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."

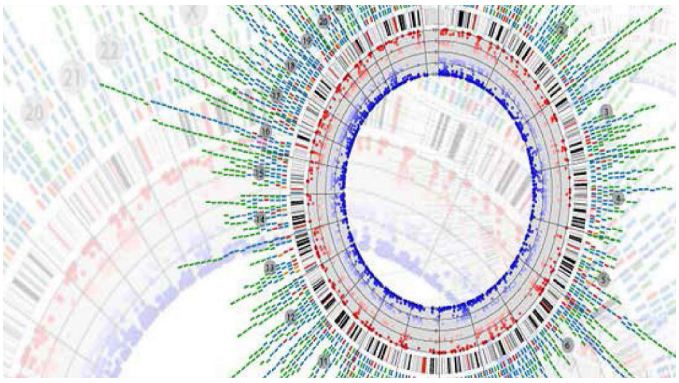
Journal Reference:

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 graftversus-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 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 higherrisk 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.ub.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-theshelf" 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 undiffereniated 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 biasing," 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.