# CELL-e'BRATION

*In - venting all that's STEMulating from NCRM*

Bulletin of Nichi-In Centre for Regenerative Medicine | XVI Anniversary Issue; Oct 2021; | Chamber XVI, Count I

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## XV Fujio Cup Won by Students of Medicine from India

*Winners of the virtual Fujio Cup Quiz (2020) Himanshu Yashavanthi Nagesh & Sufyan Ibrahim from Kasturba Medical College, India presenting the Fujio Cup awarded during the NCRM NICHE 2020 to their Dean and HOD*

The XV Anniversary of Nichi-In Centre for Regenerative Medicine (NCRM), the NCRM NICHE 2020 was conducted as a virtual event, owing to the COVID-19 pandemic on the 18th of October, 2020 as an international event organized by the Japanese firm, M/s GN Corporation, Japan based on a licensing arrangement with NCRM.

The NCRM NICHE 2020 was held in academic partnership with Shibaura Institute of Technology, Tokyo, Japan, German Society for Stem Cell Research (GSZ), Cologne, Germany, Training Program in Regenerative Medicine (TPRM), Canada and the Edogawa Evolutionary Laboratory of Science (EELS), Tokyo, Japan.

The NCRM NICHE 2020 had as its components, i. The Active Knowledge Gaining (AKG) events, Fujio Cup Quiz (FCQ) and ii. the Passive Knowledge Gaining (PKG) events of Interactive Lectures & the Inter-Disciplinary Conclave (IDC).

There was an online preliminary round of take home assignment essays on a myriad of regenerative medicine topics from which the top scoring 12 teams were selected for the next online pre-final round conducted over zoom with quiz masters from India, Japan and New Zealand. Among these 12 teams, eight teams of FCQ Elites were selected for the Pre-Final round II conducted on Webex and four teams emerged as finalists. The final round was presentations by the finalists which was held during the NCRM NICHE 2020 on the 17th of October 2020 and a jury comprising of experts including the audience selected the winners, Himanshu Yashavanthi Nagesh & Sufyan Ibrahim from Kasturba Medical College, India and the runner-up team of Juan Dennis Bahrian & Ahmad Syafiq Zuhri from Institut Teknologi Bandung, Indonesia.

## FAST FACTS OF NCRM NICHE

Year started: 2006

Venues: Chennai, India till 2016

Tokyo, Japan from 2017 onwards

Total No. of Delegates attended: 1375

Total No. of FCQites: 1500

Total No. of Institutes participated: 180

No. of Countries represented till date: 20

Peer-reviewed Publications*: 2

(*based on the event)

## In this issue....

# The FUJIO CUP Hall of Fame

## FUJIO CUP QUIZ (FCQ)

The FCQ is an exclusive Quiz on Stem Cells & Regenerative Medicine for students and scholars from Life Sciences, Biotechnology, Veterinary Science, Dentistry and Medicine conducted every year as a part of NCRM NICHE. The FCQ was named after renowned Japanese Physician Dr. Fujio Takayama.

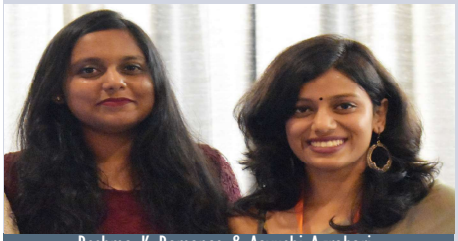
## Fifteenth FCQ 2020

Sufyan Ibrahim & Himanshu Yashavanthi Nagesh
Kasturba Medical College,India

Juan Dennis & Ahmad Syafiq Zuhri
Institute Teknologi Bandung,
Indonesia

## Fourteenth FCQ 2019

Winners



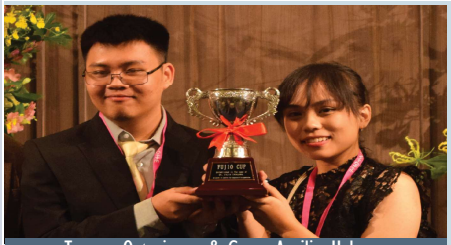
Reshma K Romanas & Aayushi Agrahari
Kasturba Medical College, India

Runners

Sandeep Rao Kordcal & Anil Dsouza
Father Muller Medical College,
Mangalore, India

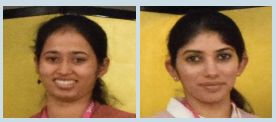
## Thirteenth FCQ 2018

Winners



Tommy Octavianus & Grace Aprilia Helena
Bandung Institute of Technology, Indonesia

Runners



Sneha K M & Sarayu R
School of Regenerative Medicine,
Bengaluru, India

## Twelfth FCQ 2017

Winners

Anirudh Pai & Siddharth Shankar
Kasturba Medical College, Mangalore, India

Runners

Khalidha Noordeen &
Nisha Harur Muralidharan
Anna University, Chennai, India

## Eleventh FCQ 2016

Winners

Rithika Rajendran & Preethi Jenifer
Sri Ramachandra University, Chennai, India

Runners

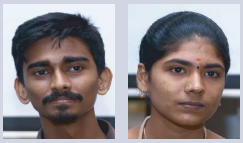
M.Lakshana & Varsha. M
MVJ Medical college & Research hospital,
Bengaluru, India

## Tenth FCQ 2015

Winners

Michelle Dsouza & Vikrant Patil
Manipal School of Regenerative Medicine, Bangalore, India

Runners



K.Sriram & S.Savithri
Rajalakshmi Engineering College,
Chennai, India

## Ninth FCQ 2014

Winners

Preethem Srinath & Vivek Ashok Kumar,
Manipal Instt. of Regenerative Medicine, Bangalore, India

Runners

Aakash Chandran C & Srivats V R
Chengalpattu Government Medical College,
Chengalpattu, India

## Eighth FCQ 2013

Winners

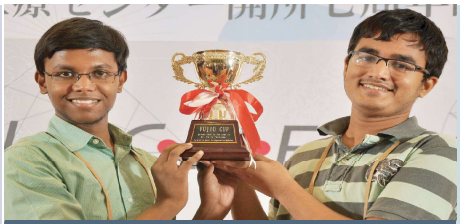
Ramakrishnan.P & Vijayendran.S,
Anna University, Chennai, India

Runners

Rupesh Kumar Natarajan & R.Sathya Sagar,
Madras Medical College,
Chennai, India

## Seventh FCQ 2012

Winners



Amith Rangarajan & P.V. Sudharsan
Chengalpattu Government Medical College, Chengalpattu, India

Runners

Nandinee Giri & N.Sunontha
Rajalakshmi Engineering College,
Chennai, India

## Sixth FCQ 2011

Winners

K. Shanmugam & V. Bhanu Prasad,
Madras Medical College, Chennai, India

Runners

Batul Yusuf & Sandhyaa V
Manipal Institute of Regnerative Medicine,
Bangalore, India

