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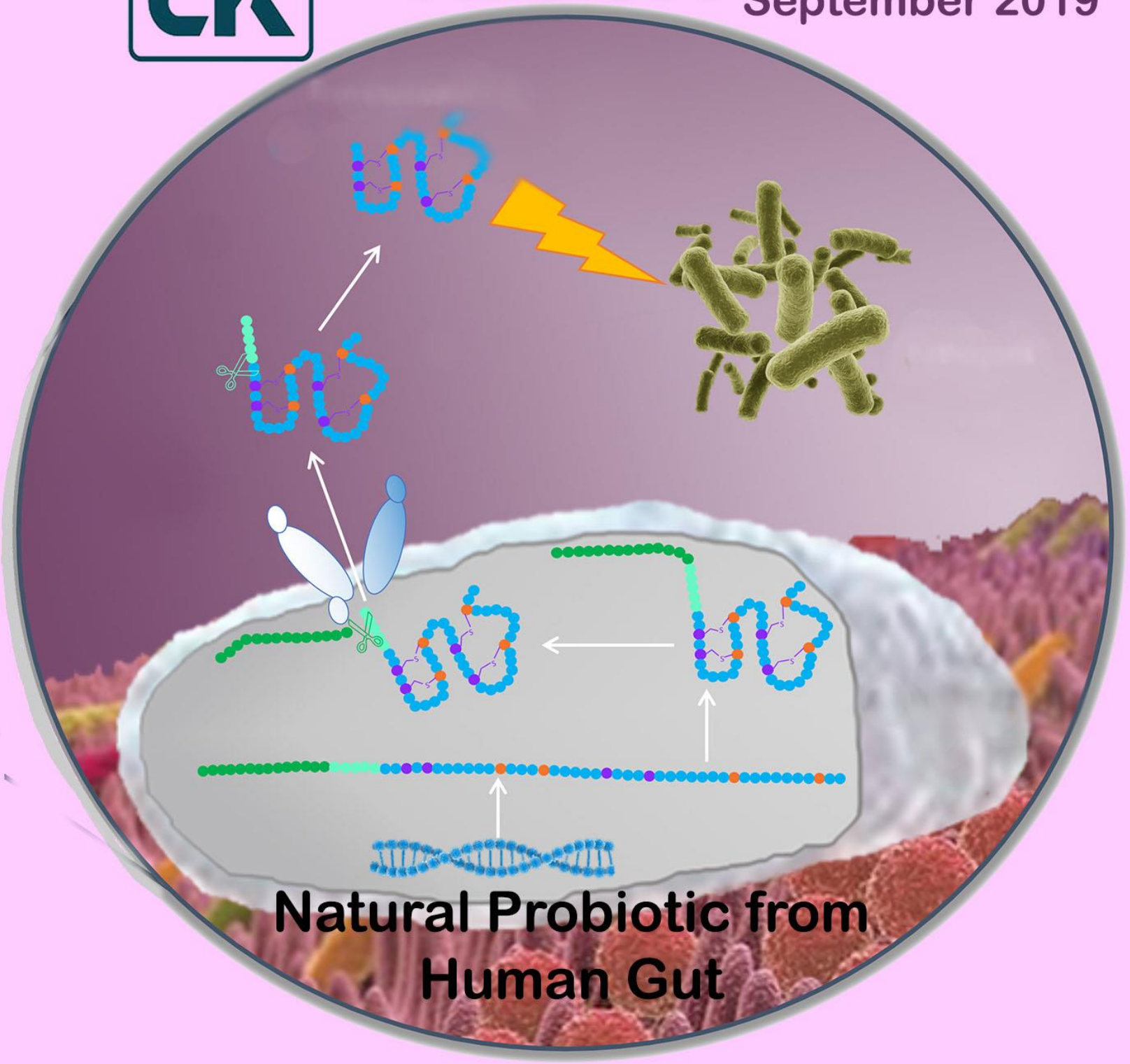

Natural Probiotic from Human Gut

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From the Publisher's Desk

Welcome to Biotechnology Kiosk!

We are ready with the fourth issue of Biotechnology Kiosk (BK) magazine. As we have been presenting in every issue, it has regular features including high-end editorials by experts, biotechnology advances around the world and industry news from pharma and biotech sectors. In this issue, biotechnology advances around the world covers cutting edge research breakthroughs in a vast array of fields in modern biotechnology that include coupling neuro-engineering and robotics, microbial science, connected organoid systems and agriculture, genetics and plant biotechnologies. We are glad that BK's presence on LinkedIn, Facebook and Twitter is growing. Please follow us on LinkedIn, Facebook and Twitter pages that get updated periodically with new information.

As we promised to introduce additional popular features to make BK more information-filled for our readers, we are happy to announce that we will soon start a Q&A series 'Entrepreneur Insight' that will include a background story and interview with

notable biotech entrepreneurs. The entrepreneur selected by BK executive publishers will be designated as entrepreneur of the month. Please stay tuned for this exciting addition of BK that will appear soon.

Please do write to us with your comments and feedback. Your suggestions are always appreciated.

We do hope that you will enjoy reading this issue of Biotechnology Kiosk.

Dr. Megha Agrawal and Dr. Shyamasri Biswas

Executive Publishers and Editors

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COLUMNS

Regenerative Medicine

By Megha Agrawal, PhD

Executive Editor

Cardiac Muscle Tissue Scaffolding helps restore Heart Functions

Myocardial infarction (MI) refers to heart attack, which is a serious medical condition. MI corresponds to the irreversible death of heart muscle after a prolonged lack of oxygen supply (ischemia). A heart attack leads to the development of scar tissue that diminishes heart muscle function, which eventually results in catastrophic heart failure. Each year, an estimated 785,000 new heart attack cases occur in the United States with a high fatality rate. This is due to the fact that there is no established treatment currently available that can be employed for repairing the resulting damage to cardiac tissue.

Researchers have employed regenerative medicine to treat patients with MI and ischemic heart failure. In the regenerative medicine based approach, researchers investigated several growth factor and gene therapeutics. However, the vast majority of trials have employed different types of stem cells. Heart tissues are not only comprised of cells but they also include a distinct scaffolding framework, which is known as the extracellular matrix (ECM). The main challenge that the researchers have faced is replicating the native cardiac ECM. The ECM has many constituents that consist of numerous proteins and proteoglycans that has a unique tissue-specific composition. This provides cues that influence all aspects of cell behavior that is necessary for proper tissue function as well as repair. An MI not only causes cell death, but also results in an inflammatory response and up-regulation of matrix metalloproteinase that ultimately degrade the native cardiac ECM [1-3].

More recently, research has focused on developing innovative biomaterials that can increase cardiac muscle, reduce fibrosis, and eventually lead to significant improvements in both global and regional function after percutaneous, trans-endocardial delivery. It also includes preclinical safety standards that comprise adequate biocompatibility, hemo-compatibility, and lack of arrhythmias. The goal of the current research efforts is to replace the abnormal microenvironment in the native cardiac ECM with healthy myocardial ECM cues to facilitate cardiac repair after an MI [4].

Injectable ECM Hydrogel Scaffold Designed to Repair Damage and Restore Cardiac Function

In a research of major impact and significance, scientists recently evaluated the safety and feasibility of trans-endocardial injections of a novel cardiac ECM hydrogel, in early and late post MI patients with left ventricular dysfunction. They successfully conducted a first-in-human, FDA-approved Phase 1 clinical trial of an injectable ECM hydrogel that is made of cardiac muscle tissue. This injectable, catheter-deliverable hydrogel is derived from porcine decellularized myocardial ECM [4].

