treat certain diseases. Stem cells are obtained from the patient's own blood bone marrow, fat and umbilical cord tissue or blood. They are progenitor cells that lead to creation of new cells and are thus called as generative cells as well.

The biological task of stem cells is to repair and regenerate damaged cells. Stem cell therapy exploits this function by administering these cells systematically and in high concentrations directly into the damaged tissue, where they

advance its self-healing. The process that lies behind this mechanism is largely unknown, but it is assumed that stem cells discharge certain substances which activate the diseased tissue. It is also conceivable that single damaged somatic cells, e.g. single neurocytes in the spinal cord or endothelium cells in vessels, are replaced by stem cells. Most scientists agree that stem cell research has great life-saving potential and could revolutionize the study and treatment of diseases and injuries.

What are the Diseases that can be treated by Stem Cell Therapy?

Stem cell therapy is useful in certain degenerative diseases like –

Cerebral Palsy - spastic, hypertonic and ataxic.
Diabetes Mellitus
Duschene Muscular Dystrophy and other Myopathies
Motor Neuron Diseases
Mental retardation
Alzheimer's
Multiple sclerosis
Transverse myelitis
Hemiplegia (Stroke)
Autism spectrum disorders
Neurological disorders due to hypoxic brain damage.
Brain Hemorrhage and Cerebral -Infarct
Spinal Cord Injury and Paraplegia
Dementia
Post Surgical Neuro-deficit

What is the Procedure of Stem Cell Therapy?

If stem cell therapy is an option, a detailed treatment plan is prepared depending on the type of treatment necessary. Once the patient has consented to the treatment plan, the next step is bone marrow extraction. Please note that this is a minimally invasive surgical procedure, so it is important that patients do not take any blood-thinning medication in the ten days prior to the appointment. It is necessary for each patient to consult their own doctor before discontinuing this type of medication.

The treatment procedure include:

Bone Marrow Extraction: Bone marrow is extracted from the hip bone by the physicians. This procedure normally takes around 30 minutes. First, local anesthetic is administered to the area of skin where the puncture will be made. Then, a thin needle is used to extract around 150-200 ml of bone marrow. The injection of local anesthetic can be slightly painful, but the patient usually does not feel the extraction of bone marrow.

Isolation, Analysis and Concentration of the Stem Cells in the Laboratory: The quality and quantity of the stem cells contained in the collected bone marrow are tested at the laboratory. First, the stem cells are isolated. Then a chromatographical procedure is used to separate them from the red and white blood corpuscles and plasma. The sample is tested under sterile conditions so that the stem cells, which will be administered to the patient, are not contaminated with viruses, bacteria or fungi. Each sample is also tested for the presence of viral markers such as HIV, hepatitis B and C and cytomegalia. The cleaned stem cells are counted and viability checks are made. If there are enough viable stem cells, i.e. more than two million CD34+ cells with over 80 percent viability, the stem cell concentrate is approved for patient administration.

Stem Cell Implantation: The method of stem cell implantation depends on the patient's condition. There are four different ways of administering stem cells:

Intravenous administration:
Administration via catheter using angiography
Direct injection into the target area
Retrobulbar Injection

It is important to understand that while stem cell therapy can help alleviate symptoms in many patients and slow or even reverse degenerative processes, it does not work in all cases. Based on additional information, patient's current health situation and/or unforeseen health risks, the medical staff can always, in the interest of the individual patient, propose another kind of stem cell transplantation or in exceptional situations cancel the treatment.

What are the Side Effects of Stem Cell Therapy?

The side effects of stem cell therapy differ from person to

person. Listed below are the side effects of stem cell therapy;
Risk of mild infection
Anemia
A sore mouth
Difficulty eating and drinking
Feeling tired and exhausted
Infertility

Is Stem Cell Therapy Legal in India?

Recently Govt has proposed to amend the laws regarding Stem Cell treatment. According to the Indian Council of Medical Research, all is considered to be experimental, with the exception of bone marrow transplants. However, the guidelines that were put into place in 2007 are largely non-enforceable. Regardless, stem cell therapy is legalized in India. Umbilical cord and adult stem cell treatment are considered permissible. Embryonic stem cell therapy and research is restricted.

Success Rates of Stem Cell Therapy in India:

There is about a 60% to 80% overall success rate in the use of stem cell therapy in both India and around the world. However, success rates vary depending on the disease being treated, the institute conducting the procedures, and the condition of the patient. In order to receive complete information you will have to contact the medical institutes and ask specific questions concerning the patient's condition.

Cost of Stem Cell Therapy in India:

People across the world are looking to India as a hub for Medical tourism for affordable stem cell therapy. Treatment here costs just 25 % of what it costs In Western countries, besides practically no waiting period for surgery here. The price varies depending upon the implantation method(s) employed.

BOX: Some Major Stem Cell clinics in India

All India Institute of Medical Science (AIIMS)

Fortis Hospital Noida

Apollo Gleneagles Hospital

Apollo Hospital Chennai

Moolchand Medcity

Fortis Vasant Kunj

Indraprastha Apollo Hospital

Advanced Health, Mumbai, India

Rejuvenesse, Mumbai, India

Global Hospitals, Hyderabad

Leader's Talk

Ready to make big changes in Biopharma industry through Stem Cell applications – Dr Subhadra Dravida, Founder, Transcell

There are few companies that can boast of being insightful, cost-effectivein the first year of operations and Transcell is one such. At present, the group comprises of 40+ members including technologists and sales personnel taking in-house research based service and product offerings to the market.

We arranged a talk with CEO of India's pioneer biotech company built on stem cell based technologies at Hyderabad, India. She talks about current govt. regulations and business revenue generation of Stem cell industry. Recently govt. has also decided to frame Stem Cell therapy guidelines with high possibility to bring it in the gamut of healthcare industry.

The purpose of this talk is to share the experience of leaders of this niche biotech business and to help nextgeneration entrepreneurs understand the nuances to take risksand stay motivated.

Image: Dr Subhadra Dravida

Brief profile of Founder of Tanscell – a stem cell based biotech organization

S Dravida, PhD is an experimentalist turned entrepreneur, Founder of Transcell group of biotech companies, www.transcellbio.science, based in Hyderabad, translating adult stem cell technologies prowess into clinical reality.

Transcell is into biobanking, R&D of drug discovery (Oncology & Neuro) and regenerative medicine research (Muscular dystrophies & Periodontal diseases) based on adult stem cell technologies as platforms.

She is a technocrat, successfully running the teams converting evidence based science to business opportunities with an intent to reach the patient communities. It is her chronic optimism; >13 yr of R&D experience from elite institutions of India, US and Canada; unwavering drive to crack the mysteries of cancers and neurodegenerative diseases using stem cells as tools (has patents to her credit) through her venture helping her to stand through the ups and lows of startup disease in India.

It is a long journey and commitment

in sciences that she has embraced while attempting to combine innovation in sciences and commerce to drive through Transcell from India that makes her stand stable in the striving ecosystem.

Outside of her work, she likes to explore monasteries, treck, write her heart out and enjoys reading science fiction. The latest one that she read was Dan Brown's Origin – Where did we come from; Where are we going?

Dr. Dravida is a biologist by education with clinical informatics research experience having associated professionally with the University of North Carolina, USA, Ottawa Health Research Institute, Canada.

Images: Transcell facilities in Hyderabad, India

First of all how you are going to describe your venture - Transcell?

Transcell Biologics (Transcell) is a biotech company, founded on original research driven hypothesis i.e processing adult stem cells for the intended applications. The emphasis was on harvesting, processing and handling the right kind for the requirement.

As a researcher and bench side scientist with my experience in the same domain of translational research, I could distinguish the domains of applications i.e regenerative medicine and drug discovery using stem cells as platforms. So, Transcell true to it's theme of pluripotency and self renewing has built capacities and Intellectual property in Cancers, Neurodegenerative diseases, Muscular dystrophies and Periodontal diseases like indications based on in-house research findings on it's proprietary platform technology (developed for both therapeutic and non-therapeutic applications).

All along, the Company has been creating the wealth of unique repository of India specific donor/patient sourced samples both for private and intended research use.

Images: Transcell facilities in Hyderabad, India

How is Transcell going to bring benefits to the biotech and healthcare industry in India?

We have been in the market, offering biobanking services for personalizing medicine along with some of the cell based products as prototype models to third party researchers in translational research and drug discovery programs. Our group has functional molecules as products in pipeline for Cancers and Neurodegenerative diseases with novel stem cell formulae in pre-clinical stage of development addressing Muscular dystrophies (Orphan disease) and Periodontal diseases.

Is stem cell therapy covered under insurance in India?

No, it is not covered under any insurance scheme. Till date, both research and applications have been treated as experimental in India and there has been no consensus with the regulations as well. So, was the resistance and confusion in the insurance providers' mind.

What are the stem cell therapies approved and what not, and what may be the 'possible' reason(s) for delay in framing regulation in India?

The only stem cell-based products that are approved for use consist of blood-forming stem cells (hematopoietic progenitor cells) derived from cord blood. It is fantastic now in India with clarity given to all the stakeholders on regulating stem cell therapies by DCGI while processed stem cells being categorized as "drugs" that have to go through the cycle of clinical trials like any new chemical entity. For hematological malignancies and for Orthopedic applications with no manipulation of stem cells to be applied, remain approved with clinical evidence proven. So, with the current regulatory regime introduced, clinical practitioner has the discretion to practice in the benefit of the patient instead of Big Pharma dumping their medicines to prescribe.

Did you ever feel accomplished on global level?

Honestly, for me, success is when the products or services from Transcell reach the suffering patients in India and do good in curing the debilitating condition. The social cause is highlighted in scoring my journey and self-assessment at any level. The awards and recognitions in sciences do not measure one's real contribution.

Did you have enough money to start your company or you had helping hand when you needed?

My story was not built on an idea like how most of the startups in other domains would have come into existence. It was logical extension of my career in research towards productization with heavy lab driven data in place. So, I brought intellectual property, proprietary data, technical knowhow, >10 yr of bench to bed side scientific and translational skills of commercial success to the venture. It is not just money that played role in starting the company and my skin is deep in the game with all savings put in. I am first generation entrepreneur and had no help till I found my true angels in 2016 boosting the very proposition.

Do you have any IP product and what are their applications?

Transcell has several first-in-class chemistry, biology platforms with protected processes and compositions for Neurodegenerative disorders, Cancers, Regenerative Medicinal applications.

What are market projections of stem cell industry?

Stem cell industry is a very heterogenous segment with varied projections based on practice area. Stem cell banking, Regenerative medicine,

Cell therapy, Basic research, Clinical research, Drug discovery are some of the practice areas pegged upto 300 b $ global market while we have no statistics available for Indian market value.

How do you see yourself and your company as a part of stem cell and biotech Industry? Or does company collaborates regularly with other players of industry?

Our collaborating partners are academia, established cross functional industry players, clinicians and patient communities than players like Transcell. We believe in strengthening our position and value proposition through complementary tie ups to complete our offerings and development.

What is your advice to young entrepreneurs who wish to look into starting a biotech company in India?

I always said, unless it is your technology and you are from the domain, don't dream to become an entrepreneur on borrowed ideas as it will be a futile attempt. Enterpreneurship in biotech space is a serious and intense practice with high stakes involved and requires not just money but conviction, belief and grip on science.

Related Video: https://www.justdial.com/photos/transcell-biologics-pvt-ltd-jubilee-hills-hyderabad-stem-cell-banks-crr5uo-pc-7176022-sco-28ldkyiu

Startup Story

NOT ALL STEM CELLS ARE CREATED EQUAL!

They grow better in Low Oxygen Conditions

by Dr. Shivinder S. Deol MD, Founder, SanoStem Global, LLC

How beneficial are Stemedica's Unique Patented Adult Hypoxic Allogeneic Immune Privileged Bone Marrow Derived Mesenchymal Stem Cells (BMMSC) in Multiple Diseases & Injuries?

Author: Dr. Shivinder S. Deol

Words: Hypoxic (Low Oxygen), Allogeneic (Donor), Immune Privileged (No immune response, act as Universal Donor Cells), Mesenchymal Stem Cells (MSC)

Introduction

Tissue oxygen tension (tPO_2) varies in different human organs & tissues from 2-7% (Figure 1) while breathing room air, which has 20% FiO2 (Fraction of inspired oxygen). Placenta & embryo tPO2 is 1-2%. This allows 1 human fertilized egg to undergo 41 divisions to become **over 2.5 Trillion cells** at time of delivery in only 9 months! This is the incredible power of stem cells!

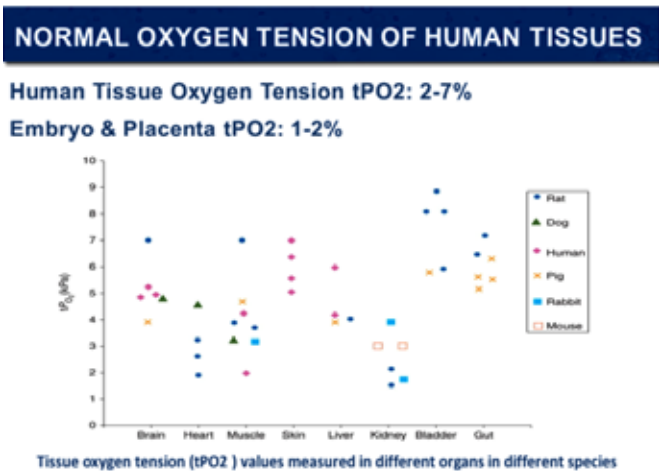


Figure 1

Wide Application Studies

Several studies have confirmed that stem cell (SC) niches in different tissues exists under hypoxic conditions, which promotes the dedifferentiated state (immature stage where the cells can divide & replicate unlimited number of times). Figure 2. Even small amounts of shift in tPO_2 stimulates early differentiation, a process by which mature cells specialize in different tissues depending on the location. Early differentiation may have some negative implications.