## Fifth FCQ 2010

Winners

Subhosmito Chakraborty & Jayastu Senapati,
Christian Medical College, Vellore, India

Runners

Hima Shah & Kavina Ganapathy
Manipal Institute of Regenerative Medicine,
Bangalore, India

## Fourth FCQ 2009

### Winners

Sumit Rai & S. Rangarajan,
Manipal Institute of Regenerative Medicine, Bangalore, India

### Runners

Taronish Dubash &
Krithika Hariharan
Manipal Institute of Regenerative Medicine, Bangalore, India

## Third FCQ 2008

### Winners

Raghavan Vallur & Ashish Ranjan,
Manipal Institute of Regenerative Medicine, Bangalore, India

### Runners

Aviral Roy & Sudharsan
Stanley Medical College,
Chennai, India

## Second FCQ 2007

### Winners

B. Senthilvelan & K. Anand,
Kilpauk Medical College, Chennai, India

### Runners

R. Krishnamoorthy & S. Subash
Dr. MGR Medical University,
Chennai, India

## First FCQ 2006

### Winners

C. Anand & A.R. Karuppiah,
PSG Medical College, Coimbatore, India

### Runners

Gautham & Joe Varghese
Christian Medical College,
Vellore, India

# NCRM NICHE 2020

## Virtual Plenary Lecture I

*Prof. Masaharu Seno*

The virtual plenary lecture I was by Prof. Masaharu Seno, Professor, Faculty of Engineering, Graduate School of Interdisciplinary Science and Engineering in HealthSystems, Okayama University, Japan on "How can you choose the fate of iPSCs and stem cells, Regeneration or Carcinogenesis?: A hypothetical insight." in which he stressed on the importance of choosing the proper conditions of culture of induced pluripotent stem cell (iPSCs) for therapy especially 3D platforms, cytokines and growth factors, apart from inhibition of stimuli that cna potentially give rise to cancer stem cells

## Virtual Plenary Lecture II

*Dr. Maria Cristina Nostro*

The virtual plenary lecture II was delivered by Dr. Maria Cristina Nostro, Scientist, McEwen Stem Cell Institute and an Assistant Professor at the University of Toronto on "Modelling human beta cell development with pluripotent stem cells" in which she described their team's work on mimicking human embryonic development to generate pancreatic progenitors (PP) with the ability to mature into insulin producing cells. They are also working on identifying markers to purify the PP populations and accelerate functionality by improving vascularization at the time of transplantation.

## Virtual NCRM NICHE Inter-Disciplinary Conclave (IDC)

*Rev Fr. Francis P Xavier SJ*

Rev Fr. Francis P Xavier SJ, a physicist who is the Founder-Director of Loyola Institute of Frontier Energy (LIFE) and Loyola- ICAM College of Engineering and Tech-nology (LICET), former Gasson Professor at Boston College; and the Vice President for Academic and Research (Jesuit Worldwide Learning), Geneva presented his views on Stress Management and COVID 19 in the Inter-Disciplinary Conclave (IDC) session 2020

Reminiscences of the Pre-COVID days: The delegates from different countries, of NCRM NICHE 2019 during the Yukata (a traditional Japanese garment) wearing ceremony

# TRAINING PROGRAM IN REGENERATIVE MEDICINE (TPRM)

The Training Program in Regenerative Medicine (TPRM) is affiliated with the University of Toronto, McMaster University and Ottawa University, Canada and consists of a series of lectures webcasted from the University of Toronto to scholars enrolled through NCRM. At the end of the programme the participants will get a certificate from the University of Toronto. For details visit *www.ncrm.org/feat/tprm/index.htm*

TPRM 2008-09 Batch

TPRM 2009-10 Batch

TPRM 2010-11 Batch


TPRM 2011-12 Batch

TPRM 2012-13 Batch

TPRM 2013-14 Batch



TPRM 2016-17 Batch

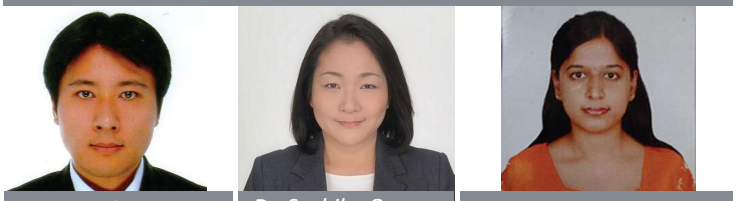
TPRM 2014-15 Batch

Dr. Sumana Premkumar | Dr. Pushkala | Dr. John Sudhakar

TPRM 2015-16 Batch

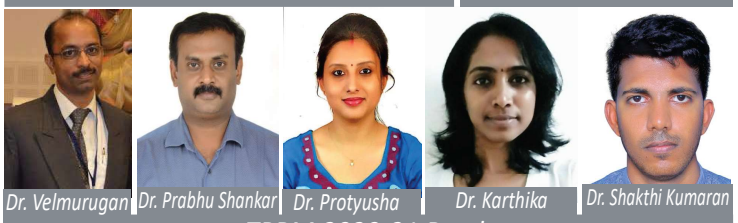
Dr. Jun Makino | Dr. Yasutaka Kakumu | Dr. Daiki Matsumaru

TPRM 2017-18 Batch



Dr. Fumihiro Ijima | Dr. Sachiko Ogawa | Ms. Sandhyaa

TPRM 2018-19 Batch | TPRM 2019-20 Batch



Dr. Velmurugan | Dr. Prabhu Shankar | Dr. Protyusha | Dr. Karthika | Dr. Shakthi Kumaran

TPRM 2020-21 Batch

Dr. Sabarinath | Dr. Kavitha | Dr. Nandini | Dr. Ramya

Dr. Varshini | Dr. Joseph | Dr. Anilkumar | Dr. Jaideep

TPRM 2021-22 Batch

# Collaborative Clinical Skills Training Program started at JAICARE, Madurai

*Fr. S. Marianathan S.J (JAICARE) and Dr. K. Raghavan (SARVEE) in the MOU signing ceremony on 1st of August, 2021*

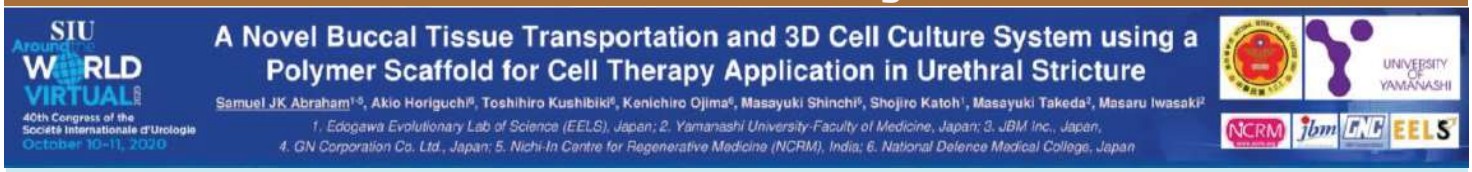
A clinical skills training program has been launched at the Jesuit Antonyraj memorial Inter-disciplinary Centre for Advanced Rehabilitation and Education (JAICARE), Madurai, India as a collaborative initiative beween JAICARE, Sarvee Integra Private Limited, Madurai and NCRM, India. This facility will serve as a perfect environment for doctors, nurses and paramedics to get hands on training in critical skills such as CPR, IV Cannulation, Catheterization, Airway management etc.