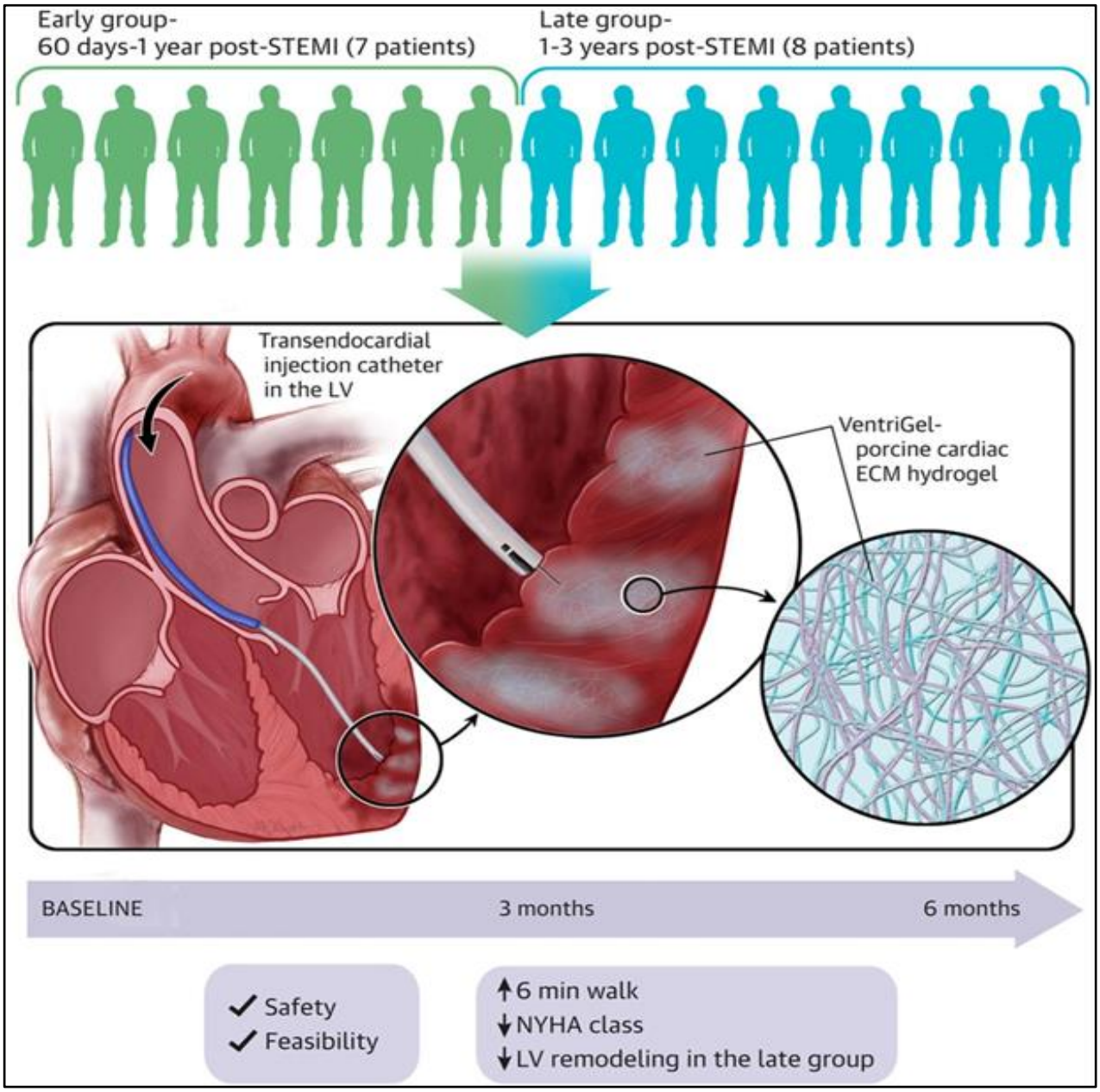

*Figure 1: The schematic process of injecting ECM hydrogel into the damaged region of heart and the phase 1 clinical trial [**Source:** JACC: Basic to Translational Science, 2019].*

This innovative hydrogel is designed to repair damage and restore cardiac function in heart failure patients who previously suffered a heart attack. The clinical trial conducted by the scientists is the first to test an ECM hydrogel designed to repair cardiac tissue in human. This research also demonstrates for the first time testing of a hydrogel made from the natural scaffolding of cardiac muscle tissue [4].

The hydrogel forms a scaffold that acts as a reparative environment where healthy cells migrate, once the gel is injected in damaged cardiac muscle. This phenomenon then leads to an increase in cardiac muscle, and less scar tissue that results in improvements in the heart function. The process of making the hydrogel involves taking cardiac connective tissue by stripping heart muscle cells through a cleansing process from pigs. It is subsequently freeze-dried and milled into powder form. The fluid which is generated can then be easily injected into heart muscle in a minimally invasive procedure that does not require surgery (Figure 1). Once it hits body temperature, the liquid turns into a semi-solid that forms a porous gel [4]. The Phase 1 trial of the hydrogel evaluated by the researchers involved 15 patients (Figure 1), who had sustained moderate damage in the left ventricle chamber of the heart following a heart attack. The trial showed that the hydrogel can be safely injected via catheter into patients who had suffered a heart attack in the past 2 to 36 months. Each patient was injected up to 18 doses of gel into the damaged region via catheter. Researchers then followed the patients for six months after this gel-based treatment [4].

This study is significant because of the fact that ECM hydrogels that have been shown in the preclinical studies have also the potential to be effective for other conditions. For example, such hydrogels could be beneficial in poor blood circulation that occurs due to peripheral artery disease.

Concluding Remarks

The field of regenerative medicine for the heart has evolved and grown from the earlier cell transplantation to increasingly preclinical studies on biomaterials or matrix-based approaches that help to recreate a more appropriate microenvironment for tissue repair. This transition of regenerative medicine in both cardiovascular and non-cardiovascular applications is further noticeable by the modern translational applications of biomaterial-alone therapies that can facilitate endogenous repair. In this regard, the latest advances in clinical trials to evaluate an injectable biomaterial hydrogel delivered via percutaneous trans-endocardial injections for cardiac repair are of immense value and interests. These new ECM technologies are expected to show significant advantages over the traditional regenerative medicine therapeutics.

References

1. E.C. Perin, L. Miller, and D.A. Taylor, et al., (2016). Stem Cell and Gene Therapy for Cardiovascular Disease. *Academic Press, Cambridge, MA,* https://doi.org/10.1016/C2014-0-00701-0
2. I.T. Swinehart and S.F. Badylak, (2016). Extracellular matrix bioscaffolds in tissue remodeling and morphogenesis. *Dev Dyn*, 245, pp. 351-360.

3. J.M. Singelyn, J.A. DeQuach, and S.B. Seif-Naraghi, et al., (2009). Naturally derived myocardial matrix as an injectable scaffold for cardiac tissue engineering, *Biomaterials*, 30, pp. 5409-5416.

4. Jay H. Traverse, Timothy D. Henry, and Nabil Dib, et al., (2019). First-in-Man Study of a Cardiac Extracellular Matrix Hydrogel in Early and Late Myocardial Infarction Patients. *JACC: Basic to Translational Science,*doi.org/10.1016/j.jacbts.2019.07.012.

Enzyme Biotechnology

By Shyamasri Biswas, PhD

Executive Editor

Can Gut Enzyme Fight Deadly Drug-Resistant Infections?