Most stem cell companies culture the cells at room air. Prolonged exposure outside of body's normal low oxygen

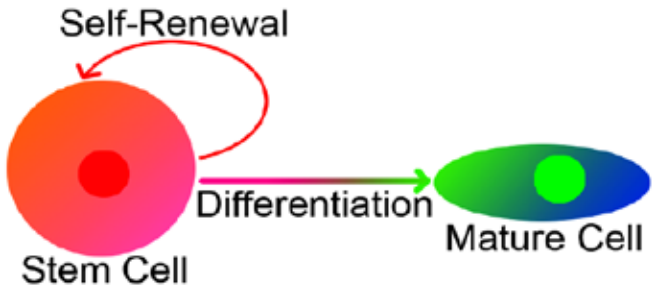
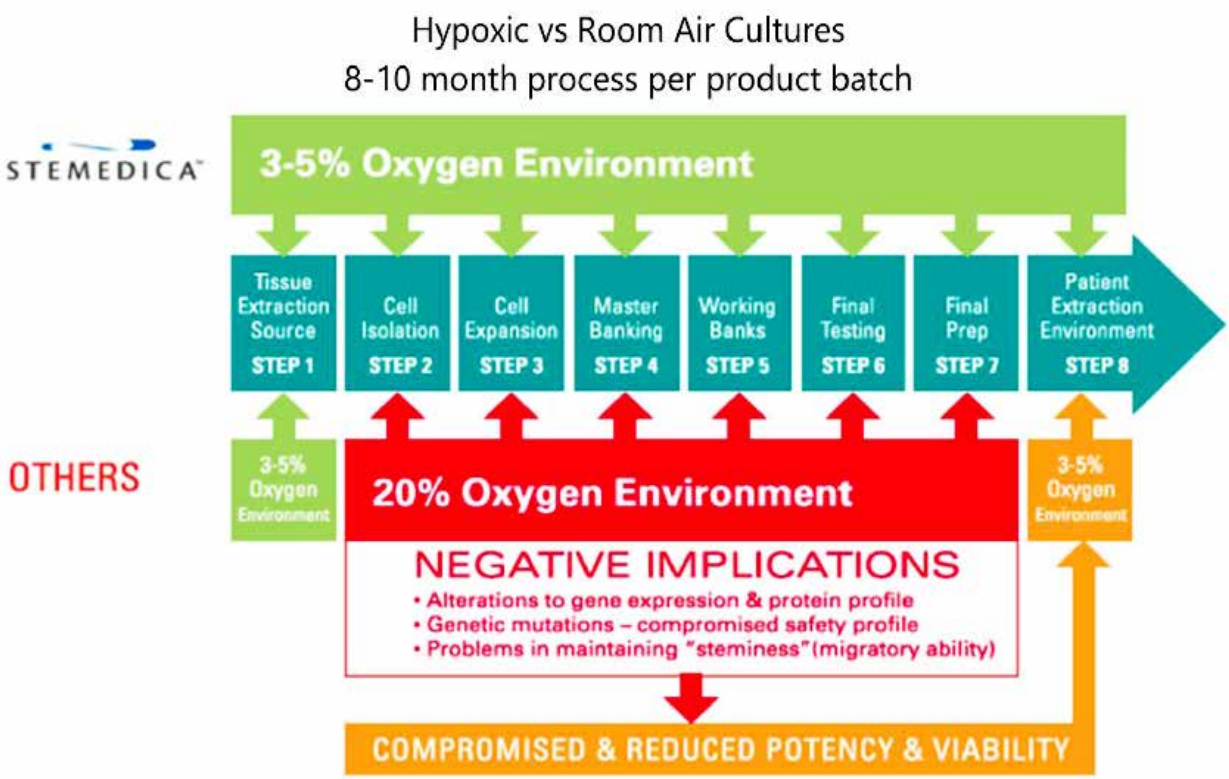


Figure 2

Figure 3



milieu (environment), can potentially lead to **smaller cell expansion,** as 1 study found that hypoxic BMMSC had 30-fold greater cell growth than regular MSC, **lower cytokines & growth factors** (different proteins body makes to stimulate or produce response far away), as 1 assay of Vascular Endothelial Growth Factor (VEGF) in hypoxic cultures showed over 50 times higher levels than normoxic MSC, **reduced angiogenesis** (new blood vessels, essential for repair & regeneration), and eventually **compromised or reduced potency and viability** (Figure 3).

There are over 300 chemokines, cytokines & growth factors identified from hypoxic MSC and over 37 in substantial amounts to be isolated. These factors are also being studied for multiple conditions, with remarkable efficacy. The low oxygen human stem cell factors will soon be available in liquids, creams, sprays, inhalers, etc. to support multiple conditions.

Stemedica has patented method of culturing cells under hypoxic conditions of 3-5% O_2, resulting in much higher efficacy, as seen in several ongoing global clinical trials and numerous case reports.

The hypoxic Stem Cells are fully characterized (Figure 4) with all major biomarkers identified (no CD34 indicating pure MSC cultures, with no hematopoietic or progenitor cells).

The low oxygen MSC are immune privileged (Figure 5) with less than 1% of cells exhibiting HLA-DR (main protein responsible for early rejections), thereby removing any risk of transfusion reactions. Over 10,000 patients have been studied in clinical trials or in case reports & no serious side effects have been observed in any patient so far. **Adult Stem Cells do NOT cause teratomas or tumors**, as occasionally can be seen with Embryonic Stem Cells.

Stemedica's Stem Cells are allogeneic, that means these have come from 1 single donor & can be given to over 10

Figure 4

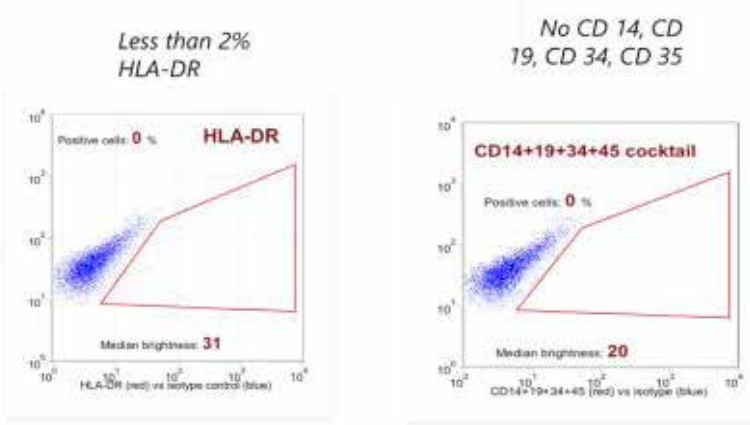
HYPOXIC MSC CHARACTERIZATION & VEGF

CHARACTERISTIC	FULLY CHARACTERIZED HYPOXIC MSCs
Biomarkers - Positive	CD29, CD44, CD73, CD90, CD105, CD166, CD106
Biomarkers - Negative	CD11B, CD14, CD19, CD31, CD34, CD45, HLA-DR
Tumorogenicity	Negative
Acute & Chronic Toxicity	Negative
Clonogenicity	High – Validation available
Potency & Differentiation	Validation: Yes Differentiates to Multiple Cell Lineages: including Adipogenisis, Osteogenisis & Chrondrogenisis
VEGF	VEGF Production: Extremely High (> 50 times than regular MSCs)
Scalability	High (> 3 times other MSCs)

million patients! Every patient gets the same proven effective thoroughly tested safe stem cells. Autologous stem cells on other hand take stem cells typically from bone marrow of the patient, process these and give back in same patient. Unfortunately, there is no way to standardize this process. Results vary considerably for autologous transplantation from no response, to mild response to occasionally good response.

Efficacy has been seen in multiple disease conditions. The US FDA has approved 6 Phase II clinical trials in USA, with 2 completions in heart failure and stroke. Kazakhstan has completed a Phase III clinical trial in myocardial infarction (MI or heart attack) and has received commercialization approval for same in August 2017. A diabetes mellitus clinical trial is being planned in India. MSC have strong anti-inflammatory properties and given intravenous can go to any area in body that is inflamed and produce beneficial response. Stem cells provide multifaceted solutions to heal the body. The body is its best healer, and stem cells may be the most ideal healer.

Figure 5



Avantages of Immune Privileged or Universal MSC

No need of HLA matching
No rejection or Transfusion reaction
No need for Dose reduction or multiple administration
Universal donor or "SELF" cells
No serious side effects in any treatment (over 10,000) so far

Stemedica also produces low oxygen foetal neural stem cells (NSC), which can assist in multiple neurological diseases & injuries, in combination with MSC or alone. The more serious or complex the disease, the need for combination treatments.

About Stemedica Cell Technologies Inc.

Stemedica Cell Technologies Inc. is a global biopharmaceutical company that manufactures best-in-class allogeneic adult stem cells and stem cell factors. The company is a government licensed manufacturer of cGMP, clinical-grade stem cells currently used in US-based clinical trials. The Company has FDA Investigational New Drug Approvals for acute myocardial infarction, chronic heart failure, cutaneous photoaging, ischemic stroke, traumatic brain injury and Alzheimer's disease. Stemedica's products are also used on a worldwide basis by research institutions and hospitals for pre-clinical and clinical (human) trials. Stemedica is currently developing additional clinical trials for other medical indications using adult, allogeneic stems cell under the auspices of the FDA and other international regulatory agencies. The company is headquartered in San Diego, California. Visit the website for more information online at www.stemedica.com.

About SanoStem Global LLC

SanoStem Global, LLC (SanoGlobal) is a global regenerative company that promotes healthy lifestyles with nutritional support, detoxification, hormonal and neurotransmitter balancing; along with cell-based therapies to promote longevity, quality of life, while reducing disability and diseases especially for diseases that have no cure or good treatment options. SanoGlobal has exclusive distribution rights from Stemedica for its proprietary stem cells products for India and several neighbouring countries. SanoStem India Pvt. Ltd (SanoStem), a subsidiary of SanoGlobal has distribution and manufacturing rights to India. SanoStem seeks to be actively engaged in stem cell clinical trials, treatments, marketing and sublicensing of these stem cells products in India. SanoStem is looking for key partners and allies to assist in clinical trials and developing the regenerative business. The company is headquartered in Bakersfield, California. Visit the website for more information online at www.sanostemglobal.com.

Guest Article

CRISPR – Theory and Technology

by Ranjani Rajasekaran1 and J. John Kirubaharan2
1PhD scholar, 2Professor and Head,
Department of Veterinary Microbiology, Madras Veterinary College, Chennai –India.

Advent of recombinant DNA technology paved way towards genome editing. Since then, genome editing technology evolved steadily with consistent improvisation of the former technology. One such improvised technology was CRISPR-Cas9 which exploited the microbial adaptive immune system – CRISPR - found in bacteria and archaea. It provides acquired immunity against foreign viruses and plasmids. It was initially found in the E.coli K12 bacterial genome as repeated motifs of <50bp that were neatly and consistently ordered. At that time, it was considered to be "exotic junk of DNA". Later, in the year 2002, this junk of DNA was named as Clustered Regularly Interspaced Short Palindromic Repeat' – CRISPR.

CRISPR Locus

The presence of CRISPR on a bacterial genome is called CRISPR locus. The figure 1 shows cmponent of a CRISPR locus:

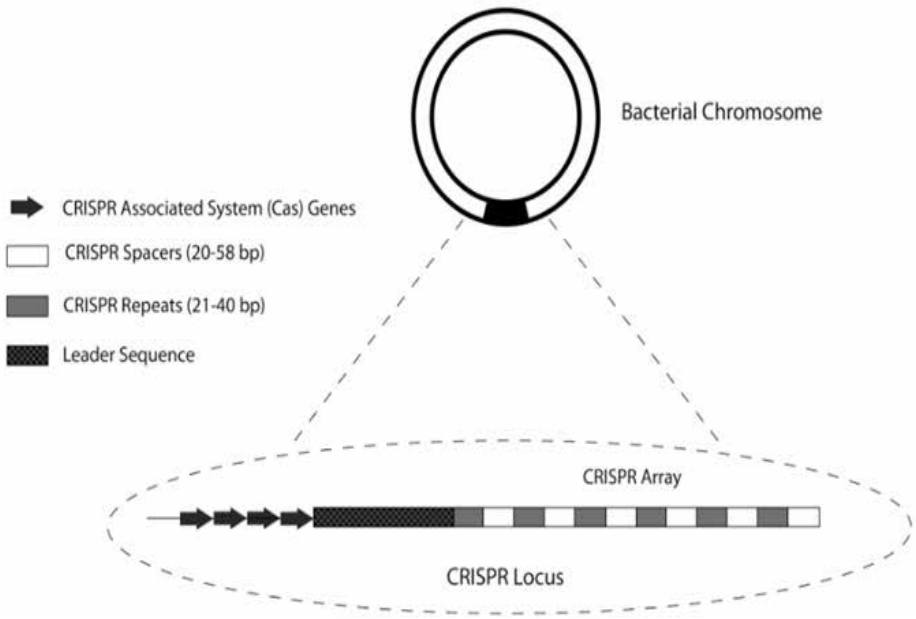


Image courtesy: Crispr-Cas9 plasmid www.systembio.com.

Components of a CRISPR locus

- **CRISPR Array**

o Spacers - Small variable sequences in the bacterial genome that are acquired from foreign nucleic acids flanked by repeats

o Leader – Includes a promoter

and contains long A-T rich region

- **Cas nuclease/ Cas proteins**

o Contains DNA endonuclease and two RNA components

o crRNA and tracrRNA

o Required for multistep defense against invasive element

- **Protospacer adjacent motifs (PAM)**

o Differentiates between self and non-self DNA

Types of CRISPR

The CRISPR-Cas system is generally divided into three types, depending on the Cas protein sequence and structure:

Type	Function	Cas proteins used
I	Cleaves and degrades DNA	Several Cas proteins
II	Cleaves DNA only	Only a single Cas protein – Cas 9
III	Cleaves DNA or RNA	Several Cas proteins

The CRISPR-Cas9 system is widely used for genome editing. It belongs to type II CRISPR-Cas system adapted from Streptococcus pyogenes.

Types of Cas proteins

There are 45 major Cas proteins identified so far. Among them, Cas 1-10 is of major importance. There are three types of Cas proteins based on the process it is involved with:

- **Universal** – Spacer acquisition – Cas 1 and 2
- **Signature** – Target interference – Cas 3, 9, 10
- **Type specific** – crRNA expression – Cas 4, 5, 6, 7 and 8

Mechanism of CRISPR mediated immunity in bacteria

CRISPR-Cas systems in bacteria target viruses, plasmids, chromosomal sequences (transposons, prophages) and produce immunity against the same.