At this centre, Kikuzo – iPax, An Auscultation cum Pulse-Palpation simulation system for Clinical skills learning of Medical Students from Japan which combines the ease of a virtual selection of the type of cardiac and/or lung sounds associated with different disease conditions while the actual listening will be using through stethoscope and pulse-palpation with fingers, exactly similar to the clinical scenario, through a highly sensitive system which has a reputation for several years of track record in medical institutions in Japan, has also been brought to the first time to India.

Breakthrough studies are being conducted as part of this collaborative initiative on novel biological response modifier glucans such as the black yeast Aureobasidium pullulans derived beta glucans for different neurological conditions. Studies have been completed on A. pullulans AFO-202 strain produced beta glucan which is a potent immune-enhancer apart from its effects on alleviating glucotoxicity. In the study conducted in children with autism, the AFO-202 strain produced beta glucan has been able to increase the levels of melatonin and alpha-synuclein apart from improving the sleep and behavioural pattern. Another variant, the A. pullulans N-163 strain produced beta glucan which is a potent immune-modulator, anti-inflammatory and lipotoxicity alleviating agent either alone and in combination with AFO-202 beta glucan has been able to mitigate the cytokine storm and produce sustained positive effects in COVID-19 patients. Studies on children with Duchenne muscular dystrophy (DMD) is underway.

Fr. Danis Ponniah S.J (Provinicial), Fr. Vargeesh Antony S.J, Dr. K. Raghavan and Fr. Marianathan S.J during the virtual event of the inauguration of JAICARE in which Fr. Francis Xavier S.J (Rector, Loyola College) joined virtually

## Pre-clinical studies of BEES-HAUS presented at the Société Internationale d'Urologie, SIU 2020.




The Buccal epithelium Expanded and Encapsulated in Scaffold-Hybrid Approach to Urethral Stricture (BEES-HAUS), a novel tissue engineering technique to repair urethral stricture has been making considerable strides towards clinical application in Japan. As a part of this progress, the pre-clinical studies on BEES-HAUS done in Japan yielded a novel transportation cocktail to transport the buccal tissues form the place of collection to the lab and after in vitro expansion back to the hospital for clinical transplantation along with transplant worthy buccal mucosal epithelial cells with higher expression of native epithelial and progenitor markers was presented at the prestigious SIU World Congress on 10-11 October, 2020.

## Progress in Tissue-engineering of cartilage presented at the BSDB/Genetics Society Annual Spring Meeting


Plasticity of in vitro tissue engineered human chondrocytes in a 3D platform, expressing increased average tissue telomere length due to increase of progenitors, more than conventional 2D culture.

Osteo-arthritis(OA) affected human cartilage derived in vitro tissue engineered chondrocytes when cultured in the unique 3D polymer scaffold, TGP was able to yield younger population of cells for transplantation evident from expressing increased average tissue telomere length was presented at the BSDB/Genetics Society Annual Spring Meeting held from 19-23 April 2021. This study proves the utility of the in vitro tissue engineered cartilage tissue in cell therapy applications such as the Autologous Chondrocye implantation (ACI) and Matrix associated ACI (MACI).

Our earlier studies have proven pluripotency and chondroprogenitors expression of osteo-arthritis(OA) affected human cartilage derived chondrocytes when cultured in a 3D polymer scaffold. When we evaluated their average telomere length in comparison with conventional culture (2D) method, in 2D, growth was fibroblast like with cells degenerating before 28 days. In 3D they formed clusters and grew as tissue, continuing beyond day 42 when were evaluated. Average telomere length increased in 2D, though they degenerated before day 28, whereas in 3D they gradually increased until day 42. The progenitor population was almost nil in 2D, whereas significant increase was observed in 3D. An increase of average telomere length in 2D needs further evaluation on the proportion of fibroblasts, whose telomere length is longer than chondrocytes. The 3D environment being conducive to progenitors, yields a relatively overall younger tissue, warranting further research of plasticity of adult cells in novel environments. This study was presented at the BSDB/Genetics Society Annual Spring Meeting held from 19-23 April 2021. This study proves the utility of the in vitro tissue engineered cartilage tissue in cell therapy applications such as the Autologous Chondrocye implantation (ACI) and Matrix associated ACI (MACI).

## Translational study of buccal cell transplant for urethral stricture at the JSRM meeting, 2021

The 20th Congress of the Japanese Society for Regenerative Medicine

JSRM

In the process of getting approval for a multi-centric clinical trial for the Buccal epithelium Expanded and Encapsulated in Scaffold-Hybrid Approach to Urethral Stricture (BEES-HAUS) in Japan, animal studies were conducted which yielded positive outcome that was presented at the 20th Congress of the Japanese Society for Regenerative Medicine, Kobe Convention Center, Japan between 11-13 March, 2021.

# Collaboration with Okayama University for studying intricacies of cancer and aging using induced pluripotent stem cell-based models

**Prof. Masaharu Seno**
**Okayama University, Japan**

A tie-up has been made with Okayama University which has offered a post-doctoral fellowship to one of the scholars of NCRM to work on studying the molecular intricacies of aging and innovative treatments for cancer. The research is led by Prof. Masaharu Seno, head of the Lab of Nano-Biotechnology at the Department of Biotechnology, Graduate School of Natural Science and Technology, Okayama University whose team has created the World's first cancer stemcell (CSC) model from induced pluripotent stem (iPS) cells. Their research on CSCs from iPSCs enables an abundant supply of many different kinds of cancer cells for experiments and such a library of CSCs will help in developing customized cancer treatments. The collaborative research will be focussed on applying novel biomaterial platforms to enable growth of CSCs in a more efficient manner, thereby enabling functional physiologically and biologically active molecules be developed for cancer treatment.