The resurgence of microbial infections caused by multidrug-resistance (MDR) strains poses a serious healthcare challenge for public. According to some survey and estimates for the public healthcare risks for the coming decades, millions of people around the world are considered at risk of serious bacterial infections due to the emergence of MDR [1, 2]. To mitigate this serious threat to the global human healthcare, biotechnologists and medical researchers are working together to discover novel antimicrobial molecules and viable natural pathways to combat this challenge. To this end, the human gut microbiome is being further researched that has largely remained unexplored so far. It has been suggested that the human gut microbiome could potentially contain a treasure trove of information about new natural molecules including ribosomally-synthesized and post-translationally modified peptides (RiPPs) that could be leveraged for the development of powerful probiotic and drugs [3]. Previous researches have shown that RiPPs can be biosynthesized from a genetically encoded precursor peptide that usually contains an N-terminal leader sequence and a C-terminal core peptide [4]. Further, researchers showed a subclass of bacteriocins among these peptides, which is known as sactipeptides [3, 5, 6]. This important subclass of peptides is believed to hold the key to exploit human gut microbiome for potential development of natural antibiotic that can fight drug-resistant infections. However, the important biological activity of the sactipeptide subclass of RiPPs is not yet fully revealed and characterized [3].

Antimicrobial Molecule Produced by the Human Microbiota Gut Offers Promise to Fight Drug-Resistant Infections

Researchers for the first time reported the *in-vivo* and *in-vitro* production of the Ruminococcin C1 (Rum C1) sactipeptide and its functional and conformational characterizations. In a research of major significance, the strong antimicrobial activity against Gram-positive pathogens including MDR strains and the lack of toxic effect toward eukaryotic cells were demonstrated. Rum C1 was shown to be promising for the

development of natural antibiotic produced by a human gut symbiont. Additionally, its producer strain *Ruminococcus gnavus E1* could potentially be used as a powerful natural probiotic for gut health enhancement, Figure 1 [3].

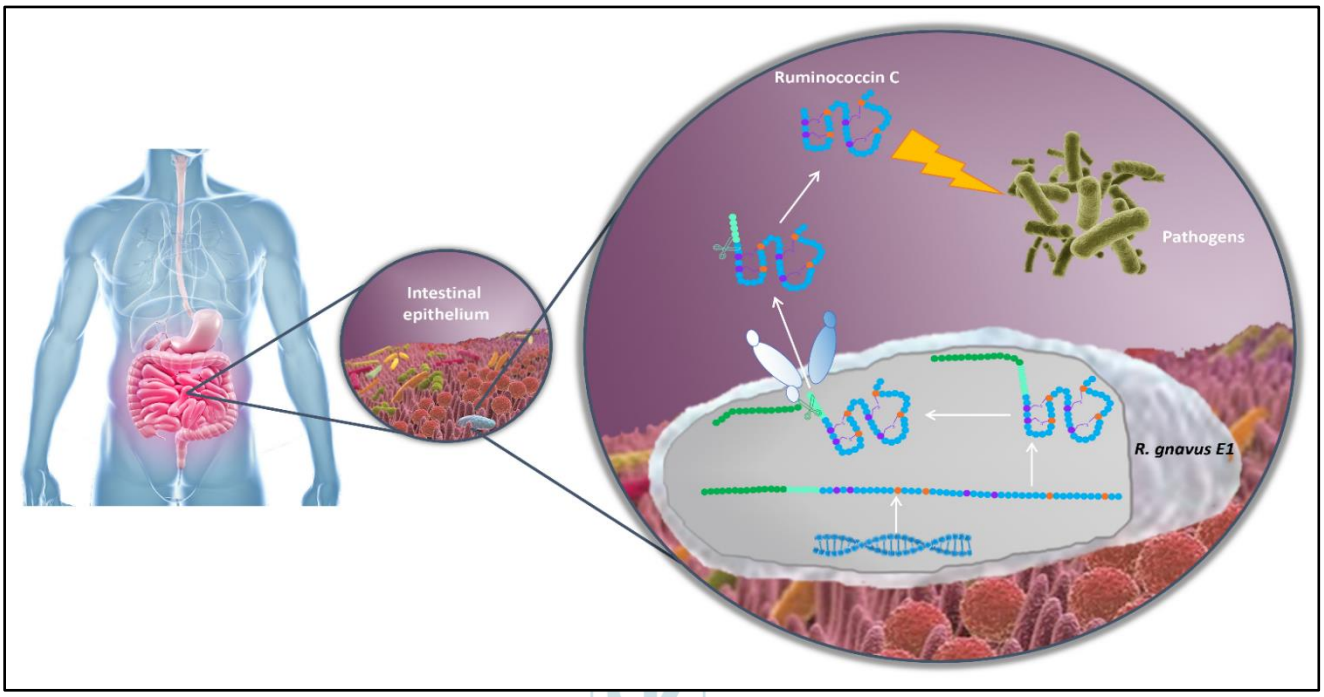

*Figure 1: A schematic illustration of the production of antimicrobial and safe sactipeptide Rum C1 from the human symbiont R. gnavus E1. It is externally activated in the gut by the host digestive system [**Source:** Science Advances 2019].*

In a significant breakthrough, researchers found broad-spectrum antimicrobial activity of RumC1 compound that was isolated from a gut bacterium of the Firmicutes group. It exhibited antimicrobial properties when employed even against antibiotic-resistant Clostridia and Staphylococci. Rum C1 that was ribosomally synthesized and post translationally modified did not show any toxicity unlike other conventional antibiotics. Most importantly, it did not show any signs of triggering towards development of drug resistance. This implies that Rum C1 could even be employed to work in tandem with other antimicrobial agents to enable minimizing bacterial resistance and to fight clinical pathogens [3].

The method employed by the researchers involved purifying Rum C1 from rat feces. This resulted in the production of an active, mature molecule identical to the peptides that naturally reside in human intestines. The antimicrobial activity was subsequently tested against a broad range of bacteria, including pathogens and strains resistant to multiple antibiotic drugs. They then performed safety assays to test its effect on human cell lines and observed that the peptide isolated from *R. gnavus* E1 fights Gram-positive bacteria quite effectively [3].

The Potential of Rum C1 for Use against Food Borne Pathogens and MDR Bacteria

The broad antimicrobial spectrum of Rum C1 was investigated on a vast array of Gram-positive and Gram-negative bacteria, including pathogens and MDR strains. Rum C1 was shown to be safe for use against pathogens and MDR bacteria. Further, researchers demonstrated the of Rum C1 against a range of pathogenic Clostridium species, which is known as the third cause of foodborne infections in the United States after Norovirus and Salmonella spp. according to the Centers for Disease Control and Prevention (CDC). Rum C1 was also observed to be active against a range of Gram-positive organisms such as *Staphylococcus aureus* and MDR strains including vancomycin-resistant *Enterococcus faecalis*, nisin-resistant *Bacillus subtilis* or methicillin-resistant *S. aureus* (MRSA) [3].

The demonstrated high potency of Rum C1 against pathogenic strains coupled with its unique functionalities of safety features that include unaffected eukaryotic cells by the applications of Rum C1 makes it a significantly promising approach to fight MDR. Further, the absence of resistance development makes Rum C1 a promising candidate either as therapeutic agent or as food safety agent. Based on these findings, it can be further envisioned that Rum C1 sactibiotics and other groups of bacteriocins could be employed in combinatorial therapies in future with other antimicrobial agents that could include antibiotics [3].