The mechanism of immunity includes 2phases:

- Immunization phase – Includes spacer acquisition
- Immunity phase – Expression and interference

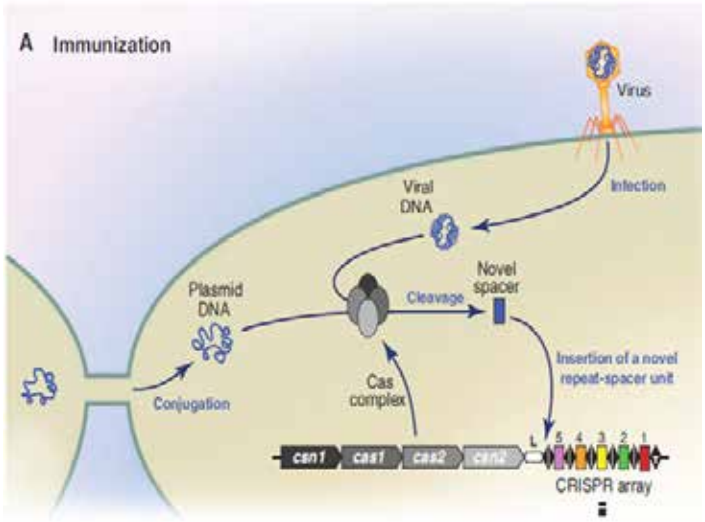


Fig: Immunization phase

Upon introduction of a foreign DNA, it is cleaved by DNA endonuclease in the Cas proteins and is inserted as spacers into the CRISPR locus.

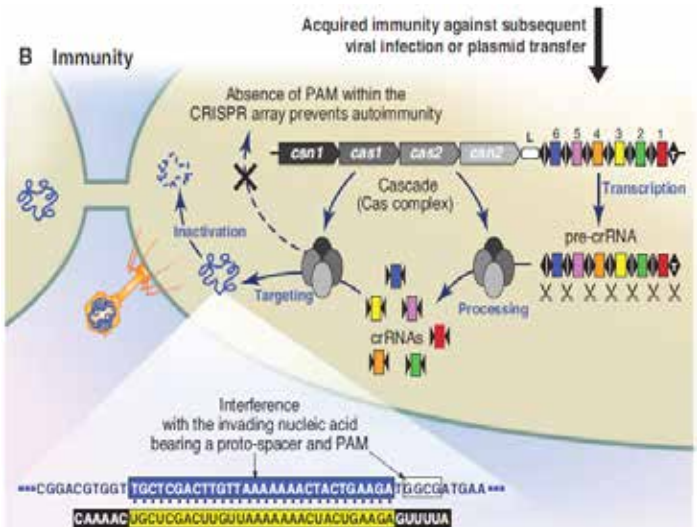


Fig B: Immunity phase:

Reinfection - Repeat spacer units transcribed - Pre-CRISPR RNA (pre-crRNA) - Cas9 binds to pre-crRNA - crRNA-tracrRNA-Cas9 complex - Foreign DNA destroyed

CRISPR-Cas9 — Technology

The ability to edit genomes precisely has been fulfilled by CRISPR-Cas9 technology. With the advent of this technology, any gene of interest can be inserted or deleted effortlessly and efficiently. It is an easy and versatile platform for genome editing when compared to the strenuous zinc finger and TALEN approaches.

Components of CRISPR-Cas9 system

Genome editing using CRISPR Cas9 technology has two components:

- an endonuclease – Cas9
- a short guide RNA (sgRNA)

Endonuclease – Cas9

The endonuclease is the bacterial Cas9 nuclease protein from Streptococcus pyogenes. The Cas9 nuclease possesses two DNA cleavage domains (the RuvC1 and HNH-like nuclease domains) that cleave double-stranded DNA, making double strand breaks (DSB).

Short guide RNA

- crRNA – 20 nucleotide guide RNA + 14 nucleotide repeat region
- tracrRNA – 14 nucleotide anti-repeat region + 3 stem loops (Loop1,2,3)

o Stem loop 1 – formation of functional sgRNA:Cas9 complex

o Stem loop 2 and 3 – stability and activity of CRISPR-Cas9 system

CRISPR-Cas9 regulation

- Last 20bp at the 5' end of the sgRNA acts as a homing device that,
- Recruits Cas9 to cleave a specific dsDNAdirectly upstream of a protospacer adjacent motif (PAM)

o The target sequences which are immediately followed by the PAM sequence will be targeted for genome editing. PAM recognition sequence differs depending on the species and the type of bacteria from which the Cas9 nuclease is derived.

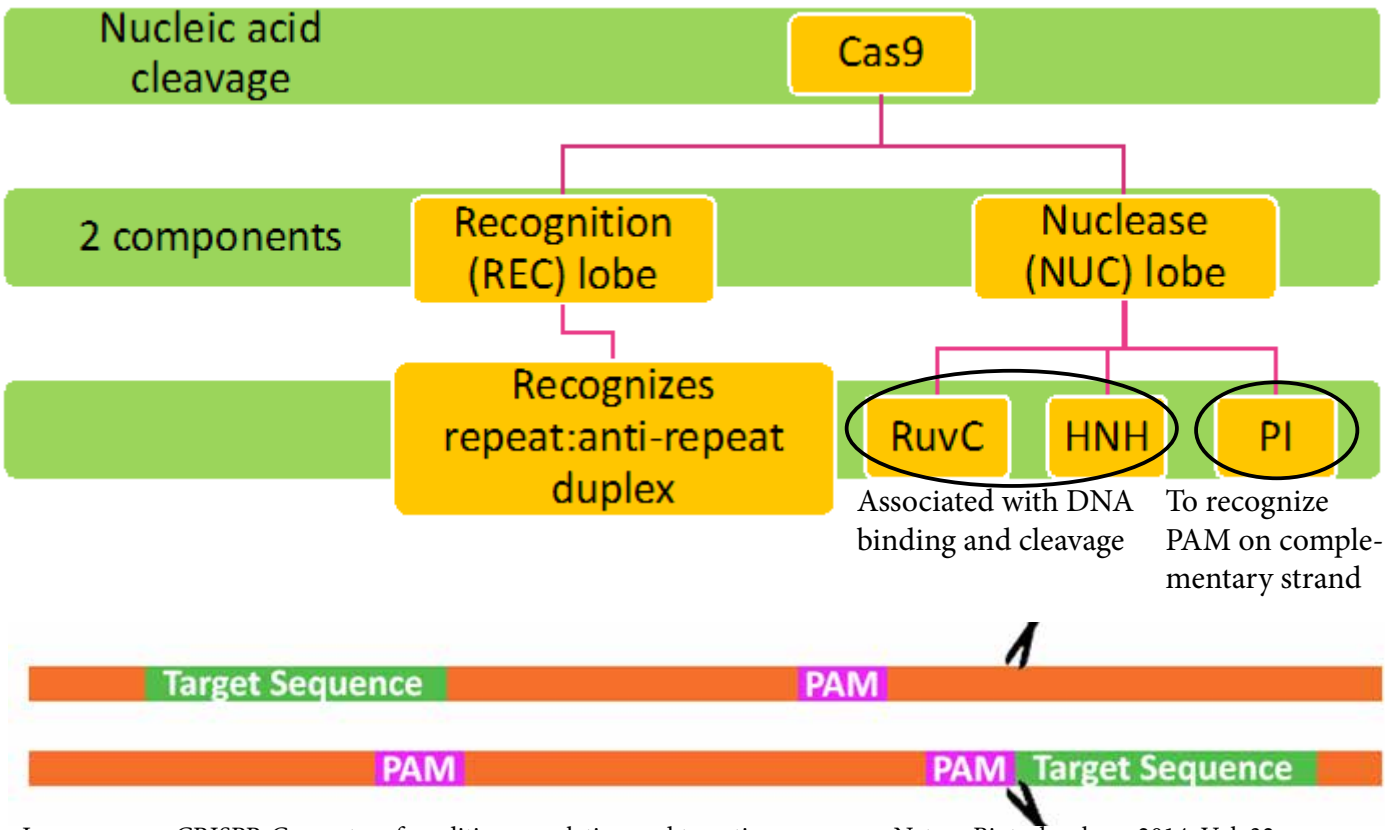


Image source: CRISPR-Cas system for editing, regulation and targeting genomes. Nature Biotechnology, 2014, Vol. 32.

• sgRNA serves as a bridge between Cas9 and target sequence
• It can be designed to recognize a particular sequence
• Successful genome editing using CRISPR-Cas9 depends on the sgRNA sequence as well as the PAM Sequence

CRISPR-Cas9 – Double strand break

Double strand break can be repaired by - Non-homologous end joining (NHEJ) or Homology directed repair (HDR)
• NHEJ: Does not use template
More error prone
Occurs with high frequency
• HR: Requires template
More accurate

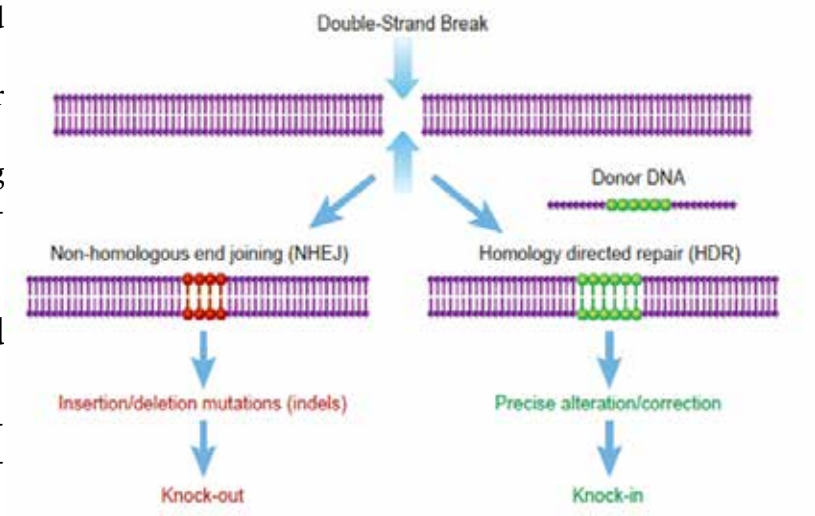
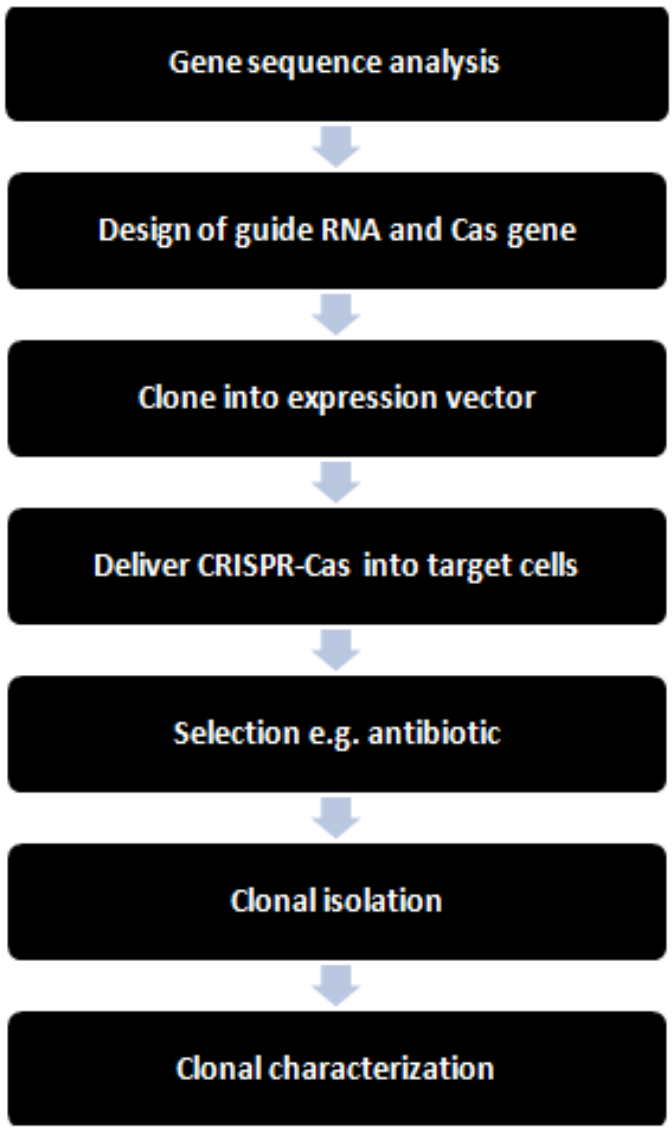


Image source: Bhaya et al., 2011. CRISPR-Cas Systems in Bacteria and Archaea : Versatile Small RNAs for Adaptive Defense and Regulation.

Workflow of CRISPR

• Gene sequence analysis
o Essential to sequence the gene of interest of the target genome
• Design of guide RNA for Cas9
o Selection criteria:
Should highly match target sequence – To minimize off target activity
Should not have more than 3 mismatches
20nt sgRNA is often used
17 or 18nt sgRNA – More specific
Designing tools for guide RNA
• Optimized CRISPR Design
• sgRNA Scorer
• sgRNA Designer
• ChopChop web tool
• E-CRISP
• CRISPR Finder
• RepeatMasker - to double check and avoid selecting target sites with repeated sequences



So, the complex of CRISPR should contain:
o sgRNA + Cas9 + Host genome sequence (identical to the host genome)

• Design of single stranded oligonucleotide DNA – Repair template

• **Choice of Cas protein**
o Cas9 – Efficient in homologous recombination
o Cas9 nickase – Double nicking with two separate gRNAs
o DeadCas9 – Transcriptional pertubation of target genes without modifying the DNA
o Light-activated Cas9 – Activation of gene transcription with light stimulation

• **Alteration of PAM**
o PAM interacting amino acids may be replaced with different a.a to improve its specificity with Cas

• **Expression vector**
o Lentiviral vectors – to transfect cells
o Recombinant adeno viral vectors – in vivo gene delivery
o All in one vector – guide RNA and Cas9 genes

• **Delivery of CRISPR into target cell**

Target cell	**Method of delivery**
Mammalian cells	-Lipofection-based transfection of DNA plasmids -Electroporation of DNA plasmids or RNP -Lentiviral transduction of DNA plasmids
Microbial organisms	Transformation of plasmids into competent cells
Yeast	Electroporation of plasmids and galactose induction of Cas9
Plants	Agrobacterium mediated transformation of sgRNA and Cas9 vector
Mouse	-Direct injection of AAV into the tissue -Electroporation in zygotes

CRISPR-Cas9 — Variations to the System

There are two variations to the system introduced above that are also commonly available today: the Cas9 Nicakse and the Cas9 Double Mutant. Each of these variants has their own benefits and applications.