## Obituary

*Mr. Eiji Osawa*
*(1933-2020)*

Mr. Osawa, Former President of YMCA who introduced Dr. Abraham, Head, NCRM to Dr. Fujio Takayama which paved way for his higher studies in Japan would always be fondly remembered by us as we all got to meet him during the 2017 NCRM NICHE conducted for the first time in Japan. Mr. Osawa graduated from Aoyama Gakuin University. He was associated with the YMCA'S Men ,Boy Scout, Gideons, Samatitans/Lifeline and Ecumenical. As a Rotarian, he is a role model for the motto "Service above Self". Mr. Osawa is survived by his wife and three daughters.

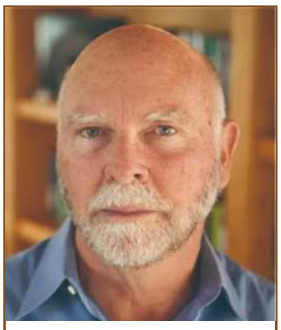
*Mr. V. Sampathkumar*
*(1972-2021)*

Words cannot express the loss of our wonderful colleague Mr. Sampathkumar who passed away due to health reasons. He served as the system-admin head at NCRM with nearly 15 years of service to the organization. His dedication to work and sincerity lauds our deepest appreciation. His contribution to the organization and NCRM NICHE for the development of the website, the registration portals, online and offline management of the event from 2006 will forever be remembered by everyone incldluing those who have come across during their participation in the event. He is survived by his wife, a son and a daughter.

# Edogawa NICHE Prize 2020

## THE EDOGAWA NICHE PRIZE

江戸川ニッシュ賞



**Dr. John Craig Venter**
*Founder, Chairman & CEO, J. Craig Venter Institute, CA, USA*
*Edogawa NICHE Prize 2020 - Recipient*

The Edogawa NICHE Prize has been jointly instituted by Edogawa Hospital- A unit of Jinseisha Social Welfare Trust (www.edogawa-hospital.jp), Tokyo, Japan and Nichi-In Centre for Regenerative Medicine (NCRM; www.ncrm.org), Chennai, India, the founding organization of NCRM NICHE (www.ncrmniche.org) to honour individuals who are physicians and/or scientists from around the world chosen by the Jinseisha-NCRM committee, based on their contribution to development of a novel solution that enables prevention or diagnosis or treatment of any disease, which is a result of an interdisciplinary interaction among different fields of science.

The Edogawa NICHE Prize for the year 2020 has been awarded to Dr. John Craig Venter for his contribution to research and development pertaining to the Human genome. This honor reflects Dr. Venter`s lifetime accomplishments in the power of the genomics and specifically in the identification of the human genome which has radically transformed healthcare.

Dr. Venter was born in Salt Lake City Utah on October 14, 1946. He started his college education at the College of San Mateo, CA and later studied Biochemistry in University of California, San Diego under biochemist Nathan O. Kaplan. After obtaining a PhD in Physiology and Pharmacology from UCSD, he became a Professor at the State University of New York and joined the National Institute of Health in 1984. He has founded Celera Genomics, The Institute of Genomic Research (TIGR), J. Craig Venter Institute (JCVI) and co-founded Human Longevity Inc and Synthetic Genomics.

His path breaking sequencing of the first human genome with the Human Genome Project further progressed to transfecting a cell with a synthetic chromosome, a feat that has opened up opportunities to develop novel solutions not only in healthcare, but also in environmental issues and energy domain.

## JOYCE AND JAMES TILL TRAVEL GRANT 2020

Dr. Rupesh Kumar Natarajan.

Dr.Natarajan's infectious enthusiasm with ceaseless and sincere efforts to attain the FCQ Elite status in 2013 after the initial participation in FCQ 2011 and willingness not to just aspire great things for himself but to inspire young minds to excel have made the Jury to decide in his favour for the J2T2 Grant 2020.

Dr. Natarajan, participated in the Fujio Cup Quiz when he was an Undergraduate Medical student at the Madras Medical College in India. He then went onto pursue residency training in the speciality of Pediatrics in the United States and is now pursuing a fellowship in Pediatric Cardiology at the University of Minnesota, Masonic Children's Hospital, USA. He has been continuing to keep himself abreast with the advances in the field of Regenerative Medicine and shares the same passion and commitment that there should be betterment of human lives, through this evolving speciality with hopes to solve many unmet medical needs.

The NCRM NICHE organizers place forth their appreciations to Dr. Natarajan for his desire to inspire young minds across the globe to pursue Inter-Disciplinary Research which would enable development of novel solutions.

**www.j2t2grant.org**

## Reversal of in vitro aging reported for the first time

394 British Society of Gerontology, 2021 Annual Meeting — Poster Session 1 Group 5, 7th July 2021, 15:15 - 16:30

Reversal of Senescence Associated B-Galactosidase (SA-ßGal) expression of human chondrocytes, in-vitro cultured in a novel 3D scaffold platform of a thermoreversible gelation polymer (TGP)

**Samuel JK Abraham* (1,2,5~8), Senthilkumar Rajappa (2), Senthilkumar Preethy (3), Hiroshi Yoshioka (4) Masaru Iwasaki (5), Atsuki Fujimaru (6), Shojiro Katoh (7)**

(1) II Dept of Surgery, Yamanashi University, Chuo, Japan (2) JBM Inc., Tokyo, Japan (3) Fujio-Eiji Academic Terrain (FEAT), Nichi-in Centre for Regenerative Medicine (NCRM), Chennai, India (4) Mebiol Inc., Hiratsuka, Japan, (5) Centre for Advancing Clinical Research (CACR), Yamanashi University, Chuo, Japan (6) Dept. of Orthopaedics, Edogawa Hospital, Tokyo, Japan (7) Edogawa Evolutionary Laboratory of Science (EELS), Edogawa Hospital, Tokyo, Japan (8)

drsam@nichimail.jp

* doi.org/10.1016/j.jor.2021.01.005
** doi.org/10.1016/j.knee.2021.02.019
*** doi.org/10.1016/j.jfs.2021.119553
# doi.org/10.1016/j.reth.2020.03.006

The first-of-its-kind report on reversal of in vitro aging of human chondrocytes, proven by decreased Senescence Associated B-Galactosidase (SA-ßGal) expression when a novel 3D scaffold platform was employed has helped to explore the potentials of the EELS-TALC method (Enriched with Essentials and Lapped in Scaffold Transplant-suitable Autologous Leveraged Chondrocytes) for elderly patients with osteoarthritis induced knee damage. This was presented at the British Society of Gerontology 50th Annual Conference on 7th of July, 2021.