Concluding Remarks

The biotech R&D advances that are being made in developing and optimizing a bio-based process to purify a natural molecule exhibiting antibiotic activity produced by a human intestinal symbiont offer tremendous promise in combating MDR in future. We anticipate that this paves the way for the development of new therapeutic strategies for human or animal health. These include drug optimization and other processes in combination with antimicrobial agents or antibiotics.

References

1. A. J. O'Neill, (2008). New antibacterial agents for treating infections caused by multi-drug resistant Gram-negative bacteria. *Expert Opin. Investig. Drugs*, 17, 297–302.
2. J. O'Neill, (2016). Tackling Drug-Resistant Infections Globally: Final Report and Recommendations (Review on Antimicrobial Resistance).
3. Steve Chiumento, Clarisse Roblin, and Sylvie Kieffer-Jaquinod, et al., (2019). Ruminococcin C, a promising antibiotic produced by a human gut symbiont, *Science Advances,* **5** (9), eaaw9969.
4. P. G. Arnison, M. J. Bibb, and G. Bierbaum, et al., (2013). Ribosomally synthesized and post-translationally modified peptide natural products: Overview and recommendations for a universal nomenclature. *Nat. Prod. Rep.* 30, 108–160.
5. M. C. Rea, R. P. Ross, and P. D. Cotter, et al., (2011). Classification of bacterocins from Gram-positive bacteria. *Prokaryotic Antimicrobial Peptides.* pp. 29–53.
6. H. Mathur, M. C. Rea, and P. D. Cotter, et al., (2015). The sactibiotic subclass of bacteriocins: An update. *Curr. Protein Pept. Sci.* 16, 549–558.

Cancer Biotechnology

By Peeyush Prasad, MSc

Contributing Editor

Can Artificial Intelligence Push the Limit in Cancer Diagnostics?

Artificial intelligence (AI) is the technology that is used for understanding the data and objects which usually requires human intelligence but with more accuracy and speed. Explosion of data and need for accurate analysis in a short duration, led to the development of AI, which can help learn and process the object or data under consideration. AI is being used for several advanced technology and security purposes such as data analysis, image processing, data security, fraud detection, speech recognition, chatbots and for algorithm trading [1]. Lately, the use of AI in healthcare has become imperative due to large amount of data in the healthcare sector and for effective diagnosis and prognosis of complex diseases such as cancer and diabetes. Cancer is one such menace to human health and one of the leading causes of death among both men and women globally. According to the World Health Organization 'WHO', approximately 9.6 million deaths occurred due to cancer in 2018. As Figure 1 suggests, low and middle income countries are worst affected by cancer with about 70% of cancer deaths reported in the developing countries [2].

Artificial Intelligence for Analyzing Data and Image Analysis for Cancer Diagnostics at an Early Stage

Complexity of cancer arises from various factors such as constantly varying mutational landscape of cancer cells, complex and dynamics tumor microenvironment, and difference in genetic background of each cancer patient. All these aspects make diagnosis and treatment of cancer very difficult. This is due to the fact that not only one cancer type varies from other cancer type in mutations but it also varies within a patient when progressed to later stage such as metastasized stage. Advanced stage diagnosis and/or misdiagnosis of cancer are two such factors which is needed to be addressed for effective therapy. Current technologies use different means that are being employed for diagnosis of cancer such as imaging (Pap smear and mammography), molecular profiling (Proteomics, Genomics, Transcriptomics and Metabolomics; tissue based biomarker), and cell free DNA analysis

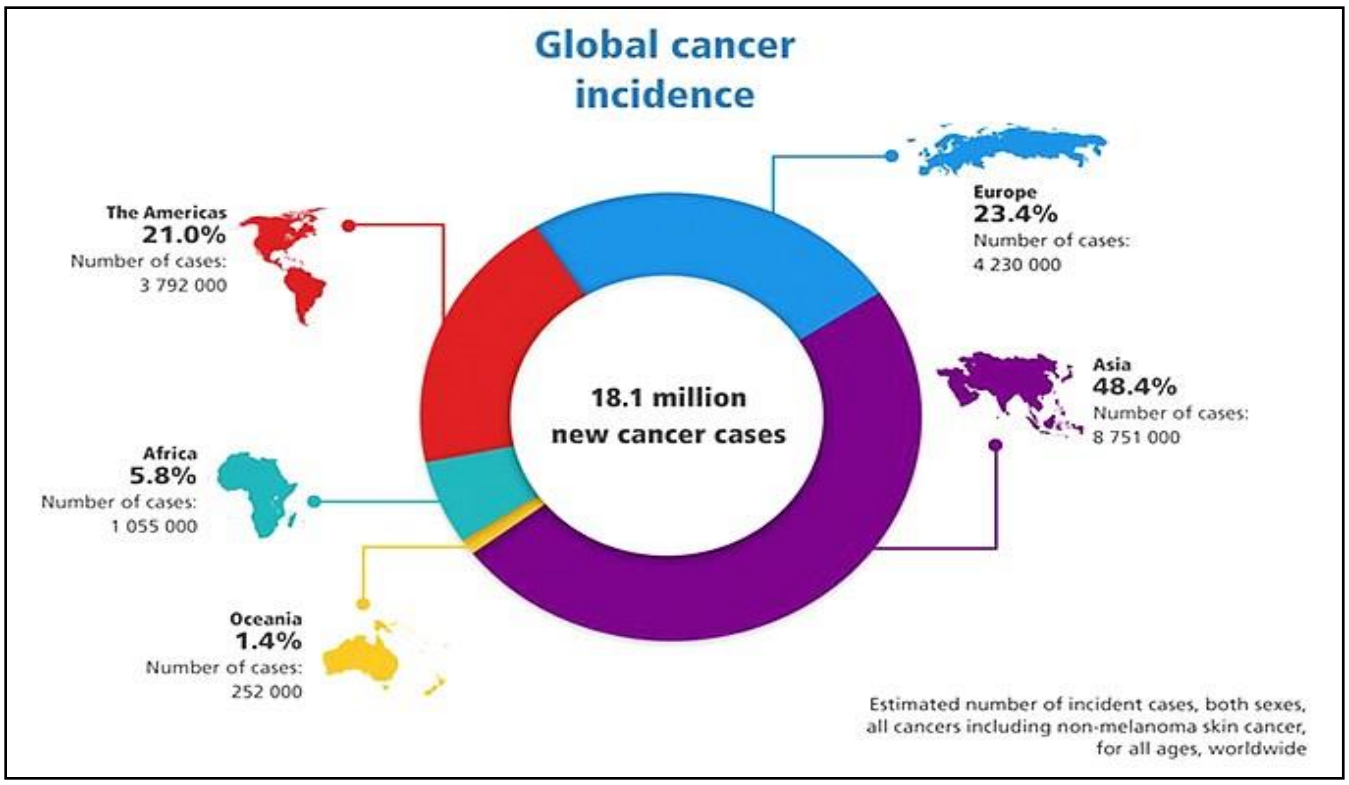

*Figure 1 Global cancer incidence [**Source:** WHO http://gco.iarc.fr/].*

(cfDNA; circulating biomarker). While, microscopic examination by pathologist can help in determining the prognosis and the treatment to some extent, it remains very challenging for effective therapy of cancer that has metastasized to different sites in the body [3]. There is no dearth of data but understanding data in meaningful and unbiased manner with accuracy is one of the time taking and labor intensive process for human intelligence. AI offers hope in analyzing these data that can go beyond human intelligence level to gain a better insight into the critically important diagnosis of cancer at its early stage. AI can be used for understanding data and image analysis in a meaningful manner with the aid of more affordable and cheap devices (democratization of technology). To this end, several computer models have been developed for cancer diagnosis that mostly focuses on image analysis, to identify the abnormalities specified by pathologist [4]. Especially, cognitive computing has been developed for dealing complex cancer data. These algorithms are created to read, memorize and advise physicians for decision making on the ever evolving medical literature. They help physicians in taking decision on relevance of data for determining appropriate cancer treatment [5]. AI can also help in determining pre-symptom cancer risk by using predictive models trained on large dataset. To explore the potential of AI technology more, let us take a look into few of the following examples.