Applications of CRISPR-Cas9 system

• Gene disruption (without donor template DNA)
• Gene knock-out (with a reporter knock-in)
• Non-protein coding gene disruption
• Specific mutations
o Desired SNP introduction or correction
o Desired insertions/deletions
• Promoter Study
o Luciferase replaced the 5' exon
• Conditional knockout
o For essential genes or tissue-specific study inserting LoxP sites
o Around the exon to be knocked-out
• Large chromosomal deletions
o Using two signature Cas9 RNAs to induce double stranded breaks at sites that flank the region of interest
• Exogenous gene Insertion
o Adeno-associated virus integration site 1 (AAVS1)

in human genome is a safe harbor for transgene integration

o A controlled Gene Knock-in e.g. controlled copy number and location

• CRISPR interference and activation of transcription

CRISPR in various disciplines

• Neuroscience

o Novel rat model for muscular dystrophy reveals new treatment targets

• Cancer biology

o Novel tumor suppressor genes and new animal models for brain tumors

• Vaccinology

o T cell engineering with CRISPR-Cas reveals a new therapeutic strategy for HIV

• Immunology

• Plant biology

o Successful adaptation of the CRISPR-Cas editing system in rice

• Therapeutics – Cancer, HIV, cardiovascular disease, SCID

• Epigenetic modifications and Stem cell differentiation

Importance of CRISPR

• High potency and specificity

• Broad applicability in vitro and in vivo

• Potential one-time curative treatment

• Ability to edit out diseases

• Ability to address any site in the genome or foreign genome

• Ability to target multiple DNA sites simultaneously

• Multi-functional programmability – Delete, insert, repair

Any enthusiastic scientist would have the curiosity and excitement to explore CRISPR technology that lead to various CRISPR based genome editing. But, considering the ethical and biosafety concerns it could raise, strict laws and regulations have been formed to exempt misuse or improper use of this technology in scientific research.

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Historical News from 12th April - 12th May

NEWS: Govt & Industry

SSIET Chairman Prof. J.Karthikeyan won the "Iconic Global Asian of the Year 2017" Award

April 18, 2018

Prof.J.Kartheekeyan, Chairman & CEO of Sree Sastha Institutions is awarded the Iconic Global Asian of the Year 2017 for embossing Asia on the world map and making a generation looking up to them, aspiring to reach the personage excellence. "Asia's Greatest Brands & Leaders 2017 – process reviewers PricewaterhouseCoopers P.L.", was held at the Roselle Junior Ballroom of Marina Bay Sands Expo and Conventions Centre, Singapore was a magnificent event highlighted by the presence of the Ambassador of Ukraine – His Excellency Dmytro Senik, and Minister-Consular of Kazakhstan Embassy in Singapore – Mr. Faizrakhman Kassenov.

About Prof. J.Karthikeyan

Prof. J.Karthikeyan, Chairman of Sree Sastha Institute of Engineering and Technology (SSIET) has widely travelled and has hand on exposure in running Industrial Units and is equally exposed to running and organizing academic Institutions. A Member of 17 Professional and Scientific Societies, has attended numerous Conferences / Seminars on Education, Leadership, Management and Industry. He was on Special Educational Mission to Singapore, Malaysia in April 2007 and later to China (Beijing, Shenyang and Shanghai in June 2007.

India signs loan agreement with World Bank for US$ 125 million for "Innovate in India for Inclusiveness Project"

by Biotech Express News Bureau

Original Source: Press Information Bureau, India and www.worldbank.org

Government of India and World Bank Sign Agreement to Invest in Technology that Addresses India's Public Health Priorities. The $125 million loan from the International Bank for Reconstruction and Development (IBRD), has a 5-year grace period, and a maturity of 19 years.

A Loan Agreement for IBRD credit of US$ 125 (equivalent) for the "Innovate in India for Inclusiveness Project" was signed with the World Bank on 24th April, 2018 in New Delhi. The Innovate in India for Inclusiveness Project (I3) was signed by Sameer Kumar Khare, Joint Secretary, Department of Economic Affairs, Ministry of Finance, on behalf of the Government of India; Mohd. Aslam, Manag-

ing Director, Biotechnology Industry Research Assistance Council (BIRAC); and Hisham Abdo, Acting Country Director, World Bank India, on behalf of the World Bank

The Objectives of the project is to nurture indigenous innovation, foster local product development and accelerate commercialization process by bridging critical skill and infrastructure gaps to promote affordable and innovative healthcare products generation for inclusive development and increasing competitiveness in India. The project would support consortia of public, private, and the academic institutions to overcome the key market failures currently holding back the development of an innovative biopharmaceutical and medical devices industry in India.

The project consists of the following parts:

(i) Strengthening of pilot-to market innovation ecosystem

(ii) Acceleration of the pilot –to-market process for specific products and

(iii) Project Management and monitoring & Evaluation.

The Innovate in India for Inclusiveness Project will support Government of India's Biotechnology Industry Research Assistance Program (BIRAC), set up five years ago to support innovative start-ups and collaborations through strategic partnerships. This project, will nurture next generation technical skills; provide companies with advanced shared facilities to conduct clinical validation; link clinical trial sites with networks of expert advisors and international bodies; and strengthen all institutions involved in the facilitation and adoption of global innovations, technologies, and licensing models.

Biohacker Who Injected Himself with Untested Herpes Vaccine Found Dead

The controversial CEO of a biohacking company was found dead Sunday in a sensory deprivation tank at a spa in downtown d.c.d.c. police responded about 11:30 a.m. Sunday and found traywick's body. A death investigation is underway, though police say they have no evidence that suggests foul play.

D.c. police responded about 11:30 a.m. Sunday and found traywick's body. A death investigation is underway, though police say they have no evidence that suggests foul play.

Traywick ran ascendance biomedical, which encouraged non-scientists to conduct their own medical research. In february, he took off his pants in front of a crowd at a biohacking conference in texas and injected himself in the thigh with an experimental, non-fda-approved treatment for herpes.

Borlaug Global Rust Initiative Honors Women In Wheat Research

April 25, 2018, BGRI

Image: Dr Urmi Bansal

The Borlaug Global Rust Initiative (BGRI) awarded a group of women who have made significant contributions in wheat research and development. The winners of the 2018 Women in Triticum Award were honored at the 2018 BGRI Technical Workshop in Marrakech, Morocco.

The Early Career Awards were given to the following researchers:

Meriem Aoun, who applied both conventional and molecular breeding techniques toward the release of resistant durum varieties to rusts and Fusarium head blight;

Radhika Bartaula, a plant geneticist working to unravel the genetic mechanism of resistance to wheat stem rust pathogen in barberry;

Sreya Gosh, work focuses on understanding and exploiting genes controlling resistance to leaf rust in wheat;

Raheela Rehman, who conducts studies to better understand and characterize the differences in root absorption and translocation of zinc in wheat and maize plants, as well as in various wheat genotypes with high grain zinc concentrations; and

Hannah Robinson, who engages with researchers throughout Australia and across the globe to develop research projects aimed at improving wheat and barley production.

Dr. Urmil Bansal, a molecular geneticist at the University of Sydney Plant Breeding Institute, was hailed with the Mentor Award. Aside from developing and validating closely linked markers for more than 20 rust resistance genes to facilitate marker-assisted pyramiding to control of rust diseases in wheat, she has mentored 29 M.Sc. and Ph.D. students mostly from developing countries including South Asia and Africa.

FDA Approves Application for AquaBounty Salmon Facility in Indiana

April 26, 2018

The U.S. Food and Drug Administration today approved a supplemental New Animal Drug Application (NADA) submitted by AquaBounty Technologies, Inc. The supplemental NADA requested FDA approval to raise AquAdvantage Salmon – a product under an application previously approved in 2015 – at a land-based contained facility near Albany, Indiana. While the Indiana facility is approved for production, the company is prohibited from importing the eggs necessary for producing genetically engineered (GE) salmon at the facility because of a requirement in FDA's current appropriations law.

Plant Scientists Boost Malaria Drug Yield In Plant

May 2, 2018, BBC

Scientists from Shanghai Jiao Tong University and other research institutions in China modified the genetic sequence of the plant *Artemisia annua* to make it produce high levels of a key drug for malaria. Their research study is published in *Molecular Plant*.

According to the World Health Organization (WHO), malaria has affected about 216 million people in 91 countries in 2016, and caused around 445,000 deaths all over the globe in the same year only. *A. annua* is the main source of artemisinin, the only WHO recommended treatment for the devastating disease. Thus, the researchers identified the genes involved in making artemisinin and modified the plant to make it produce three times more drug than the usual amount. They did this by simultaneously increasing the activity of three genes, HMGR, FPS, and DBR2.

ICRISAT's top Honour for Two Women Scientists

APRIL 17, 2018 , The Hindu

Both bag Doreen Margaret Mashler Award for their work in plant pathology and biotechnology

Women scientists Mamta Sharma and Pooja Bhatnagar-Mathur are the joint recipients of Doreen Margaret Mashler Award for 2018, for significant work in plant pathology and biotechnology respectively at the International Crops Research Institute for the Semi-Arid Tropics (ICRISAT)

In 2017, she led a team that developed the Loop-Mediated Isothermal Amplification (LAMP) method to identify a pathogen affecting chickpea and over 500 crops globally. She also established the Centre of Excellence on Climate Change Research for Plant Protection to address the effects of climate change on insect-pests and diseases.

Dr. Bhatnagar-Mathur, led an international, multi-institutional effort, for innovative biotechnology solutions to combat aflatoxin in groundnut using a 'double-defence' approach. This breakthrough resulted in resistance to fungal infection as well as remarkably low levels of aflatoxin contamination.

Janssen Strikes Deal to Acquire BeneVir and its Oncolytic Virus Platform in Deal Worth Up to $1 Billion

Published: May 02, 2018 By Alex Keown

Janssen Biotech, a subsidiary of Johnson & Johnson's Janssen Pharmaceuticals, cut the deal in order to acquire **BeneVir's proprietary T-Stealth Oncolytic Virus Platform** that can be used to develop oncolytic viruses used to infect and destroy cancer cells. The deal was facilitated by Johnson & Johnson Innovation LLC.

Oncolytic viruses are a growing field in immuno-oncology. Oncolytics have been shown to make a difference in treating various cancers. In 2015 the U.S. Food and Drug Administration approved the first oncolytic virus therapy for melanoma, Amgen**'s Imlygic**. Multiple companies have jumped into the field, including Merck, which in February acquired Australia-based Viralytics Limited and its oncolytic immunotherapy treatments for **$394 million**.

While Janssen was mum on the financial details of the transaction, HC2 said the deal could be **worth up to $1.04 billion** when milestones are included. Under the terms of the agreement, Janssen will make an upfront cash payment of $140 million and additional contingent payments of up to $900 million based on achievement of certain predetermined milestones, HC2 announced. The deal is expected to close in the second quarter of 2018.

DuPont & ADM Open Biobased FDME Pilot production Facility in Illinois

April 30, 2018, http://www.dow-dupont.com.

DuPont Industrial Biosciences (DuPont) and Archer Daniels Midland Company (ADM) announced the opening of the world's first biobased furan dicarboxylic methyl ester (FDME) pilot production facility in Decatur, Illinois.

Nearly one-tenth of the world's oil is used to make the plastic products we use every day. From shampoo bottles to frozen food containers, fossil-fuel-based plastics are virtually impossible to avoid because of a lack of commercially available alternatives — a significant gap in the marketplace that DuPont and ADM's new biobased FDME will help address. FDME is a molecule derived from fructose that can be used to create a variety of biobased chemicals and materials, including plastics, that are ultimately more cost-effective, efficient and sustainable than their fossil fuel-based counterparts.

Sterling Biotech suspended on BSE

Earlier Sterling Biotech was warned by BSE and last date was given to comply with the norms of stock exchange. Last date was 12th April 2018, but it seems that Sterling Biotech could not comply and thus BSE suspended account of company from Bombay Stock Exchange.

New Medical Hub proposed in Ghaziabad Uttar Pradesh

A new pharma industry cluster will come soon in the industrial area of Madhuban Bapudham, near NH-58. The GDA has started the process already, we will roll out bid call in May, said Ritu Maheshwari, GDA vice-chairperson.

The space allotted to develop industries here is nearly 1 lakh 14 thousand sqm. Along the line, a multispeciality hospital hub has also been proposed to develop in 3 hectare of area in this region. For this, single or group of bidders can bid for the space. Earlier it was proposed to be develop on PPP model.

Kymriah® first-in-class CAR-T therapy from Novartis, receives second FDA approval to treat large B-cell lymphomas

May 01, 2018

Kymriah is an innovative immunocellular therapy that is a one-time treatment manufactured individually for each patient using the patient's own T cells. Kymriah uses the 4-1BB costimulatory domain in its chimeric antigen receptor to enhance cellular expansion and persistence. In 2012, Novartis and Penn entered into a global collaboration to further research, develop and commercialize CAR-T cell therapies, including Kymriah, for the investigational treatment of cancers.

KYMRIAH™
(tisagenlecleucel) Suspension for IV infusion

Novartis announced the US Food and Drug Administration (FDA) has approved Kymriah® (tisagenlecleucel) suspension for intravenous infusion for its second indication - the treatment of adult patients with relapsed or refractory (r/r) large B-cell lymphoma after two or more lines of systemic therapy including diffuse large B-cell lymphoma (DLBCL), high grade B-cell lymphoma and DLBCL arising from follicular lymphoma. Kymriah is not indicated for the treatment of patients with primary central nervous system lymphoma. Kymriah, developed in collaboration with the University of Pennsylvania, became the first chimeric antigen receptor T cell (CAR-T) therapy to receive regulatory approval in August 2017 for the treatment of patients up to 25 years of age with B-cell precursor acute lymphoblastic leukemia (ALL) that is refractory or in second or later relapse. Kymriah is now the only CAR-T cell therapy to receive FDA approval for two distinct indications in non-Hodgkin lymphoma (NHL) and B-cell ALL.

"Today's FDA approval of Kymriah provides another opportunity for Novartis to build on its leadership in CAR-T development, delivering a potentially transformative therapy with durable and sustained response rates and a well-characterized safety profile to help patients in dire need of new treatment options," said Liz Barrett, CEO, Novartis Oncology. "We look forward to leveraging all of our learnings and new capabilities from the initial launch of Kymriah in pediatric and young adult B-cell ALL for this larger group of patients."