# RECENT PUBLICATIONS OF NCRM-GNC-JBM CONSORTIUM


**Citation:** Katoh S, Fujimaru A, Iwasaki M, Yoshioka H, Senthilkumar R, Preethy S, Abraham SJK. **Reversal of senescence-associated beta-galactosidase expression during in vitro three-dimensional tissue-engineering of human chondrocytes in a polymer scaffold.** Scientific Reports 2021. Sci Rep 11, 14059 (2021)

**URL**: *https://doi.org/10.1038/s41598-021-93607-9*

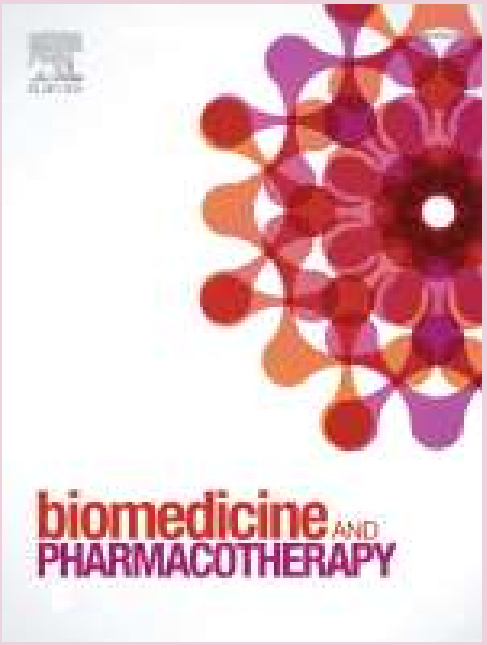
**Keywords:** Cellular senescence; In vitro culture; Senescence-associated beta-galactosidase (SA-βgal); Thermo-reversible gelation polymer (TGP); Aging reversal

**Summary:** Regenerative medicine applications require cells that are not inflicted with senescence after in vitro culture for an optimal in vivo outcome. Methods to overcome replicative senescence include genomic modifications which have their own disadvantages. We have evaluated a three-dimensional (3D) thermo-reversible gelation polymer (TGP) matrix environment for its capabilities to reverse cellular senescence. The expression of senescence-associated beta-galactosidase (SA-βgal) by human chondrocytes from osteoarthritis-affected cartilage tissue, grown in a conventional two-dimensional (2D) monolayer culture versus in 3D-TGP were compared. In 2D, the cells de-differentiated into fibroblasts, expressed higher SA-β gal and started degenerating at 25 days. SA-βgal levels decreased when the chondrocytes were transferred from the 2D to the 3D-TGP culture, with cells exhibiting a tissue-like growth until 42–45 days. Other senescence associated markers such as p16INK4a and p21 were also expressed only in 2D cultured cells but not in 3D-TGP tissue engineered cartilage. This is a first-of-its-kind report of a chemically synthesized and reproducible in vitro environment yielding an advantageous reversal of aging of human chondrocytes without any genomic modifications. The method is worth consideration as an optimal method for growing cells for regenerative medicine applications.

**Citation:** Raghavan K, Dedeepiya VD, Suryaprakash V, Rao KS, Ikewaki N, Sonoda T, Levy GA, Iwasaki M, Senthilkumar R, Preethy S, Abraham SJK. **Beneficial Effects of novel aureobasidium pullulans strains produced beta-1,3-1,6 glucans on interleukin-6 and D-Dimer levels in COVID-19 patients; results of a randomized multiple-arm pilot clinical study. Biomedicine and Pharmacotherapy 2021.**

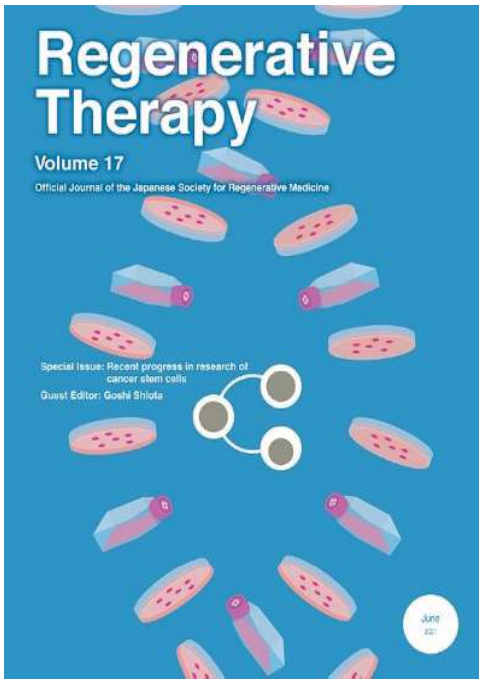
**URL** : https://pubmed.ncbi.nlm.nih.gov/33835468/

**Keywords:** COVID-19; IL-6; D-Dimer; Cytokine storm; Coagulopathy; Immuno-modulation; Beta Glucans; Adjunct treatment




**Summary:** In this pilot clinical study, we report the beneficial effects of beta glucans derived from two strains AFO-202 and N-163 of a black yeast Aureobasidium pullulans on the biomarkers for cytokine storm and coagulopathy in COVID-19 patients. A total of 24 RT-PCR positive COVID-19 patients were recruited and randomly divided into three groups (Gr): Gr. 1 control (n=8) – Standard treatment; Gr. 2: Standard treatment + AFO-202 beta glucan (n=8); and Gr. 3, Standard treatment + combination of AFO-202 and N-163 beta glucans (n=8) for 30 days. There was no mortality or requirement of ventilation of the subjects in any of the groups. There was a decrease in D-Dimer values (751 ng/ml to 143.89 ng/ml) and IL-6 values (7.395 pg/ml to 3.16 pg/ml) in Gr. 1 in 15 days but the levels increased to abnormal levels on day 30 (D-Dimer: 202.5 ng/ml; IL-6 55.37 pg/ml); which steadily decreased up to day 30 in groups 2 (D-dimer: 560.99 ng/dl to 79.615; IL-6: 26.18 pg/ml to 3.41 pg/ml) and 3 (D-dimer: 1614 ng/dl to 164.25 ng/dl; IL-6: 6.25 pg/ml to 0.5 pg/ml). The same trend was observed with ESR. LCR and LeCR increased while NLR decreased significantly in Gr. 3. CD4+ and CD8+ T cell count showed relatively higher increase in Gr.3. There was no difference in CRP within the groups. As these beta glucans are well known food supplements with a track record for safety, larger multi-centric clinical studies are recommended to validate their use as an adjunct in the management of COVID-19 and the ensuing long COVID-19 syndrome.