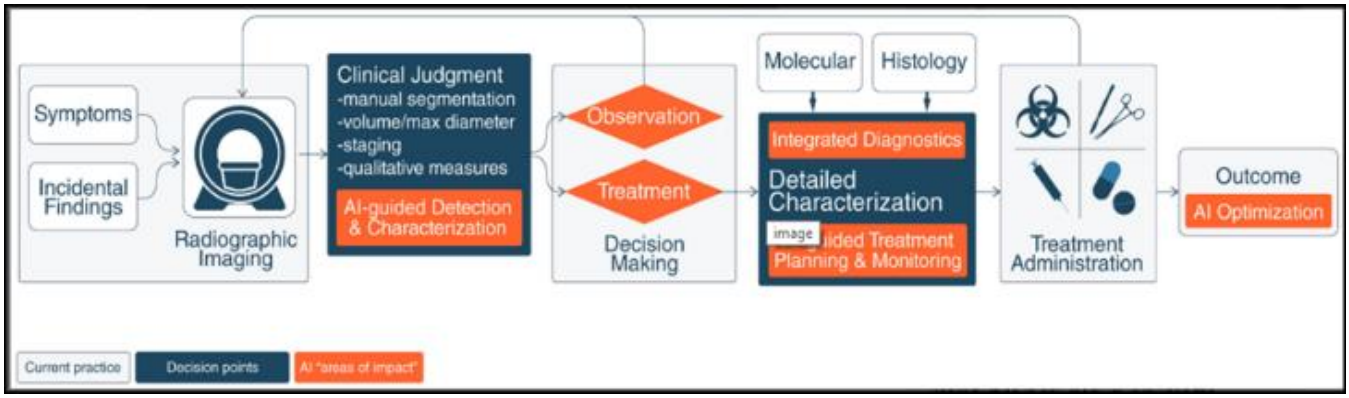

*Figure 2: Potential Enhanced Clinical Workflow With Artificial Intelligence (AI) Interventions. [**Source:** CA Cancer J Clin. 2019].*

Lunit, an AI company, which has analyzed 1,700,000 images, working in the field of breast and lung cancer, has developed INSIGHT algorithm for analyzing chest X-rays and mammography images. Lunit INSIGHT algorithm can analyze mammography for diagnostic purpose with 97% accuracy. It is a self-learning algorithm for finding nodules in specific region with fewer false negative results (Table 1) [6].

Table 1: AI based company in cancer diagnosis.

Company	Function
Google AI https://ai.google/healthcare/	Working in the field of digital pathology. Assisting pathologist for detecting breast cancer in lymph node biopsy.
IBEX Medical Analytics https://ibex-ai.com/	Work on the data from digitized glass slide and electronic medical records to reveal underlying pattern and clinical insights for personalized treatment and diagnosis.
logy.AI https://logy.ai/	AI based company working on diagnosis of cancer and malaria
Philips https://www.usa.philips.com/healthcare/innovation/artificial-intelligence	Philips teamed up with PathAI for improving breast cancer diagnosis.
Paige.AI https://paige.ai/	Creating large scale machine learning algorithm on digital slides for cancer diagnosis and therapy.
Lunit https://www.lunit.io/	AI based medical company. Developing powerful data driven imaging biomarkers

Google has also developed the deep learning-based approach to improve diagnostic accuracy for detecting nodal metastasis (LYmph Node Assistant or LYNA) (Table 1). In breast cancer, nodal metastasis affects the treatment decisions such as radiation therapy, chemotherapy and surgical removal of additional lymph node. Convolutional neural network (CNN) architecture was used in this AI system which gave excellent results with 8 false positive and 92.4% tumor detection (Camelyon 16 dataset). Human pathologist on the other hand achieved only 73.2% sensitivity for tumor detection [3, 7]. In another study, deep convolutional neural network is used for skin lesions. CNN was trained on 129,450 clinical images and its performance was tested against 21 board-certified dermatologists on biopsy proven clinical samples. Keratinocyte carcinomas versus benign seborrheic keratoses (common cancers) and malignant melanomas versus benign nevi (deadly skin cancer) were used as two critical binary classifications. Here, AI system proved to be as excellent as experts in classifying skin cancers [8].

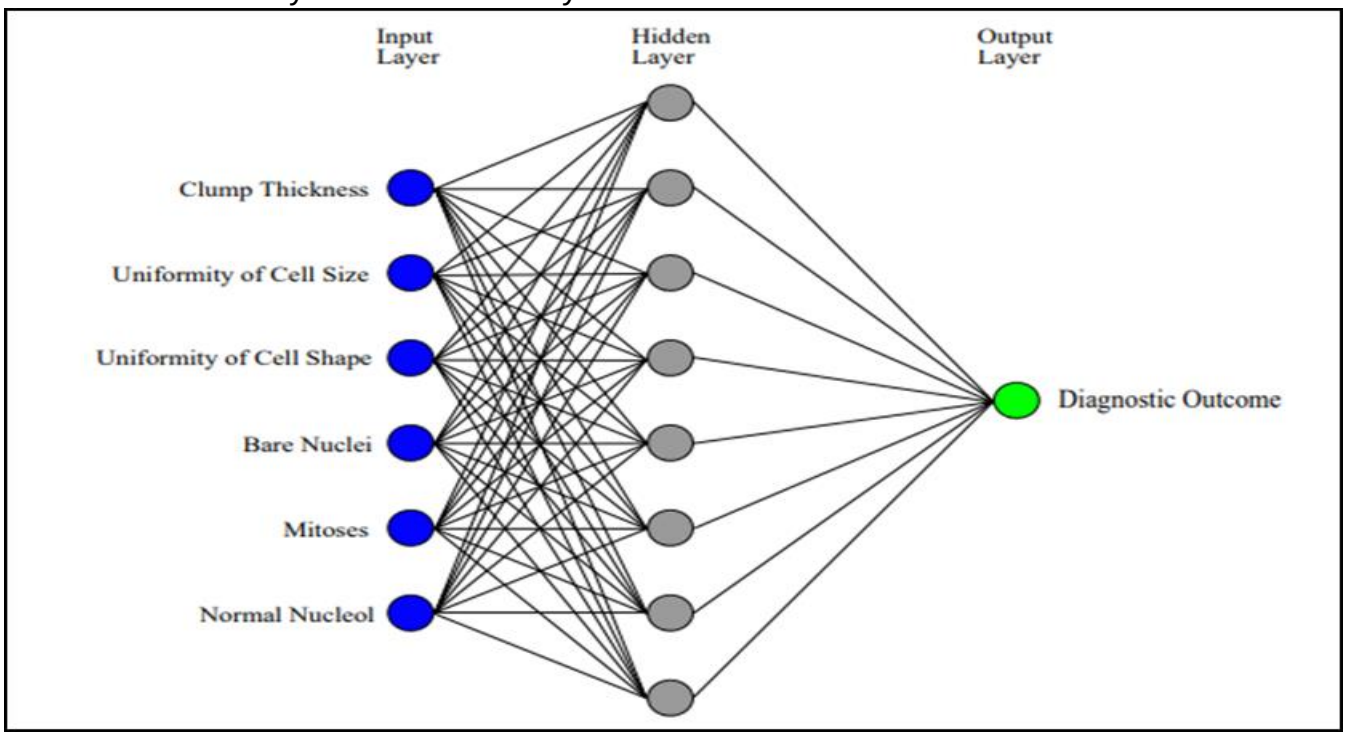

*Figure 3: A simple example of how Artificial Neural Network (ANN) is trained to predict the diagnostic outcome from six inputs and one hidden layer with 8 neurons [**Source:** Designs 2018]*