Kymriah is manufactured for each individual patient using their own cells at the Novartis Morris Plains, New Jersey facility. In the US, the target turnaround time for manufacturing Kymriah is 22 days. The reliable and integrated manufacturing and supply chain platform for Kymriah allows for an individualized treatment approach on a global scale. The process includes cryopreservation of a patient's harvested (or leukapheresed) cells, giving treating physicians and centers the flexibility to initiate therapy with Kymriah based on the individual patient's condition. Novartis has significant CAR-T manufacturing experience and has demonstrated a reproducible product. Novartis has manufactured CAR-T cells for more than 300 patients from 11 countries. Novartis continues to advance its CAR-T manufacturing expertise in Morris Plains where we have been supplying CAR-T cells for global clinical trials and where we continue to invest in support of the anticipated demand to meet the needs of patients.

GSK's Shingles Vaccine generated most revenue in First Quarter of 2018

Apr 25, 2018,

Despite strong sales of shingles vaccine Shingrix, GlaxoSmithKline reported its **sales and earnings**

fell 2 percent in the first quarter of the year, largely due to challenges in respiratory sales as well as significant currency impact.

GSK said Shingrix saw sales of about $153 million in the first quarter. The first quarter of 2018 is the first full quarter that Shingrix has been on the market in the United States. It has quickly replaced rival drugmaker Merck's shingles vaccine Soztavax. Since its launch about six months ago the GSK vaccine has seen significant growth in the United States and has won approximately 90 percent of the market share in this country. The company anticipates Shingrix will become its biggest vaccine of all time.

While the first quarter of the year was tough but expected for GSK, the company has been making moves to ensure future long-term growth. During the first quarter of this year, GSK took full control of its consumer health business.

According to news earlier in month of April 2018, the company announced it has **divested its rare disease gene therapy portfolio** to Orchard Therapeutics. As part of the agreement Orchard, which **launched in 2016**, received a number of gene therapy programs as part of the deal, which is expected to complement its existing pipeline of clinical and preclinical gene therapies for primary immune deficiencies and inherited metabolic disorders.

Under terms of the deal, GSK will receive a 19.9 percent equity stake in Orchard, as well as a seat on that company's board of directors. Additionally, GSK will receive undisclosed royalties and commercial milestone payments related to the portfolio. By taking over the GSK programs Orchard will assume all obligations from GSK's 2010 collaboration agreement with the Ospedale San Raffaele and Fondazione Telethon, as well as from GSK's collaboration agreement with MolMed, GSK announced.

Top Biotech Influencers to Watch on Twitter

Kiran Mazumdar-Shaw
Followers:1.44M

Dr. C. Michael Gibson, M.D., Harvard professor of medicine
Followers: 394K

Dr. Tedros Adhanom Ghebreyesus, Director-General of the World Health Organization
Followers:322K

Dr. Atul Gawande, surgeon and public health official, he's also the author of four New York Times bestselling books
Followers:241K

Dr. Eric Topol, M.D., Executive Vice President and Professor of Molecular Medicine at the world-renowned Scripps Research Institute
Followers:129K

Dr. Robert R. Redfield, M.D., head of Centers for Disease Control and Prevention
Followers:119K

Dr. Linda Girgis, M.D., family physician
Followers: 100K

Robin Y. Smith, CEO of Orig3n
Followers: 105K

Dr. Francis S. Collins, M.D., 16th Director of the National Institutes of Health
Followers: 86.2

Dr. Michael Mosley, BBC-affiliated influencer
Followers: 85.4K

Matthew Herper, Senior Editor covering Healthcare, Pharma, and Medicine for Forbes.com and Forbes magazine
Followers: 81.4K

Dr. Atanas G. Atanasov, Head of the Department of Molecular Biology at the Institute of Genetics and Animal Breeding within the Polish Academy of Sciences
Followers: 91.4K

Amgen Announces Rhode Island Will Be Location of First US Next-Generation Biomanufacturing Plant

April 10, 2018, Amgen

Amgen (NASDAQ:AMGN) today announced plans to build a new state-of-the-art next-generation biomanufacturing plant at its campus in West Greenwich, R.I. The new plant, the first of its kind in the United States (U.S.), will employ Amgen's proven next-generation biomanufacturing capabilities and manufacture products for the U.S. and global markets.

A next-generation biomanufacturing plant incorporates multiple innovative technologies into a single facility, and therefore is built in half the construction time with approximately one half of the operating cost of a traditional plant. Next-generation biomanufacturing plants require a smaller manufacturing footprint and offer greater environmental benefits, including reduced consumption of water and energy and lower levels of carbon emissions.

"Amgen has three decades of experience in biologics manufacturing, and we are proud of our track record of providing a reliable supply of high-quality medicines for patients around the world," said Esteban Santos, executive vice president of Operations at Amgen.

Amgen opened its first next-generation biomanufacturing plant in Singapore in 2014. The existing Amgen Rhode Island plant was licensed by the U.S. Food and Drug Administration in September 2005 and houses one of the world's largest mammalian protein manufacturing facilities. The facility manufactures commercial and clinical bulk drug substance. Amgen has invested more than $1.5 billion in its Rhode Island site, adding more than 500,000 square feet of manufacturing, utility, administrative and laboratory space to the campus. There are 625 full-time staff members employed at the Amgen Rhode Island campus.

Advaxis recruits Kenneth Berlin as New CEO

Apr 23, 2018

The company announced **Kenneth A. Berlin** will take over the helm of the company as president and CEO effective immediately. The announcement of a new CEO was not the only change to Advaxis' leadership team announced today. In addition to Berlin's appointment, Advaxis also announced Andres A. Gutierrez has been named chief medical officer.

With Berlin at the helm, Advaxis will be looking to harness his experience to drive growth. The company highlighted some of his corporate successes as a pharma executive for other companies. While at Rosetta Genomics Berlin spearheaded the effort to reposition the company with various microRNA-based oncology diagnostic products. Additionally, he raised nearly $100 million in capital to fund these efforts, Advaxis noted. Before Rosetta Genomics, Berlin was the Worldwide General Manager at cancer diagnostics developer Veridex, LLC, a subsidiary of Johnson & Johnson. At Veridex he grew the organization to more 100 employees, launched three cancer diagnostic products, led the acquisition of its cellular diagnostics partner, and delivered significant growth in sales as Veridex transitioned from an R&D entity to a commercial provider of oncology diagnostic products and services.

U.S. Supreme Court: Patent Office Allowed To Cancel Bad Patents

Source: Purch

In one of the most important patent cases in recent years, the Supreme Court ruled that the Patent Office can not only issue patents, but can also retract them. The ruling should deter aggressive patent holders from going after other companies, unless they are certain that their patents will withstand a review, which should result in less litigation across industries.

In a recent case between two oil drilling companies, Oil States Energy Services and Greene's Energy Group, the

former argued that it was unconstitutional for an administrative law board of the Patent Office to retract patents, because that should be the job of the courts. This administrative law board, called the Patent Trial and Appeal Board (PTAB), was created in 2012 as part of the America Invents Act as a way to lower the costs of litigation.

The Supreme Court disagreed because the way patents are granted has been decided by Congress all this time, not courts, and therefore Congress can also control how the bad patents are retracted.

Sanofi to Sell its Generic Division Zentiva to Advent for $2.4 Billion

April 2017, Reuters

Sanofi said the sale was expected to be completed before the end of the year, and Advent's offer was binding and fully financed. The 1.9 billion euros price is an enterprise value, including equity and debt.

"Following a comprehensive review of strategic options for our generics unit in Europe, we have determined that transferring this business to Advent is the best option to ensure its long-term success," Sanofi Chief Executive Olivier Brandicourt said in a statement.

Novartis appoints John Tsai Head of Global Drug Development and Chief Medical Officer

Source: http://www.novartis.com.

Novartis announced today the appointment of John Tsai, M.D. as Head of Global Drug Development (GDD) and Chief Medical Officer. Dr. Tsai will join Novartis on May 1, 2018, and will be based in Basel, Switzerland. He will report to Vas Narasimhan, M.D., CEO of Novartis and will become a member of the Executive Committee of Novartis (ECN). He succeeds Dr. Narasimhan who became CEO of Novartis on February 1, 2018.

Dr. Tsai has been Chief Medical Officer and Senior Vice President of Global Medical at Amgen Inc., since May 2017 and oversees all clinical and medical functions across multiple sites worldwide. At Novartis, he will be responsible for advancing the company's industry-leading pipeline of innovative medicines and biosimilars. Dr. Tsai will also lead the GDD organization's ongoing transformation embracing the power of advanced data sciences and digital technologies to create a more agile model for drug development.

Image: John Tsai, M.D.
Source: Front Line Genomics

"I am delighted to welcome John to Novartis," said Dr. Narasimhan. "As we continue to reimagine drug development, his expertise across multiple therapeutic areas, including cardiovascular, oncology and neuroscience combined with his background in electrical engineering will be a source of great strength for Novartis.

Dr. Tsai said: "I feel honored to have the opportunity to lead the Novartis Global Drug Development organization and do my part in bringing forward the company's strong pipeline of medicines that address some of humanity's biggest health challenges. I am also excited to work with my colleagues at Novartis to pioneer novel paradigms for drug development with data and digital technologies at the core."

Upcoming Big BioEvent

Partnered by Biotech Express

BioSD 2018

International Conference on

Biotechnological Research and Innovation for Sustainable Development & XV BRSI Convention

22-25th November, 2018

Organized by
CSIR-Indian Institute of Chemical Technology
Hyderabad, India

In Association with
The Biotech Research Society, India (BRSI)

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Important Dates

Deadline for abstracts submission	**31.08.2018**
Acceptance notification	**15.09.2018**
Deadline for registration (early bird)	**30.09.2018**
Accommodation Reservation	**10.10.2018**
Cancellation Before	**31.10.2018**

Registration

Registration will be open from 1st July 2018. Participants can register by filling the registration form and paying the registration fee as detailed below on the conference website. Registrations will be made on first come first serve basis, till the maximum number of participants (~400) have been reached.

OVERSEAS PARTICIPANTS	Till 30th Sep 2018	From 1st Oct 2018	On the spot
Full Delegate	US $ 200	US $ 300	US$ 400
Accompanying person	US $ 100	US $ 150	US$ 200
Student	US $ 100	US $ 150	US$ 200

PARTICIPANTS FROM INDIA (Non - BRSI)	Till 30th Sep 2018	From 1st Oct 2018	On the spot
Full Delegate	Rs 6000	Rs 7000	Rs 8000
Accompanying person	Rs 3000	Rs 3500	Rs 4000
Student	Rs 5000	Rs 6000	Rs 7000
Bio- Entrepreneurs Conclave	Rs 15000	Rs 17500	Rs 20000

BRSI MEMBERS	Till 30th Sep 2018	From 1st Oct 2018	On the spot
Full Delegate	Rs 5000	Rs 6000	Rs 7000
Accompanying person	Rs 3000	Rs 3500	Rs 4000
Student	Rs 4000	Rs 5000	Rs 6000

Paid delegates (full delegates and students) would be eligible to receive conference kit, attend all the scientific sessions and social programs as well as refreshments, lunch and dinner. Registered accompanying persons would be eligible to attend cultural programs as well as refreshments, lunch and dinner. The payment should be made online using the link available on the conference website.

Groundbreaking from 12th April - 12th May

RESEARCH NEWS

From other High Impact Journals

Stem cells from adults function just as well as those from embryos

April 24, 2018

A review of research on induced pluripotent stem cells (iPSCs) finds that donor age does not appear to influence their functionality. This validates iPSCs as a viable alternative to embryonic stem cells in regenerative medicine, and highlights the enormous potential of iPSCs derived from elderly patients to treat their age-related diseases.

The 2006 discovery of induced pluripotent stem cells -- which can be derived directly from a patient -- offers an attractive alternative. Their use has already been proved in a young patient: a boy suffering from a rare genetic disease, in which the skin blisters and tears off, recovered completely after receiving a skin transplant grown from his own gene-corrected stem cells.

However, questions remained about the impact of donor age on iPSC functionality -- an especially relevant point given that the elderly stand to benefit the most from these stem cells. Kränkel and colleagues therefore critically analyzed the available research to date, to summarize what is known and identify future research needs.

The analysis revealed that the age of the donor may reduce the efficiency at which their body cells can be reprogrammed into iPSCs. However, once generated, the stem cells appear to be rejuvenated -- with typical signs of aging reversed.

"iPSCs show improved functionality compared to the donor's regular body cells, and can be differentiated into mature body cells with a similar efficiency to younger stem cell donors," says Kränkel. "This means that stem cells from an elderly patient can be developed into other cells and returned to the patient for treatment."

Despite this promising conclusion, it is still a matter of debate as to whether cells from older donors have accumulated more damaging mutations than those of younger donors. "This seems logical," says Elisabeth Strässler, co-author of the study. "There is also the issue of whether such mutations persist during the transformation to stem cells, or whether they are repaired."

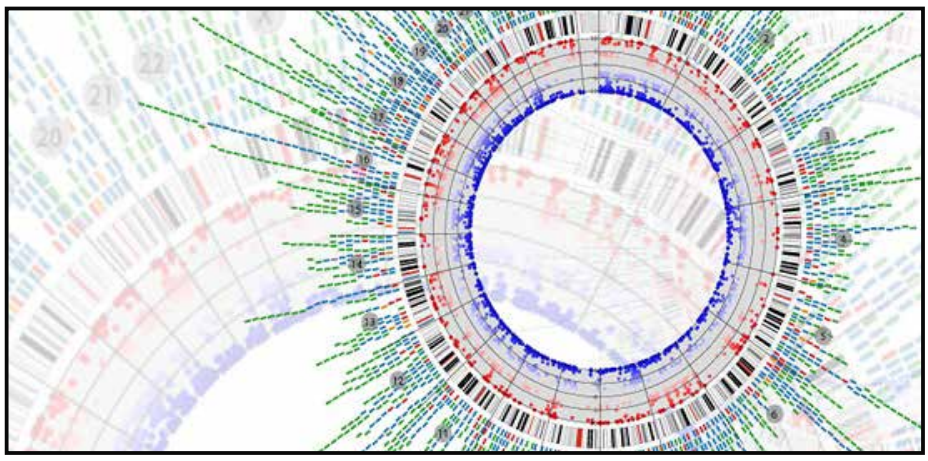
Journal Reference:

Age Is Relative—Impact of Donor Age on Induced Pluripotent Stem Cell-Derived Cell Functionality. Frontiers in Cardiovascular Medicine, 2018; 5 DOI: 10.3389/fcvm.2018.00004

Scientists generate Atlas of the human genome using stem cells

April 23, 2018

Scientists from the Hebrew University of Jerusalem have generated an atlas of the human genome using a



state-of-the-art gene editing technology and human embryonic stem cells, illuminating the roles that our genes play in health and disease.