# RECENT PUBLICATIONS OF NCRM-GNC-JBM CONSORTIUM




**Citation:** Horiguchi A, Ojima K, Shinchi M, Kushibiki T, Mayumi Y, Miyai K, Katoh S, Takeda M, Iwasaki M, Suryaprakash V, Balamurugan M, Rajmohan M, Preethy S, Abraham SJK. **Successful engraftment of epithelial cells derived from autologous rabbit buccal mucosal tissue, encapsulated in a polymer scaffold in a rabbit model of a urethral stricture, transplanted using the transurethral approach.** Regen. Ther. 2021; 18:127-132

**URL**: *https://doi.org/10.1016/j.reth.2021.05.004*

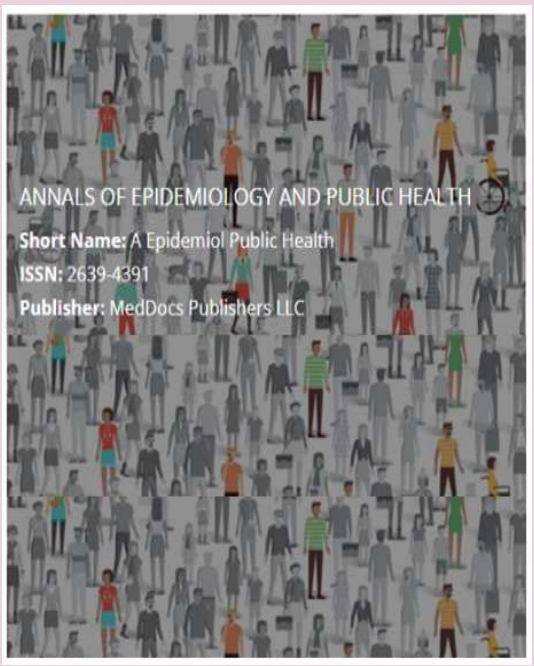
**Keywords:** Animal model, Urethral stricture, Buccal cell transplantation, BEES-HAUS, Thermo-reversible gelation polymer (TGP)

**Summary:** A pilot study reported an autologous buccal mucosal cell transplant in humans through the trans-urethral route using the buccal epithelium expanded and encapsulated in scaffold—hybrid approach to urethral stricture (BEES-HAUS), a minimally invasive approach to treat urethral stricture. Although successful outcomes were achieved in that study, for further validation, it is essential to prove that the transplanted buccal epithelium was engrafted over the urothelium through histological examination of the urethra, harvested post-transplant, which is infeasible in humans. Herein, we report the successful creation of an animal model of urethral stricture and the engraftment of epithelial cells derived from autologous buccal mucosal tissue, encapsulated in a thermo-reversible gelation polymer (TGP) scaffold, transplanted by trans-urethral route.

**Citation:** Raghavan K, Dedeepiya VD, Suryaprakash V, Rao KS, Ikewaki N, Sonoda T, Levy GA, Iwasaki M, Senthilkumar R, Preethy S, Abraham SJK. **Analysis of Perception of Government Run Public Healthcare Set-Ups in a Southern State of India - A Cross - Sectional Questionnaire-Based analysis.** A Epidemiol Public Health. 2021; 4(1): 1059.

**Keywords:** Tamil Nadu, Public health care system, Private vs public healthcare facilities, Preference of health care facility, Cross-sectional analysis

**Summary:** Public healthcare set-ups in India face formidable challenges and is lagging far behind from private set-ups. However, in some states, there is a difference. Tamil Nadu, a southern state in India has been christened as the Medical capital of India as it has one of the best healthcare services in India and a very well-established public-health care system. Several studies have outlined the facilities of public-healthcare set-ups in Tamil Nadu as being superior to that found in other states in India but there is no study so far that has captured the perception of people in the state of Tamil Nadu on them. We therefore sought to evaluate the people' perception of public-healthcare set-ups & their level of usage of such facilities in Tamil Nadu. Result showed that most of the respondents (> 60%) though were hospitalised in private health care-set ups for the previous illnesses, when asked of their preference specifically for each type of health care set ups, choice of private healthcare was only marginally high (74.2%) compared to public health care facilities (68.1%). Further, ease of access to public-health care set-ups was higher than private. Expenditure in private set-ups since is nearly 70% higher than in public health care set-ups, respondents want issues like lower hygiene in public-health care set-ups be rectified enable them use those facilities to the fullest.



# RECENT PUBLICATIONS OF NCRM-GNC-JBM CONSORTIUM


**Citation:** Katoh S, Rao KS, Suryaprakash V, Horiguchi A, Kushibiki T, Ojima K, Iwasaki M, Takeda M, Senthilkumar R, Rajmohan M, Karthick R, Preethy S, Abraham S. **A 3D polymer scaffold platform for enhanced in vitro culture of Human & Rabbit buccal epithelial cells for cell therapies.** Tokai J Exp Clin Med 2021; 46(1):1-6

**URL** : *https://pubmed.ncbi.nlm.nih.gov/33835468/*

**Keywords:** Buccal Mucosa, Epithelial cells, Polymers, Tissue Engineering

**Abstract:** Background: Buccal mucosal epithelial cells show promising application for various regenerative medicine approaches. In this study, we examined the feasibility of culturing rabbit and human buccal mucosal epithelial cells in a novel thermoreversible gelation polymer (TGP) scaffold, without feeder layers or other foreign proteins.

Methods & Results: The results of this 28-day in vitro culture, using the conventional technique (2D) and TGP (3D) showed that the epithelial cell morphology could be maintained only in the TGP group while cells in the 2D group de-differentiated to fibroblast morphology in both human and rabbit samples. CK3 expression, a marker for epithelial differentiation was higher in 3D-TGP cultured cells than 2D.

Conclusion: TGP based in vitro cell culture is a prospective methodology to culture buccal mucosal epithelial cells efficiently without using foreign biological components for tissue engineering applications.

**Citation:** Katoh S, Yoshioka H, Senthilkumar R, Preethy S, Abraham S. **Enhanced miRNA-140 expression of osteoarthritis-affected human chondrocytes cultured in a polymer based three-dimensional (3D) matrix.** Life Sciences 2021. 119553.

**URL** : *https://doi.org/10.1016/j.lfs.2021.119553*

**Keywords:** COVID-19; inflammation; mental health; neurological; psychological.

**Abstract:** We have evaluated the potential of a three-dimensional (3D) thermoreversible gelation polymer (TGP) matrix in enhancing miRNA 140 expression (a biomarker correlating with homeostasis and cartilage regeneration) during the in vitro expansion of osteoarthritis (OA)-affected human chondrocytes.

Materials and methods: OA-chondrocytes were cultured in two-dimensional (2D) monolayer followed by culture in 3D-TGP. miRNA 140 expression levels in cell culture supernatant followed by expression in the cell lysate of both 2D and 3D-TGP cultures were analyzed.

Key findings: The expression of miRNA 140 in cell culture supernatant from the 3D-TGP group was 0.001 to 0.002% that in 2D culture supernatant while in the cell lysate, miRNA 140 expression in the 3D-TGP was nearly 30-fold higher than that of 2D group.

# RECENT PUBLICATIONS OF NCRM-GNC-JBM CONSORTIUM


**Citation:** Ikewaki M, Iwasaki M, Kurosawa G, Rao KS, Beitia JL, Preethy S, Abraham SJ. **β-Glucans: Wide-spectrum Immune-balancing Food-supplement-based Enteric (β-WIFE) Vaccine Adjuvant Approach to COVID-19.** Human Vaccines & Immunotherapeutics 2021; 17(9).