Quantgene, on the other hand provides precision technology and looks into the cell free DNA (cfDNA) for determining genetic predisposition to cancer. cfDNAs expelled by cells and are found in the circulating blood. Cancer cells also expel cfDNA which can act as circulating biomarker. Qunatgene looks at each copy of cfDNA present in blood sample [9]. CanSAR is another AI system developed to look into molecular profile (proteins) that can be targeted by drugs. MD Anderson and Memorial Sloan Kettering launched Oncology Expert Advisor (OEA) which can be used for incorporating all information of more than 1

million patients for generating support system for research and patient care [5]. Table 2 summarizes the important research and developments in cancer diagnosis using AI.

Table 2: Recent AI based research and developments in the field of cancer diagnosis.

Research	Type of Cancer	Comments	Reference
Cancer diagnosis with AI and spectroscopy	Breast Cancer	Biopsy data were analyzed by supervised and unsupervised algorithm to identify changes associated with lipids, collagen and nucleic acid content. Specificity accuracy were found for luminal A (70%), B (100%), HER2 (90%) and TNBC (90.7%).	[10]
Lesion-based Convolutional Neural Network	Early Gastric Cancer	Visual geometry group (VGG)-16 model was employed to classify endoscopic images as EGC or non-EGC. Evaluation of diagnostic performance and factors affecting AI diagnosis. 90.1% sensitivity is observed in this study.	[11]
Image based deep learning framework for individualizing radiotherapy dose	Cancer in lung	Image (CT) distinct subpopulations were identified that have differential sensitivity to radiotherapy. Use of medical image for individualization of radiotherapy dose.	[12]
MR based AI model for therapy assessment	Locally advanced Rectal Cancer	AI model analyzes texture of high-resolution T2 weighted MR images for identifying patients who will show complete response and no response at an early stage of treatment.	[13]
Radiomics MRI phenotyping with Machine learning for predicting lower grade glioma (LGG)	Glioma	For predicting LGG, machine learning classifiers were trained on radiomics features of glioma where best classifier assessed by area under the curve (AUC).	[14]
Machine learning analyzing immune-histochemistry of suspected thyroid nodules	Thyroid cancer	This model can be used for identifying benign and malignant thyroid nodules which is noninvasive prediction based on the CT images.	[15]

Conclusion

Considering the extraordinary challenges in cancer diagnosis at an early stage, it is important to outline how AI system can be developed for future healthcare. One viable path could be that instead of developing separate AI based system by different group, an integrated AI system could be developed

for better data sharing. Further, healthcare data should be shared freely among different AI system with fewer hurdles although security of data is one of the concerns. Instead of using only cancer patient data for training algorithm, it is also important to train AI system on healthy individual data for predictive analysis. For detecting predisposition, it is imperative to explore more individual's data related to food habit, substance abuse such as tobacco or alcohol intake and family history. Researchers also need to generate data more responsibly, minimizing human error and faster the hospitals will adopt AI technology more lives will be saved.

Author's Biography:

Peeyush Prasad is a biomedical scientist with research experience in multiple areas. Currently, he is a scientific consultant at Kolabtree. He had completed his M.Sc. in Biomedical Sciences from Dr. B.R. Ambedker Center for Biomedical Research (ACBR), University of Delhi. He has explored LC-MS based proteomics approach for neuro-infectious diseases at Institute of Bioinformatics and worked on various bioinformatics tools. Further, he joined Shiv Nadar University where worked on signaling pathways in breast cancer and colon cancer. He has published 6 papers and 5 conference proceedings. His papers are published in highly reputed journals such as ACS Applied Material and Interfaces and Oxford Carcinogenesis. He is an avid reader of technological development in healthcare and likes to ideate on future of healthcare sciences".

References

1. Golden JA. (2017). Deep Learning Algorithms for Detection of Lymph Node Metastases From Breast Cancer: Helping Artificial Intelligence Be Seen. *JAMA.* 12;318 (22):2184-2186.
2. https://www.who.int/news-room/fact-sheets/detail/cancer
3. Martin Stumpe, (2018). Applying Deep Learning to Matastatic Breast Cancer Detection. Google AI Blog.
4. LeCun Y, Bengio Y, Hinton G, (2015). Deep learning. *Nature*. 521(7553):436-444.
5. Kantarjian H, Yu PP, (2015). Artificial Intelligence, Big Data, and Cancer. *JAMA Oncol.* 1(5):573-4.
6. https://lunit.prezly.com/lunit-opens-lunit-insight-for-mammography-for-public-access
7. Liu Y, Gadepalli K, and Norouzi M, et al., (2017). Detecting Cancer Metastases on Gigapixel Pathology Images. arXiv.org >cs> arXiv:1703.02442
8. Esteva A, Kuprel B, and Novoa RA, et al., (2017). Dermatologist-level classification of skin cancer with deep neural networks. *Nature.* 2;542 (7639):115-118.
9. https://www.quantgene.com/
10. Talari ACS, Rehman S, and Rehman IU, (2019). Advancing cancer diagnostics with artificial intelligence and spectroscopy: identifying chemical changes associated with breast cancer. *Expert Rev Mol Diagn.* 19(10):929-940.
11. Yoon HJ, Kim S and Kim JH, et al., (2019). A Lesion-Based Convolutional Neural Network Improves Endoscopic Detection and Depth Prediction of Early Gastric Cancer. *J Clin Med.* 26;8 (9). pii: E1310.

12. Lou B, Doken S and Zhuang T, et al., (2019). An image-based deep learning framework for individualizing radiotherapy dose. *Lancet Digit Health.* 1(3):e136-e147.
13. Ferrari R, Mancini-Terracciano C, and Voena C, et al., (2019). MR-based artificial intelligence model to assess response to therapy in locally advanced rectal cancer. *Eur J Radiol.* 118:1-9.
14. Park YW, Choi YS, and Ahn SS, et al., (2019). Radiomics MRI Phenotyping with Machine Learning to Predict the Grade of Lower-Grade Gliomas: A Study Focused on Nonenhancing Tumors. Korean J Radiol. 20(9):1381-1389.
15. Gu J, Zhu J, and Qiu Q, et al., (2019). Prediction of Immunohistochemistry of Suspected Thyroid Nodules by Use of Machine Learning-Based Radiomics. *AJR Am J Roentgenol.* 28:1-10.

Biotechnology Advances around the World

Editor's Picks

Every issue of Biotechnology Kiosk presents select latest research news picked by the executive editors on significant research breakthroughs in different areas of biotechnology around the world. The aim is to promote further R&D in all of these cutting edge areas of biotechnology. The editors have compiled and included the following innovations and breakthroughs to highlight the recent biotechnology advances.