The researchers analyzed virtually all human genes in the human genome by generating more than 180,000 distinct mutations. To produce such a vast array of mutations, they combined a sophisticated gene-editing technology (CRISPR-Cas9 screening) with a new type of embryonic stem cells that was recently isolated by the same research group. This new type of stem cells harbors only a single copy of the human genome, instead of two copies from the mother and father, making gene editing easier thanks to the need of mutating only one copy for each gene.

The researchers show that a mere 9% of all the genes in the human genome are essential for the growth and survival of human embryonic stem cells, whereas 5% of them actually limit the growth of these cells. They could also analyze the role of genes responsible for all hereditary disorders in early human development and growth. Furthermore, they showed how cancer-causing genes could affect the growth of the human embryo.

Another key finding of the study was the identification of a small group of genes that are uniquely essential for the survival of human embryonic stem cells but not to other cell types. These genes are thought to maintain the identity of embryonic stem cells and prevent them from becoming cancerous or turning into adult cell types.

"This study creates a new framework for the understanding of what it means to be an embryonic stem cell at the genetic level," said Dr. Atilgan Yilmaz, PhD, postdoctoral fellow and a lead author on the paper. "The more complete a picture we have of the nature of these cells, the better chances we have for successful therapies in the clinic."

Journal Reference:

Defining essential genes for human pluripotent stem cells by CRISPR–Cas9 screening in haploid cells. Nature Cell Biology, 2018; DOI: 10.1038/s41556-018-0088-1

New process to differentiate stem cells

April 17, 2018

As scientists try to find early therapy options to fight degenerative disc disease, there has been considerable interest in harnessing stem cells to restore nucleus pulposus, or NP. Previous research shows human induced pluripotent stem cells (hiPSCs) -- generated directly from adult cells -- can express markers for a wide variety of cells, including those that secrete NP.

Setton's lab exposed the hiPSCs to a variety of different growth factors and culture media to coax them into first developing markers for, and then fully forming into, notochord cells. Once the scientists had the notochord cells, they used a similar chemical exposure process to develop those into NP-type cells. The lab tracked the differentiating process using fluorescent cell imaging, which tested for the necessary markers during each step.

"You can think of it as a push-pull," Setton said. "You can push it in one direction, but you have to pull it from the other direction as well. I could push it toward a nerve, but I have to pull it from becoming bone. We didn't know what combination would work. It's like cooking in the kitchen, and you have to add things to the gravy. It took us a really long time to figure out that perfect recipe. But now that we did, it's very repeatable."

Setton says the multistep process her lab used to derive NP-type cells from the hiPSCs provides the necessary quality control as scientists seek additional uses for stem cell therapies. Setton says the research's next steps include assessing environmental cues -- such as the stiffness of the culture surface, cell topography and how a cell attaches -- and observe their effects in transforming hiPSCs.

Journal Reference:

Differentiation of human induced pluripotent stem cells into nucleus pulposus-like cells. Stem Cell Research & Therapy, 2018; 9 (1) DOI: 10.1186/s13287-018-0797-1

Incompatible donor stem cells cure adult sickle cell patients

April 25, 2018

Doctors at the University of Illinois Hospital have cured seven adult patients of sickle cell disease, an inherited blood disorder primarily affecting the black community, using stem cells from donors previously thought to be incompatible.

With the new protocol, patients with aggressive sickle cell disease can receive stem cells from family members if only half of their human leukocyte antigen (HLA) markers match. Previously, donors had to be a family member with a full set of matching HLA markers, or a "fully-matched" donor.

"We have made great strides curing adults with sickle cell disease with stem cell transplants, but the unfortunate truth is that the majority of these patients have, until now, been unable to benefit from this treatment because there are no fully-matched HLA-compatible donors available in their family," said corresponding author Dr. Damiano Rondelli, the Michael Reese Professor of Hematology and director of the Blood and Marrow Transplant program at the University of Illinois at Chicago.

The doctors screened 50 adult sickle cell patients as candidates for a half-matched stem cell transplant between January 2014 and March 2017. Ten patients received a transplant. Following two unsuccessful transplants, the doctors adopted the new treatment protocol, which included modifications to a process first developed at Johns Hopkins University.

"We modified the transplant protocol by increasing the dose of radiation used before the transplant, and by infusing growth factor-mobilized peripheral blood stem cells instead of bone marrow cells," Rondelli said. "These two modifications helped ensure the patient's body could accept the healthy donor cells."

Of the eight patients who underwent the revised transplant, one experienced

chronic graft-versus-host disease following the transplant and died of unknown causes. The other seven patients are alive and maintain 95 percent or higher stable engraftment -- acceptance of donor cells -- with improved blood work at least 12 months following the transplant.

"These patients are cured of sickle cell disease," Rondelli said.

"The takeaway message is twofold. First, this transplant protocol may cure many more adults patients with advanced sickle cell disease," he said. "Second, despite the increasing safety of the transplant protocols and new compatibility of HLA half-matched donors, many sickle cell patients still face barriers to care -- of the patients we screened, only 20 percent underwent a transplant."

Rondelli says that medical insurance denial accounted for 20 percent of the lack of access to the transplant.

Journal Reference:

Haploidentical Peripheral Blood Stem Cell Transplantation Demonstrates Stable Engraftment in Adults with Sickle Cell Disease. Biology of Blood and Marrow Transplantation, 2018; DOI: 10.1016/j.bbmt.2018.03.031

Identity of brain stem cells clarified

May 4, 2018

Unfortunately, when brain cells are damaged by trauma or disease they don't automatically regenerate. This can lead to permanent disability. But within the brain there are a small number of stem cells that persist into adulthood, offering a possible source of new cells to repair the damaged brain.

Work by researchers at the University of Calgary Faculty of Veterinary Medicine sheds new light on the identity of the brain cells that exhibit neural stem cell function.

One type, astrocyte neural stem cells, can self-renew and generate new neurons, particularly following brain injury. The other type -- called ependymal cells -- provide a supportive lining between the brain and the fluid that bathes the brain.

"Importantly, ependymal cells that line the caverns of the brain also sit right next to neural stem cells, suggesting that they might be important regulators of neural stem cell function,

"However, several high-profile studies have suggested that ependymal cells can actually become neural stem cells themselves, when activated by an injury to the brain. Our work provides evidence this is not the case and provides new insight into how they might contribute to brain function."

In the study, the researchers developed a process allowing them to specifically label ependymal cells within the adult brain, while avoiding astrocyte stem cells. Biernaskie says the research not only clarifies the identity of the adult neural stem cell, it also provides a new model to study the function of ependymal cells and their role in maintaining normal brain function.

Journal Reference:

Single-Cell Transcriptomics and Fate Mapping of Ependymal Cells Reveals an Absence of Neural Stem Cell Function. Cell, 2018; 173 (4): 1045 DOI: 10.1016/j.cell.2018.03.063

Fasting boosts stem cells' regenerative capacity

May 3, 2018

The age-related loss of stem cell function can be reversed by a 24-hour fast, according to a new study from MIT biologists. The researchers found that fasting dramatically improves stem cells' ability to regenerate, in both aged and young mice.

In fasting mice, cells begin breaking down fatty acids instead of glucose, a change that stimulates the stem cells to become more regenerative. The researchers found that they could also boost regeneration with a molecule that activates the same metabolic switch.

"Intestinal stem cells are the workhorses of the intestine that give rise to more stem cells and to all of the various differentiated cell types of the intestine. Notably, during aging, intestinal stem function declines, which impairs the ability of the intestine to repair itself after damage," Yilmaz says. "In this line of investigation, we focused on understanding how a 24-hour fast enhances the function of young and old intestinal stem cells."

After mice fasted for 24 hours, the researchers removed intestinal stem cells and grew them in a culture dish, allowing them to determine whether the cells can give rise to "mini-intestines" known as organoids.

The researchers found that stem cells from the fasting mice doubled their regenerative capacity.

Further studies, including sequencing the messenger RNA of stem cells from the mice that fasted, revealed that fasting induces cells to switch from their usual metabolism, which burns carbohydrates such as sugars, to metabolizing fatty acids. This switch occurs through the activation of transcription factors called PPARs, which turn on many genes that are involved in metabolizing fatty acids.

The researchers found that if they turned off this pathway, fasting could no longer boost regeneration. They also found that they could reproduce the beneficial effects of fasting by treating mice with a molecule that mimics the effects of PPARs.

The findings suggest that drug treatment could stimulate regeneration without requiring patients to fast, which is difficult for most people. One group that could benefit from such treatment is cancer patients who are receiving chemotherapy, which often harms intestinal cells. It could also benefit older people who experience intestinal infections or other gastrointestinal disorders that can damage the lining of the intestine.

Journal Reference:

Fasting Activates Fatty Acid Oxidation to Enhance Intestinal Stem Cell Function during Homeostasis and Aging. Cell Stem Cell, 2018; 22 (5): 769 DOI: 10.1016/j.stem.2018.04.001

Experimental arthritis drug prevents stem cell transplant complication

April 24, 2018

An investigational drug in clinical trials for rheumatoid arthritis prevents a common, life-threatening side effect of stem cell transplants, new research from Washington University School of Medicine in St. Louis shows.

Studying mice, the researchers found the drug prevented what's known as graft-versus-host disease, a debilitating, sometimes lethal condition that develops when transplanted stem cells attack the body's own organs or tissues.

In past work, this research team defined the role of molecules called JAK1/2 kinases and their signaling pathways in immune cell activation and graft-vs-host disease. In the new study, these same researchers evaluated ruxolitinib and baricitinib, and found baricitinib to be the superior of the two drugs in reducing and preventing graft-versus-host-disease in mice. Both drugs belong to a class of pharmaceuticals called JAK inhibitors that are known for dialing down inflammation.

Surprisingly, baricitinib did more than shut down graft-versus-host disease. It actually boosted the ability of the donor T cells to fight the cancer.

"We don't know yet exactly how this happens, but we're working to understand it," said first author Jaebok Choi, PhD, an assistant professor of medicine. "We think at least part of the explanation is the drug strips the leukemia cells of their immune defenses, making them more vulnerable to attack by the donor T cells. At the same time, the drug also stops the donor T cells from being able to make their way to important healthy tissues, such as the skin, liver and gastrointestinal tract, where they often do the most damage."

In other words, the drug appears to stop graft-versus-host disease by simply keeping the donor T cells circulating in the bloodstream, away from vital organs. Simultaneously, the drug makes the leukemia cells more vulnerable to immune attack from the donor T cells, which are now mostly confined to the bloodstream, where the cancer is.

The drug also appeared to boost levels of specific immune cells that put the brakes on a runaway immune response that can make graft-versus-host disease worse. These apparently independent effects are specific to baricitinib and may explain why other JAK inhibitors did not work as well, according to DiPersio, who is also deputy director of Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine.

The researchers emphasized the finding that the drug not only prevented graft-versus-host disease from developing in the mice but reversed established disease, suggesting possible options for patients already affected by it.

"We were surprised to achieve 100 percent survival of mice with the most severe model of graft-versus-host disease," Choi said. "We are now studying the multi-pronged ways this drug behaves in an effort to develop an even better version for eventual use in clinical trials."

Journal Reference:

Baricitinib-induced blockade of interferon gamma receptor and interleukin-6 receptor for the prevention and treatment of graft-versus-host disease. Leukemia, 2018; DOI: 10.1038/s41375-018-0123-z

Earth BioGenome Project aims to sequence genomes of 1.5 million species

April 23, 2018

An international consortium of scientists is proposing a massive project to sequence, catalog and analyze the genomes of all known eukaryotic species on the planet, an undertaking the researchers say will take 10 years, cost $4.7 billion and require more than 200 petabytes of digital storage capacity. There are an estimated 10-15 million eukaryotic species on Earth.

The proposed initiative, described in a paper in the Proceedings of the National Academy of Sciences, would require the cooperation of governments, scientists, citizen scientists and students from around the globe. The authors of the proposal compare it to the Human Genome Project, an international scientific research project from 1990 to 2006 that cost roughly $4.8 billion in today's dollars and generated an estimated return-on-investment ratio of 141-to-1.

A similar initiative, the Earth Microbiome Project, has enlisted the support of more than 500 scientists to sequence bacterial and archaeal genomes across the globe.