**URL** : *https://doi.org/10.1080/21645515.2021.1880210.*

**Keywords:** Covid-19; vaccine adjuvant; AFO-202 Beta glucan; trained Immunity; immune enhancement

**Abstract:** Conventional vaccines to combat COVID-19 through different approaches are at various stages of development. The complexity of COVID-19 such as the potential mutations of the virus leading to antigenic drift and the uncertainty on the duration of the immunity induced by the vaccine have hampered the efforts to control the COVID-19 pandemic. Thus, we suggest an alternative interim treatment strategy based on biological response modifier glucans such as the Aureobasidium pullulans AFO-202-derived β-glucan, which has been reported to induce trained immunity, akin to that induced by the Bacille Calmette-Guérin vaccine, by epigenetic modifications at the central level in the bone marrow. These β-glucans act as pathogen-associated molecular patterns, activating mucosal immunity by binding with specific pathogen recognition receptors such as dectin-1 and inducing both the adaptive and innate immunity by reaching distant lymphoid organs. β-Glucans have also been used as immune adjuvants for vaccines such as the influenza vaccine. Therefore, until a conventional vaccine is widely available, an orally consumable vaccine adjuvant that acts like biosimilars, termed as the wide-spectrum immune-balancing food-supplement-based enteric (β-WIFE) vaccine adjuvant approach, with well-reported safety is worth in-depth investigation and can be considered for a clinical trial.

**Citation:** Namitha B, Chitra MR, Bhavya M, Katoh S, Yoshioka H, Iwasaki M, Senthilkumar R, Rajmohan M, Karthick R, Preethy S, Abraham SJK. **A novel human donor cornea preservation cocktail incorporating a thermo-reversible gelation polymer (TGP), enhancing the corneal endothelial cell density maintenance and explant culture of corneal limbal cells.** Biotechnology Letters 2021

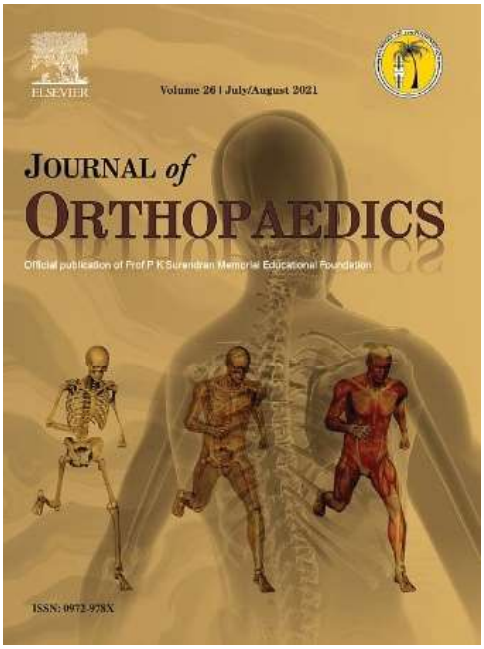

**URL** : *https://doi.org/10.1007/s10529-021-03116-y*

**Keywords:** Corneal storage, MK medium, Optisol - GS, TGP, Corneal limbal cell culture

**Abstract:** Purpose: McCarey-Kaufman's (MK) medium and Optisol-GS medium are the most commonly employed media for human donor corneal preservation. In this study, we evaluated the preservation efficacy of discarded human donor corneas using a Thermo-reversible gelation polymer (TGP) added to these two media.
Methods: Thirteen human corneal buttons collected from deceased donors, which were otherwise discarded due to low endothelial cell density (ECD) were used. They were stored in four groups: MK medium, MK medium with TGP, Optisol-GS and Optisol-GS with TGP at 4 °C for 96 h. Slit lamp examination and specular microscopy were performed. Corneal limbal tissues from these corneas were then cultured using explant methodology one with and the other without TGP scaffold, for 21 days.
Results: MK + TGP and Optisol-GS + TGP preserved corneas better than without TGP, which was observed by maintenance of ECD which was significantly higher in Optisol-GS + TGP than MK + TGP (p-value = 0.000478) and corneal thickness remaining the same for 96 h. Viable corneal epithelial cells could be grown from the corneas stored only in MK + TGP and Optisol-GS + TGP. During culture, the TGP scaffold helped maintain the native epithelial phenotype and progenitor/stem cell growth was confirmed by RT-PCR characterization.
Conclusion: TGP reconstituted with MK and Optisol—GS media yields better preservation of human corneal buttons in terms of relatively higher ECD maintenance and better in vitro culture outcome of corneal limbal tissue. This method has the potential to become a standard donor corneal transportation-preservation methodology and it can also be extended to other tissue or organ transportation upon further validation.

***The full list of publications are available at: ww.ncrm.org/feat/pub***

# RECENT PUBLICATIONS OF NCRM-GNC-JBM CONSORTIUM




**Citation:** Katoh S, Yoshioka H, Iwasaki M, Senthilkumar R, Rajmohan M, Karthick R, Preethy S, Abraham SJ. **A three-dimensional in vitro culture environment of a novel polymer scaffold, yielding chondroprogenitors and mesenchymal stem cells in human chondrocytes derived from osteoarthritis-affected cartilage tissue.** Journal of Orthopaedics 2021; 23 (2021):138-141.

**URL** : *https://doi.org/10.1016/j.jor.2021.01.005.*

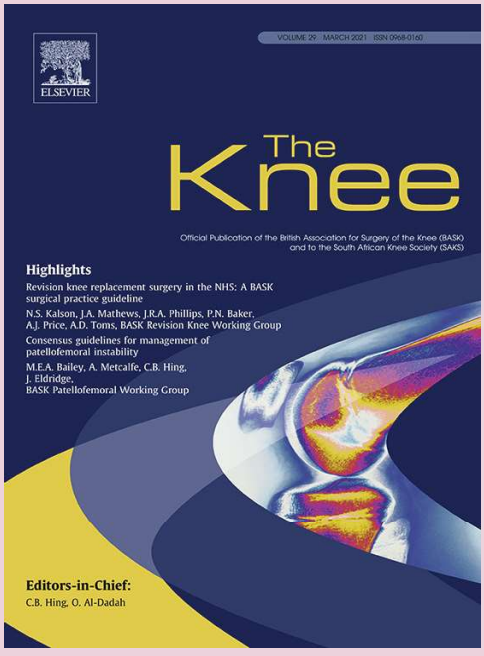
**Keywords:** Osteoarthritis; Chondrocytes; Thermo-reversible gelation polymer (TGP);Chondroprogenitors; CD49e; Mesenchymal stem cells

**Abstract:** Objective: We evaluated the expression of stem/progenitor biomarkers in osteoarthritic tissue derived chondrocytes cultured using a three-dimensional (3D) thermo-reversible gelation polymer (TGP).
Methods: The chondrocytes from discarded biopsy tissues obtained from human elderly patients with osteoarthritis were cultured using the 3D-TGP up to six weeks.
Results: The chondrocytes grew in a tissue-like manner, without de-differentiation into fibroblasts, and the cells thus tissue-engineered were proven positive for CD49e, OCT4, CD-105 and STRO-1 by immunohistochemistry.
Conclusion: This study establishes the efficacy of this 3D-TGP platform for clinically useable in-vitro tissue-engineered cartilage for improvising the clinical outcome of cell therapy for cartilage repair.