Dr. Megha Agrawal
Executive Editor

Dr. Shyamasri Biswas
Executive Editor

Neuro-engineering and Robotics

New neuroprosthetic technology for smart artificial hand for amputees

Researchers at Ecole Polytechnique Fédérale de Lausanne 'EPFL', Switzerland have recently demonstrated a new neuroprosthetic technology that opens up possibilities of combining robotic control with user's voluntary control to develop robotic smart hands especially for amputees. This research is published in the September's issue of Nature Machine Intelligence (Nature Machine Intelligence, 2019; 1 (9): 400 DOI: 10.1038/s42256-019-0093-5) that can potentially start a new interdisciplinary field of shared control for neuroprosthetic technologies.

The scientists from EPFL employed new approaches that showed improved control of robotic hands that can have applications particularly for amputees. The developed technology allows combination of individual finger control and automation for improved grasping and manipulation. Researchers then successfully tested this interdisciplinary proof-of-concept technology that merges concepts drawn from two different fields of neuroengineering and robotics on three amputees and seven healthy subjects.

This smart technology uses the concept from neuroengineering that involves deciphering intended finger movement from muscular activity on the amputee's stump for individual finger control of the prosthetic hand and the concept from robotics that leverages robotic hand for objects and maintain contact with them for robust grasping. Researchers showed that the robotic hand can react within 400 milliseconds by the applications of pressure sensors that were placed on the fingers. This enabled the object to react and stabilize before the process where brain can actually perceive and send the signal that the object is slipping.

The EPFL researchers envision that the shared approach that allows controlled robotic hands could be employed in future in several advanced neuroprosthetic applications including bionic hand prostheses and brain-to-machine interfaces. It is believed that further development of the technology would increase the clinical impact and usability of these devices.

Microbial Biotechnology

Antimicrobial-resistance infections on rise in Asia, Latin America and Africa

With the rising economic growth and wealth in the lives of people in the developing world, meat and dairy consumption has also risen considerably in India, China, Latin America and Africa. Animal husbandry has been identified as one of the key sectors that is growing because of the consumer demands in these countries. Animal husbandry farmers largely rely on the use of antimicrobials to treat and prevent infections for animals that

are particularly raised in shared and crowded conditions. However, these antimicrobial drugs are excessively and indiscriminately used to cause weight gains because of the reason it improves the profitability of the farmers. Such overuse of antimicrobials makes the bacteria resistant to antimicrobials which has serious consequences not only for the health of animals but also for humans.

A research team at ETH Zurich recently attempted to address these issues. They published a map of antimicrobial resistance in animals in low- and middle-income countries in the journal Science (Science, 2019; 365 (6459): eaaw1944 DOI: 10.1126/science.aaw1944). This important research sheds light on the growing antimicrobial-resistant infections in animals in low and middle income countries. In this research, the first global data of resistance rates, and identified regions are published, where urgent interventions are recommended.

In their research, The ETH team adopted an approach of assembling a large literature database. This was aimed to identify the affected regions and also which animal species show resistance to the common foodborne bacteria such as Salmonella, E. coli, Campylobacter and Staphylococcus. Researchers found the most affected regions associated with high rates of antimicrobial resistance in animals were northeast China, northeast India, southern Brazil, Iran and Turkey.

The alarming observations are that the listed bacteria are found to be resistant to a large number of drugs that are currently used in these countries not only in animals but also in human medicine. Researchers also analyzed and observed emergence of few resistance hotspots in Africa excluding Nigeria and the surroundings of Johannesburg, South Africa. They found highest resistance rates that were attributed to be associated with the antimicrobials that are most frequently used in animals. These include tetracyclines, sulphonamides, penicillins and quinolones. Notably, these antimicrobial compounds were noticed to have almost completely lost their efficacy to treat infections in certain regions.

This very important research by the ETH scientists have raised a valid concern of rising antimicrobial resistance in developing and emerging countries that needs to be checked before it goes out of control. One viable way to regulate the access to veterinary antimicrobials in these countries where meat consumption is rapidly rising.

Beyond the scenario in developing and emerging economies, it can be said that antimicrobial resistance is a global problem, and equal participation of elimination of the problem in the developed countries is needed. Researchers conclude that making considerable efforts to reduce it on one side of the world will substantially help manage the antimicrobial resistance problems on the other side of the planet, and this would lead to achieve the goals of mitigating the serious problem of antimicrobial resistance.

Organoid Biotechnology

First multi-organoid system offers exciting possibilities for future precision medicine

Organoids correspond to tiny 3D formations of human tissue that are grown from stem cells. They are known to perform important functions of multiple cells types found in full-sized organs. In a recent breakthrough, biomedical researchers working in the field of organoid science at Cincinnati Children's Hospital Medical Center in the United States published first report of the development of three-organoid system in the journal Nature (Nature, 2019; DOI: 10.1038/s41586-019-1598-0).

In this research of major significance, researchers demonstrated growing a connected set of three organs including the liver, pancreas and biliary ducts. This approach is different from growing mini human organs independently in separate lab dishes.

The researchers designed a method that allowed for producing pre-organ formation stage tissues to develop organs naturally. The connectivity of multiple organs is critically important part of this new multi-organoid system. The ability to make an integrated organ system was the real breakthrough in this work. This opens up a real research perspective and opportunity that allows to study normal human development.

This major step forward in connected organoid development is expected to push the concept of precision medicine that would lead to transplantable tissues grown in labs in future. In precision medicine, for example, using this approach, a set of gut organoids could potentially be grown for a specific patient that could allow more precise diagnosis and customized treatment. Similarly, this concept of multi-organoid system could be employed in liver regenerative medicine approaches that suffer from the absence of bile duct connectivity. In this regard, a multi-organoid transplant system could be employed to address this issue that could potentially provide a long-term solution for cure for patients with complex liver diseases.

Agriculture, Genetics & Plants

Tomato jumping genes can be harnessed to breed drought-resistant crops

In a major discovery that can impact the field of plant and agriculture biotechnology, researchers have found a family of 'jumping genes' in tomatoes that can potentially accelerate crop breeding with important attribute of generating crops with improved drought resistance.

Researchers from the University of Cambridge in the U.K. have reported an important phenomenon involving drought

stress that is recently published in the journal PLOS Genetics (PLOS Genetics, 2019; 15 (9): e1008370 DOI: 10.1371/journal.pgen.1008370). This research has shown that the drought stress can trigger the activity of a family of jumping genes that are known as Rider retrotransposons. Transposons are essentially mobile snippets of DNA code. They have the property of copying themselves into new positions within the genome, which is the genetic code of an organism. Previous researches have shown that they can change, disrupt or amplify genes. This family of genes was also previously known to agricultural and plant researchers for its contribution to fruit shape and color in tomatoes.

The characterization of Rider by the Cambridge based researchers revealed interesting and previously unknown facts that the Rider family is present and potentially active in other crops also. This shows the potential of transposons for crop improvement and especially as a source of new trait variations that could be leveraged to grow plants with better ability to cope with extreme weather conditions such as drought. This identification of transposons activity that is triggered by drought suggests the possibility of creating an important pathway for new gene regulatory networks to help a plant respond to drought. This implies that Rider could be harnessed to breed crops that are drought resistance. This could be achieved by providing drought responsiveness to genes already present in crops. This is quite significant especially in the regions, where more weather-resilient crops need to be breed that can withstand and combat the severe weather conditions.

Thus, transposons can potentially play an important role in the evolutionary process including altering gene expression and the physical characteristics of plants. This research also shows that using the jumping genes that are already present in plants to generate new characteristics could pave the way to develop new breeding techniques that would help generate crops traits for uniform shapes, colors and sizes. This would eventually impact the harvesting technologies to make them more efficient that could result in maximum yields.