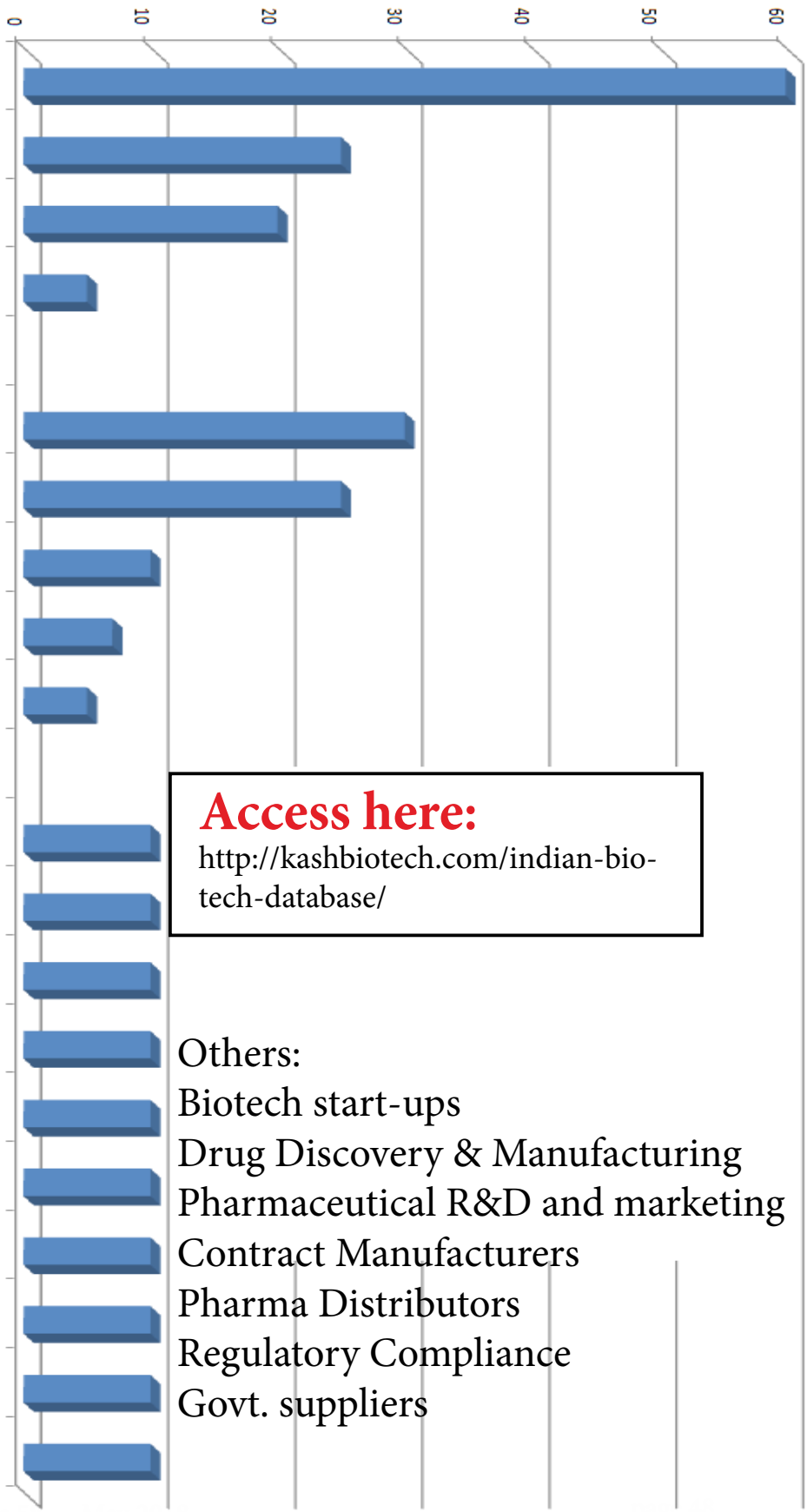
The EBP project will support and promote international protocols for data storage and sharing. A coordinating council with members from Africa, Australia, Brazil, Canada, China, the European Union and the United States will head a global network of collaborators. The council also will include representatives of several current large-scale genomics projects including the Global Genome Biodiversity Network, the Global Invertebrate Genomics Alliance, the i5K Initiative to Sequence 5,000 Arthropod Genomes and the Genome 10K Project.

Journal Reference:

Earth BioGenome Project: Sequencing life for the future of life. Proceedings of the National Academy of Sciences, 2018; 201720115 DOI: 10.1073/pnas.1720115115

For how long will the USA remain the Nobel Prize

Biotech LISTING



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Govt. suppliers

leader?

May 9, 2018

Since first being awarded in 1901, most Nobel Prizes for science have gone to the USA, the United Kingdom, Germany and France. An empirical study by Professor Claudius Gros from the Institute for Theoretical Physics at the Goethe University in Frankfurt has now shown that the Nobel Prize productivity in these countries is primarily determined by two factors: a long-term success rate, and periods during which each country has been able to win an especially large number of Nobel Prizes.

For the study, Nobel Prizes for physics, chemistry and medicine were assigned proportionately, since up to three scientists can share the prize. The success rates were calculated on the basis of population figures. For France and Germany, the periods of increased scientific creativity occurred around 1900, whereas for the USA it occurred in the second half of the 20th century.

"The US era is approaching its end," states Claudius Gros. "Since its zenith in the 1970s, US Nobel Prize productivity has already declined by a factor of 2.4." According to his calculations, a further decline is foreseeable. "Our model predicts that starting in 2025 the productivity of the USA will be below that of Germany, and from 2028, below that of France as well."

With a nearly constant, very high success rate per capita, Great Britain occupies a special position with regard to Nobel Prizes. It remains uncertain, however, whether Great Britain will be able to maintain this success, especially in view of the increasing industrialization of research.

"National research advancement can undoubtedly also be successful independent of Nobel Prize productivity," Claudius Gros stresses. "Especially because new areas of research such as the computer sciences -- a typical US domain -- are not included." It therefore remains open whether the decline in Nobel Prize productivity is cause for concern, or merely an expression of a new orientation toward more promising research fields.

Journal References:

Claudius Gros. An empirical study of the per capita yield of science Nobel prizes: is the US era coming to an end? Royal Society Open Science, 2018; 5 (5): 180167 DOI: 10.1098/rsos.180167

Claudius Gros. Pushing the complexity barrier: diminishing returns in the sciences. Complex Systems, 2012; 21: 183

Genetic roadmap to building an entire organism from a single cell

April 26, 2018

Now, in three landmark studies Harvard Medical School and Harvard University researchers report how they have systematically profiled every cell in developing zebrafish and frog embryos to establish a roadmap revealing how one cell builds an entire organism.

Using single-cell sequencing technology, the research teams traced the fates of individual cells over the first 24 hours of the life of an embryo. Their analyses reveal the comprehensive landscape of which genes are switched on or off, and when, as embryonic cells transition into new cell states and types.

The researchers leveraged the power of InDrops, a single-cell sequencing technology developed at HMS by Klein, Kirschner and colleagues, to capture gene expression data from each cell of the embryo, one cell at a time. The teams collectively profiled more than 200,000 cells at multiple time points over 24 hours for both species.

To map the lineage of essentially every cell as an embryo develops, along with the precise sequence of gene expression events that mark new cell states and types, the teams developed new experimental and computational techniques, including the introduction of artificial DNA bar codes to track the lineage relationships between cells, called TracerSeq.

In the study co-led by Schier, the research team used Drop-Seq -- a single-cell sequencing technology developed by researchers at HMS and the Broad Institute of MIT and Harvard -- to study zebrafish embryos over 12 hours at high time resolution. Teaming with Aviv Regev, core member at the Broad, Schier and colleagues reconstructed cell trajectories through a computational method they named URD, after the Norse mythological figure who decides all fates.

Schier and colleagues profiled more than 38,000 cells, and developed a cellular "family tree" that revealed how gene expression in 25 cell types changed as they specialize. By combining that data with spatial inference, the team was also able to reconstruct the spatial origins of the various cells types in the early zebrafish embryo.

Journal References:

The dynamics of gene expression in vertebrate embryogenesis at single-cell resolution. Science, 2018; eaar5780 DOI: 10.1126/science.aar5780

Systematic mapping of cell state trajectories, cell lineage, and perturbations in the zebrafish embryo using single cell transcriptomics. Science, 2018

Single-cell reconstruction of developmental trajectories during zebrafish embryogenesis. Science, 2018; eaar3131 DOI: 10.1126/science.aar3131

Genomics is disrupting the healthcare sector

May 4, 2018

The independent report shows that genomics is already driving a remarkable paradigm shift in health practices and outcomes.

In the last 15 years, the cost of reading an individual's DNA sequence -- their genome -- has plummeted from hundreds of millions of dollars to around the cost of a shoulder MRI. This is ushering in a new era of precision healthcare, in which treatments, prevention strategies and health advice will reach the right person at the right time.

Applications of genomics in cancer, rare disease and reproductive services are

booming, the report finds, with other clinical areas set to follow suit. The report shows that over 250 FDA-approved drugs are now labelled for prescribing based on the patient's genetics -- a number that has tripled since 2014.

A comprehensive resource, the report draws on patents, scientific publications, and clinical trials data to map out the emerging medical and consumer health applications of genomics.

The report shows that practical biomedical applications for genomics have stimulated the formation of hundreds of new companies globally -- particularly in the US. It surveys the diverse business models being used to transform fundamental discoveries into commercial products. It also ranks leading research organizations involved in genomic discovery and quantifies their R&D relationships with industry.

Story Source:

Materials provided by Garvan Institute of Medical Research.

Scientists discover gene controlling genetic recombination rates

April 21, 2018

Researchers hypothesize that crossover rates have evolved to balance the benefits of crossing over with the risks of selfish DNA.

Presgraves and PhD candidate Cara Brand recently accomplished an important milestone in learning about these evolutionary dynamics. By studying two species of fruit flies, they discovered a gene, MEI-218, that controls the rate of recombination. In a paper published in Current Biology, they explain how MEI-218 controls differences in the rate of crossing over between species and the evolutionary forces at play. "This is the first gene I know of that anyone has shown to be responsible for the evolution of recombination rates," Presgraves says.

The team focused on two closely related species of fruit flies -- Drosophila melanogaster and its sister species, Drosophila mauritiana -- because large differences have evolved in their rates of recombination: D. mauritiana does about 1.5 times more crossing over than D. melanogaster. When they compared genes in the two different species, the researchers found that the DNA sequences of MEI-218 were extraordinarily different.

Brand and Presgraves hypothesize that the change in recombination rates between D. mauritiana and D. melanogaster may have evolved because the species have different amounts of transposons in their genomes. The D. melanogaster genome has more transposons than D. mauritiana, so D. melanogaster may therefore have evolved a lower rate of crossing over in order to avoid the higher risk of harmful crossovers between transposons.

This means, then, that the MEI-218 gene is constantly evolving to an ever-changing optimum. The evolution of MEI-218 is similar to genes involved in immunity, Presgraves says. "That should make some intuitive sense because genes involved in immunity are constantly adapting to the changing community pathogens that are challenging us all the time."

The MEI-218 gene has so far only been investigated in fruit flies, but the research into recombination has applications for humans. "During meiosis at least one crossover per chromosome, in general, is required to make sure the chromosomes separate properly," Brand says. "Either a lack of crossing over or crossing over in the wrong regions of the genome is what leads to many birth defects like Down Syndrome."

Journal Reference:

Molecular Evolution at a Meiosis Gene Mediates Species Differences in the Rate and Patterning of Recombination. Current Biology, 2018; DOI: 10.1016/j.cub.2018.02.056

Solving the structure of ATP synthase

April 17, 2018

"Understanding how the enzyme actually works requires the knowledge of its three dimensional molecular structure at the atomic level," said Dr. Mueller, principal investigator for the study that used cryo-electron microscopy (cryo-EM) to reveal the enzyme at near atomic resolution.

The first complete structure of ATP synthase provides evidence for the mechanism by which the drug oligomycin inhibits the enzyme and how disease-causing mutations disrupt the function of the molecule. Solving the structure overcomes a barrier to understanding its likely broader function in disease and drug mechanisms.

They used cryo-EM analysis to decipher the engineered ATP synthase, which was synthesized in yeast and reconstituted into nanodiscs to allow for structural analysis. While cryo-EM isn't new, advancements in technology have made it possible to solve the structure at near atomic resolution.

Journal Reference:

High-resolution cryo-EM analysis of the yeast ATP synthase in a lipid membrane. Science, 2018; eaas9699 DOI: 10.1126/science.aas9699

Researchers describe genetic clockwork in germ cell development

April 16, 2018

To reproduce, *C. elegans* must produce gametes, that is male sperm and female eggs. These develop from undifferentiated dividing stem cells. Extensive intracellular restructuring is required to realize these processes, which have to mesh faultlessly if the cells are to develop successfully," Eckmann continues. A highly intricate clockwork mechanism with many interlocking gears gives some idea of the level of sequencing complexity involved.

These processes are controlled by RNA-binding proteins. Outside of the nucleus, in the cytoplasm, these proteins regulate selective gene activation. For a germ cell to develop out of a stem cell, two specific RNA-binding proteins need to be destroyed to reorganise the cell's genetic programme. How, when and why the signal for this developmental switch is given was previously unclear. The researchers from Halle have now figured out that the already familiar MAP kinase signalling pathway plays a central role. Eckmann summarises the process as follows: "A protein degradation cascade is initiated via this molecular pathway, at the end of which the two target proteins CPB-3 and GLD-1 are recognised, inactivated, and destroyed."

The geneticists at MLU were able to demonstrate that this process already operates at a very early stage in meiosis and corresponds temporally to the sexual differentiation onset of female germ cells. The processes are thus optimally co-ordinated. According to Eckmann, "The special thing about these processes is that they involve known molecules with very long evolutionary histories, previously receiving attention as suppressors of tumour formation within the context of normal cell division. In C. elegans, these molecules were interleaved in an innovative way. The processes were adapted and temporally co-ordinated to facilitate optimized, rapid germ cell production." These findings of the MLU research group on Developmental Genetics suggest that the same genetic program may operate in germ cells of other, more complex organisms as well -- albeit in a timely less compressed form.

Journal Reference:

MAPK signaling couples SCF-mediated degradation of translational regulators to oocyte meiotic progression. Proceedings of the National Academy of Sciences, 2018; 115 (12): E2772 DOI: 10.1073/pnas.1715439115

New cell therapy to aids heart recovery -- without cells implant

Medical researchers have designed a creative new approach to help injured hearts regenerate by applying extracellular vesicles secreted by cardiomyocytes rather than implanting the cells. The study shows that the cardiomyocytes derived from human pluripotent stem cells (derived in turn from a small sample of blood) could be a powerful, untapped source of therapeutic microvesicles that could lead to safe and effective treatments of damaged hearts.

Cell-secreted microvesicles are easy to isolate and can be frozen and stored over long periods of time. Such an "off-the-shelf" product has several major advantages over cell therapy -- 1) it can be used immediately in an acute-care setting, unlike cells that can take months to isolate and grow; 2) it does not cause arrhythmia (which often occurs when cells are transplanted); and 3) the regulatory path towards clinical application is much simpler than for a cell-based therapy.

It is well known from numerous clinical studies that most of the implanted stem cells are washed away within hours of the treatment, but there still are beneficial effects. This has led to the informal "hit-and-run" hypothesis, meaning that the cells deliver their cargo of regulatory molecules before leaving the site of injury. "Consistent with this hypothesis, we postulated that the benefits of cell therapy of the heart could be coming from the secreted bioactive molecules (such as micro RNAs), rather than the cells themselves,

"We reasoned that the cardiomyocytes would be the best source of molecules driving the recovery of injured heart, as it is well known that these cells can build muscle when used in tissue-engineering models,

The interdisciplinary team, which included bioengineers, clinicians, and systems biology scientists, derived cardiomyocytes from adult human stem cells and cultured these cells to allow them to secrete extracellular vesicles. The vesicles secreted by undifferenciated stem cells were used for comparison. The researchers then used next-generation sequencing to read their messages and instructions. They found that the extracellular vesicles from cardiomyocytes -- but not from stem cells -- contained cardiogenic and vasculogenic microRNAs that are very powerful regulatory molecules.

Building on the expertise of Vunjak-Novakovic's lab in biomaterials and hydrogels, the team encapsulated the vesicles in a collagen-based patch that slowly released them over the course of four weeks when implanted onto the injured heart in rat models of myocardial infarction. The researchers monitored the heart to measure blood-pumping function and look for any signs of arrhythmia.

"We were really excited to find that not only did the hearts treated with cardiomyocyte extracellular vesicles experienced much fewer arrhythmias, but they also recovered cardiac function most effectively and most completely," says Vunjak-Novakovic. "In fact, by four weeks after treatment, the hearts treated with extracellular vesicles had similar cardiac function as those that were never injured."

Journal Reference:

Cardiac recovery via extended cell-free delivery of extracellular vesicles secreted by cardiomyocytes derived from induced pluripotent stem cells. Nature Biomedical Engineering, 2018; DOI: 10.1038/s41551-018-0229-7

World's smallest optical implantable biodevice

April 25, 2018

Japanese researchers describe a new implantable device no bigger than the width of a coin that can be used to control brain patterns. The device, which can be read about in AIP Advances, converts infrared light into blue light to control neural activity and is both the smallest and lightest wireless optical biodevice to be reported.

The new device made by Tokuda's research team uses a complementary metal-oxide semiconductor that controls photovoltaic power. "We integrated two sets of photovoltaic cells onto semiconductor chips. Ten cells were integrated for powering, and seven cells for bias-

ing," he said.

The device includes an InGan LED chip, which causes the device to emit blue light. A more distinguishing feature of the device, however, is that it can be activated with infrared light. Infrared is used in many light therapies, because it can penetrate deep in the body, whereas blue light cannot go much deeper than the surface. Therefore, the device can be implanted several centimeters into the body.

Journal Reference

1 mm3-sized optical neural stimulator based on CMOS integrated photovoltaic power receiver. AIP Advances, 2018; 8 (4): 045018 DOI: 10.1063/1.5024243

3-D printed food now

April 24, 2018

Jin-Kyu Rhee, associate professor at Ewha Womans University in South Korea, discussed his new research and the potential of 3-D printing technology for food production at the American Society for Biochemistry and Molecular Biology annual meeting during the 2018 Experimental Biology meeting held on April 21-25 in San Diego.

"We built a platform that uses 3-D printing to create food microstructures that allow food texture and body absorption to be customized on a personal level," said Rhee. "We think that one day, people could have cartridges that contain powdered versions of various ingredients that would be put together using 3-D printing and cooked according to the user's needs or preferences."

3-D printing of food works much like 3-D printing of other materials in that layers of raw material are deposited to build up a final product. In addition to offering customized food options, the ability to 3-D print food at home or on an industrial scale could greatly reduce food waste and the cost involved with storage and transportation. It might also help meet the rapidly increasing food needs of a growing world population.

For the new study, the researchers used a prototype 3-D printer to create food with microstructures that replicated the physical properties and nanoscale texture they observed in actual food samples. They also demonstrated that their platform and optimized methods can turn carbohydrate and protein powers into food with microstructures that can be tuned to control food texture and how the food is absorbed by the body.

Story Source:

Experimental Biology 2018.

New take on early evolution of photosynthesis

April 24, 2018

A team of scientists from Arizona State University's School of Molecular Sciences has begun re-thinking the evolutionary history of photochemical reaction centers (RCs). Their analysis was recently published online in Photosynthesis Research and describes a new pathway that ancient organisms may have taken to evolve the great variety of photosynthetic RCs seen today across bacteria, algae, and plants.

There are two types of RCs that exist today: Type I RCs support metabolism by moving electrons to soluble proteins, while Type II RCs move electrons to membrane-associated molecules. However, evidence has been building in the lab of professor Kevin Redding that the RC from the heliobacteria may be able to perform both of these functions, making it a functional hybrid of the two RC types.

The heliobacterial RC is thought to be one of the simplest RCs still around today. It is homodimeric, meaning that its core is composed of two copies of the same protein. This contrasts with the two RCs from oxygen-producing organisms like plants whose core is heterodimeric, having their core composed of two similar, but not identical, proteins.

The team believes that the ancestral reaction center (ARC) was simpler than the versions that exist today. This ARC was probably homodimeric and interacted with molecules in the membrane, like the modern Type II RCs (and the heliobacterial RC), instead of with soluble proteins.

It is very difficult to reconstruct these evolutionary steps, which took over 3 billion years to occur. One way in which this is generally done is to compare the amino acid sequences of the proteins and note the number of differences between them, assuming that more similarity means that they are more closely related. In their study, however, the team cautions against relying heavily on this method for RCs. The sequence differences are just too numerous and too much time has passed to obtain reliable information from this method.

They instead compared the positions of protein structural elements and chlorophylls within the RCs.

The team envisions that the ARC, in its simplest form, was probably rather inefficient at its chemistry. Its job was to use the energy of sunlight to provide two electrons to a membrane-associated molecule called a quinone. However, the ARC likely could loosely bind two quinone molecules, one on each side of the core. With two identical-looking quinones, the ARC was not able to prioritize which quinone would get electrons, making it less likely that either would get the two it needed.

This problem was solved in two different ways. In the lineage that led to the modern Type II RCs, the core changed from homodimeric to heterodimeric, which allowed the RC to prioritize which quinone it gave electrons to, accelerating the chemistry. In the lineage that led to the modern Type I RCs, the core remained homodimeric, but a metal cluster was added so that the first electron would end up there, facilitating its delivery to the quinone that received the next electron.

Once the ARC had acquired the metal cluster, thus becoming the ancestor to all modern Type I RCs, more changes occurred to further direct electrons to a soluble acceptor, which resulted in extracting more energy for the cell's metabolism. These included changes in the positions and identities of the chlorophyll cofactors. Much of the later changes in the Type I RCs were driven by the need to deal with the presence of oxygen, as the unstable intermediates within RCs can react with oxygen to generate very

damaging molecules. In the opinion of the ASU team, the heliobacterial RC retains clear vestiges of the changes leading to the early Type I RC and that understanding the fine details in how modern RCs work allows for informed hypotheses about how they evolved.

Journal Reference:

Gregory S. Orf, Christopher Gisriel, Kevin E. Redding. Evolution of photosynthetic reaction centers: insights from the structure of the heliobacterial reaction center. Photosynthesis Research, 2018; DOI: 10.1007/s11120-018-0503-2

Newly improved microscopic glass slide works as a thermometers too

May 2, 2018

A new study describes how an updated version of the microscope slide can enable scientists to see tiny objects while also measuring their temperature. The advancement, made possible by a new transparent, has the potential to streamline and enhance scientific research worldwide, from clandestine government biology labs to high school chemistry classes. It may also have implications in computers, electronics and other industries.

The new coating is made of a layer of acrylic glass (the same material used in most eyeglasses) that's sandwiched between two layers of transparent gold. The gold is transparent because it's only 20 nanometers thick; a typical sheet of paper is 100,000 nanometers thick.

Engineers fabricated the coating so that "exceptional points" -- the sweet spots where unusual light behavior happens -- can develop within the tri-layered structure. The coating, which significantly enhances the slide's sensitivity to light detection, would be added to slides during the manufacturing process. Either the slide or cover slip could receive the coating.

To make use of the new coating, a laser is needed. Zhao says a common helium-neon laser, which can be seamlessly integrated with most microscopes, will do the job.

Common slides, which are often bought in bulk, typically cost around 5 cents. The new coating would likely add a few pennies to the cost, Zhao says.

Journal Reference:

Exceptional point engineered glass slide for microscopic thermal mapping. Nature Communications, 2018; 9 (1) DOI: 10.1038/s41467-018-04251-3

Biophysics -- lighting up DNA-based nanostructures

April 24, 2018

The term 'DNA origami' refers to a method for the design and self-assembly of complex molecular structures with nanometer precision. The technique exploits the base-pairing interactions between single-stranded DNA molecules of known sequence to generate intricate three-dimensional nanostructures with predefined shapes in arbitrarily large numbers. The method has great potential for a wide range of applications in basic biological and biophysical research. Thus researchers are already using DNA origami to develop functional nanomachines.

With the aid of a super-resolution technique called DNA-PAINT, the researchers are able to visualize nanostructures with unprecedented spatial resolution, allowing them to image each of the strands in the nanostructures.

The results obtained with the DNA-PAINT method revealed that variations in several physical parameters -- such as the overall speed of structure formation -- have little influence on the overall quality of the assembly process. However, although its efficiency can be enhanced by the use of additional staple strands, not all strands were found in all of the nanoparticles formed, i.e. not all available sites were occupied in all of the final structures. "When assembling nanomachines it is therefore advisable that the individual components are added in large excess and the positions of the modifications chosen in accordance with our mapping of incorporation efficiency," Strauss says.

The DNA-PAINT method thus provides a means of optimizing the construction of DNA nanostructures. In addition, the authors believe that the technology has great potential in the field of quantitative structural biology, as it will allow researchers to measure important parameters such as the labelling efficiency of antibodies, cellular proteins and nucleic acids directly.

Journal Reference:

Quantifying absolute addressability in DNA origami with molecular resolution. Nature Communications, 2018; 9 (1) DOI: 10.1038/s41467-018-04031-z

Witness forgery data fabrication and scientific misconduct in Calcutta University

Source: www.kashbiotech.com

Jayita Barua has accused assistant professor Anindita Ukil and her laboratory colleagues of fabricating data to generate scientific papers intended for submission to research journals and claimed she had also been part of "this game".

Barua had sent an email to the Journal of Biological Chemistry on April 12, seeking withdrawal of her name as co-author of the paper, claiming it contained fabricated data, and attaching raw data to back her claim. She also alleged in the email that her colleagues, responding to a request from the JBC's art editor, had used pencil marks to cover up the data fraud.

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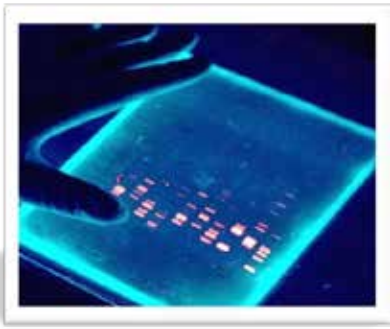

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Training Topics

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- Sterility Test
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- Environmental Monitoring of Clean Room Areas
- Growth promotion test
- Microbiological Analysis of Pharmaceutical Grade Water
- Maintenance and Preservation of Microbial Cultures
- Morphological, Cultural & Biochemical Identification of Microorganisms
- Genomic Identification of bacterial and fungal species using 16 sDNA & ITS tool sequencing
- Phylogenetic analysis of microorganism by BLAST & FASTA
- Calibration/ Validation of instruments
- Good Microbiological Laboratory Practices
- Good Documentation Practices

Chemistry & Phytopharmaceutical

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- UV-Spectrophotometry
- FTIR-Spectrophotometry
- HPLC
- HPTLC
- NMR
- GC
- GC-MS
- LC-MS
- ICP-MS
- Dissolution
- Disintegration Test
- Polarimetry
- Microscopy
- Extraction of Herbal drugs
- Identification of herbal drugs using HPTLC & DNA barcoding
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- Good Laboratory Practices
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- Biotechnology Training: 6,000 Rs
- Chemistry Training: 6,000 Rs
- Phytopharmaceutical Training: 6,000 Rs

Contact

For any further query regarding training program please contact.
Mr. Pradeep Sharma
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NOTIFICATIONS

ADMISSIONS

Friedrich Miescher Institute International PhD Program in Switzerland 2018
(Last date: 01/05/2018)

PhD Fellowships for Excellence at Biozentrum University of Basel in Switzerland, 2018
(Last date: 20/06/2018)

Swiss National Science Foundation Ambizione Research Grants for Foreign Researchers
(Last date: 01/11/2018)

National University of Singapore Scholarships for International Students, 2018
(Last date: May 15, 2018)

Commonwealth Distance Learning Scholarships
(Last date: June 20, 2018)

http://kashbiotech.com/articles-in-magazine/recent-biotech-notifications/

CSIR-Indian Institute of Chemical Technology

(Council of Scientific & Industrial Research)

Hyderabad 500007

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CSIR-IICT: PhD-August 2018

PhD Program

Invites Application for Ph.D. Programme under AcSIR

CSIR-IICT invites online applications from highly talented research oriented candidates to join as Research Fellow (RF) for PhD programme (Academic Session August 2018) in the areas of (i) Science (ii) Pharmacology and (iii) Engineering under the Academy of Scientific and Innovative Research (AcSIR).

Area of Research

- **Organic Chemistry/Analytical Chemistry/ Polymers & Functional Materials**
- **Inorganic & Physical Chemistry/ Medicinal Chemistry & Pharmacology**
- **Molecular Modelling/Computational Chemistry**
- **Biology/ Chemical Biology/ Bioinformatics**
- **Biochemical Engineering and Environmental Sciences & Engineering**
- **Chemical Engineering/Chemical Technology/Petro Chemical**

Essential Qualifications:

1. **PhD Program in Science (Chemical / Biological Sciences/Pharmacology):** M.Sc./ M.Pharm or equivalent degree in Chemistry (Organic/Inorganic/ Physical/Analytical/Medicinal and Polymers): Biology/ Biotechnology/ Microbiology/ Environmental/ Genetic/ Zoology/ Physics or Allied Sciences with a Valid rank in CSIR/UGC NET JRF examination, or a valid DST-INSPIRE/ICMR/DBT Fellowship.
2. **PhD Program in Engineering (through CSIR-JRF-GATE Fellowship):** BE/B.Tech. or equivalent degree in Chemical Engineering/Biochemical Engineering/ Environmental Engineering/Biotechnology/Petrochemical Engineering with a valid GATE score/NET (Engg). ***(ME/M.Tech degree holders are not eligible for JRF GATE fellowship)***

   However: ME/M.Tech in the above disciplines with a valid PhD Fellowship are eligible to apply for PhD Program.

Note:

The candidates who have passed CSIR-UGC-NET examination, under the "Lectureship category" are NOT eligible.

Application procedure:

Candidates who fulfil the eligibility criteria may apply for PhD Admission in AcSIR at CSIR-IICT through AcSIR online portal www.acsir.res.in/admission-process/ by giving the CSIR-IICT as first preference on or before **May 24, 2018**

Selection Procedure at CSIR-IICT

List of shortlisted candidates along with the date of Interview is expected to be displayed in CSIR-IICT website by **June 04, 2018.**

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