This research also revealed that economically important crops such as rapeseed, beetroot and quinoa have also transposons is present in these plant species. So, the technique shown in this work can be extended to further investigations into these important crops on how a controlled activation or reactivation of transposons can be achieved into plants that have Rider elements idle. This also includes the re-introduction of Rider elements. This approach of engineering Rider elements can impact significantly to reduce plant breeding time and make the breeding far more superior compared to the existing methods.

Compiled and Edited by Dr. Megha Agrawal and Dr. Shyamasri Biswas.

Biotech and Pharma Industry Roundup

mRNA immunotherapy research established at Harvard University in Collaboration With Moderna

A multi-year research collaboration with the biotech company Moderna, Inc. has been established at Harvard University. The goal of this industry-university research initiative is to identify and develop novel therapeutic approaches that could improve the lives of patients with immunological diseases. Moderna, Inc. will give funding to Harvard Medical School (HMS) to establish an initiative at HMS called the Alliance for RNA Therapies for the Modulation of the Immune System (ARTiMIS). This strategic alliance is focused on enabling basic science research in the field of immunology using Moderna's mRNA and nanoparticle delivery technology [https://otd.harvard.edu/news/harvard-university-establishes-mrna-immunotherapy-research-collaboration-wi].

Bavarian Nordic gets approval for monkeypox and smallpox vaccine

In a major boost for the Denmark-based Bavarian Nordic A/S, the U.S. Food and Drug Administration (FDA) recently approved its first vaccine that is designed to prevent smallpox and monkeypox disease in adults. These adults are considered at high risk of the viruses and are viewed as bioterrorism threats. The FDA approved Jynneos vaccine of Bavarian Nordic, which is the only approved non-replicating smallpox vaccine in the U.S. and the only approved monkeypox vaccine anywhere in the world. People with weakened immune systems and those with eczema can use Jynneos. The vaccine can also be used by household members with eczema to protect them for further contraction from the viruses in disease prone places [Source: https://www.biopharma-reporter.com/Article/2019/09/26/First-ever-monkeypox-vaccine-approval].

Meissa Vaccines raised $30 million for pipeline of vaccines

In a recent significant fund raiser for vaccines, Meissa Vaccines that resulted from Johnson & Johnson's JLABS incubator in South San Francisco raised $30 million. It is to advance a pipeline of vaccines that is anticipated to help prevent viral respiratory infections. Meissa will use the series A to run phase 1 and 2 trials that will involve a respiratory syncytial virus vaccine. The funding will also be used to move other potential candidates based on its synthetic biology technology requirements towards the clinical applications [Source: https://www.fiercebiotech.com/biotech/meissa-raises-30m-to-take-rsv-vaccine-into-clinic].

Eko gets $20M for digital stethoscope

Eko's digital stethoscope and electrocardiogram (ECG) device have been popular with the doctors to screen patients for heart disease. However, the company is making further advances to expand its footprint. It recently raised $20 million to invest in the development of machine-learning algorithms for futuristic plans. The ambitious goal is to gain technological ability that would provide digital diagnoses of heart conditions as accurately as possible. The series B funding comes from ARTIS Ventures, DigiTx Partners, NTT Venture Capital, 3M Ventures, Mayo Clinic, Seraph Group and XTX Ventures. This funding is also expected to support the commercial manufacturing of Eko's device, called Duo that will be supplied to more clinics and health systems. While the ambitious diagnostic algorithms aren't FDA-cleared yet, it is expected that the expansion into digital stethoscope will set the stage for their eventual commercialization [source: https://www.fiercebiotech.com/medtech/eko-bags-20m-to-expand-digital-stethoscope-grow-footprint].

FDA clears Abbott's highly sensitive troponin blood test aimed to prevent heart attacks

The US FDA has cleared Abbott's highly sensitive troponin blood test. This test is superior to previous methods that is designed to identify heart attacks hours earlier than the existing methods. More specifically, the test is designed for patients in such a way that after entering an emergency room with symptoms, it helps doctors to confirm the presence and severity of myocardial infarction within two to four hours of admission. It works on the Stat test that searches for even small elevations in the levels of the protein troponin-I, which is released by heart muscle cells when they are damaged. Abbott has also announced that it is launching a training partnership program that will help U.S. hospital staff to incorporate the automated blood test into their ER workflows to diagnose heart attacks [source: https://www.fiercebiotech.com/].

GlaxoSmithKline (GSK) investing $120M on new manufacturing hub for drug pipeline for cancer

GlaxoSmithKline (GSK) is investing $120 million with a goal to expand a biopharmaceutical manufacturing facility in Upper Merion, Pennsylvania. This is the latest investment made by the British pharma that is designed to support research and developments further into cancer and specialty drugs. This investment by the GSK is expected to develop a manufacturing facility that will bring together its manufacturing and R&D teams under one roof. This will enable them to share equipment and rapidly produce a new medicine which is in the process [Source: https://www.biopharmadive.com/).

Novartis integrating AveXis into its global quality control organization

Novartis is integrating AveXis into its global quality control organization. This move is seen as part of the Swiss pharma's response to a data scandal. This scandal clouded the gene therapy biotech company that Novartis bought last year for $8.7 billion. The plan of integrating AveXis is believed to be a positive

step towards resolving the issues with the FDA. The plan laid out in a company response to concerns about data issues raised by the FDA will involve several measures. It will have employee retraining and the hiring of a data integrity officer. AveXis' data oversight will be conducted by a third-party manufacturing consultant in a broadened assessment [Source: https://www.biopharmadive.com/)].

Evotec and Takeda entering into major drug discovery deal worth $850M

In a recent announcement, Evotec SE and Takeda Pharmaceutical Company Ltd said that they have signed a deal to enter a strategic drug discovery collaboration potentially worth $850M. Evotec SE is a Hamburg, Germany based Biotech company. Under this agreement, it is stated that Evotec will develop at least five small molecule discovery programs. This will be against targets that are identified by Takeda in oncology, gastroenterology, neuroscience and rare diseases. Further, Takeda will have the option to assume responsibility at lead series and upon Evotec delivering a pre-clinical candidate [Source: https://european-biotechnology.com/].

French company Microphyt raised €28.5M to develop its microalgae portfolio for nutrition and cosmetics

In the wake of a booming global market of anti-aging creams and weight-loss supplements, natural products for nutrition and cosmetics are of high demands. French microalgae company Microphyt is focusing on to harness the active molecules present in microalgae. This approach was rewarded by the investors with a €28.5M financing round. Using the funds, Microphyt is expected to focus on accelerating the product development portfolio with an aim to expand sales network globally along with increasing production capacity of its industrial platform [Source: https://european-biotechnology.com/].

Polish Skincare Company starts operations in the U.S

A Poland-based company, BANDI Laboratories that has made skincare products for more than 30 years has opened its first branch office in the United States. They recently started its initial sales and distribution center in Martinsburg, WV. The future plans of BANDI are aimed at establishing a U.S. manufacturing facility, which is expected to happen over the next five years [Source: https://businessfacilities.com/].

Pharmaceutical Product Development investing $63.7 million in the U.S.

Pharmaceutical Product Development, LLC (PPD), which is a global contract research organization has announced that it will invest $63.7 million to expand its bioanalytical lab in Henrico County, VA in the US. This new investment by the company will create 200 new jobs [Source: https://businessfacilities.com/].

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