**Citation:** Katoh S, Yoshioka H, Senthilkumar R, Preethy S, Abraham S. Katoh S, Yoshioka H, Senthilkumar R, Preethy S, Abraham S. **Enhanced expression of hyaluronic acid in osteoarthritis-affected knee-cartilage chondrocytes during three-dimensional in vitro culture in a hyaluronic-acid-retaining polymer scaffold.** The Knee 2020; 29 : 365-73.

**URL** : *https://doi.org/10.1016/j.knee.2021.02.019*

**Keywords:** Chondrocytes; Cartilage; Hyaluronic acid; Three-dimensional polymer scaffold; Thermo-reversible gelation polymer (TGP)




**Abstract:** Background: Chondrocyte transplantation to address cartilage damage is an established solution. Because hyaluronic acid (HA) is an essential component for homeostasis of the cartilage, in order to arrive at methodologies to utilize its advantages in cell-based therapies, we compared the HA retention capability of a thermoreversible gelation polymer scaffold-based environment (3D-TGP) with conventional in vitro cell culture methodologies.
Methods: Chondrocytes derived from osteoarthritis-affected knee joint cartilage of elderly patients were used and accomplished in three phases. In Phase I, the levels of HA secreted by chondrocytes were measured in culture supernatant. In Phase II, retention capacity of externally added HA was quantified indirectly by measuring the HA released in culture supernatant, and in Phase III, the expression of CD44 on cells was analysed by immunohistochemistry.
Results: In Phase I, the average HA in the 3D supernatant was 3% that of 2D. In phase II, 80% of externally added HA was detected in the 2D on day 7, while in 3D-TGP, only 0.1% was released until day 21. In Phase III, 2D yielded individual cells that started degenerating from the third week; in 3D-TGP cells grew for a longer duration, formed a tissue-like architecture with extracellular matrix with significantly intense staining of CD44 than 2D.
Conclusion: The capability of the 3D-TGP culture environment to retain HA and support chondrocytes to grow with a tissue-like architecture expressing higher HA content is considered advantageous as it serves as an in vitro culture platform that enables tissue engineering of cartilage tissue with native hyaline phenotype and higher HA expression. The in vitro environment being conducive, based on this data, we also recommend that the TGP be tried as an encapsulation material in clinical studies of chondrocyte implantation for optimal clinical outcome.

# A SELECT LIST OF PRESENTATIONS IN PROMINENT MEETINGS

| | |
|---|---|
| 15th WSCTS; Lithuania, 2004 | Our progress in research on cell therapeutics and its possible applications in treating ischemic myocardium. |
| 4th Annual meeting of ISSCR; Toronto, Canada, 2006 | Survival and function of encapsulated hepatocytes, transplanted in Acute Liver failure (ALF) models |
| ARVO; Florida, USA, 2006 | Comparative Study on Growth Characteristics of Cadaveric Human Corneal Limbal Stem Cells in a Polymer Scaffold versus Human Amniotic Membrane |
| 1st Annual Meeting of GSZ; Cologne, Germany, 2006 | In vitro expansion of clinically usable stem cells and progenitor cells for cell therapeutics and in vivo implantation in animal models; our experience. |
| Russian Academy of Ophthalmology; Moscow Russia, 2007 | Cell therapeutics for corneal epithelial and endothelial diseases - Our approach |
| 5th Annual Meeting of ISSCR;Cairns, Australia, 2007 | In vitro expansion of human chondrocytes in a three dimensional polymer and molecular characterization. |
| ASIA ARVO; Singapore, 2007 | Successful transport and in vitro expansion of corneal endothelial precursor cells, using a novel thermogelation polymer(TGP) based cocktail. |
| 13th Annual meeting of ISCT; Sydney, Australia, 2007 | Autologous Bone Marrow Mononuclear Cells for spinal cord injury- A case report |
| 4th Intl. Meeting Stem Cell Network; Germany, 2007 | Autologous stem cells for spinal cord injury |
| 6th Annual Meeting of ISCT; Philadelphia, USA, 2008 | In Vitro Expansion of Human Saphenous Vein Endothelial cells using a Novel Thermo Reversible Gelation Polymer (TGP) and Their Characterization. |
| Seminar on RM, Yamaguchi University; Ube, Japan, 2008 | Indian scenario of RM and research work on stem cells |
| 7th Annual Meeting of JSRM; Nagoya, Japan, 2008 | One year follow up of 2 diabetic patients treated with lower limb autologous bone marrow stem cells for Ischemic Ulcer - Case report. |
| 6th Annual Meeting of ISCT; Philadelphia, USA, 2008 | Autologous Bone Marrow Stem Cells in Oral Submucous Fibrosis – Our experience in three cases with six months follow-up. |
| 7th Biennial ISAKOS Congress; Osaka, Japan, 2009 | In vitro Culture and molecular characterization of human Chondrocytes using a 3D Thermo Gelation Polymer (TGP) scaffold. |
| 8th Annual Meeting of JSRM; Tokyo, Japan, 2009 | Autologous Bone Marrow Stem Cells for the Treatment of Oral Sub-Mucous Fibrosis - A Case Report |
| BioHealth; Mauritius, 2009 | What does the future hold for stem cell research and therapies? |
| Bio Asia 2010; Hyderabad, India, 2010 | Biomimicry - Our perspectives on biomimicking nano materials and environments favouring tissue engineering |
| RGCON; Delhi, India, 2010 | Autologous Immune Enhancement Therapy (AIET) for Cancer. Strategies for Preservation of Organ Structure and Function in Cancer |
| Stem Cell GBC; Toronto, Canada, 2010 | Autologous Bone Marrow Mono-Nuclear Cells (ABMMNC) for Spinal cord injury- Our experience, thoughts & suggestions for future steps. |
| 1st Annual Meeting of BHS; Dhaka, Bangladesh, 2010 | In vitro expansion of CD34 cell population of human cord blood and bone marrow derived mononuclear cells using synthetic scaffolds. |
| CITIM Conference; Budapest, Hungary, 2011 | Ex vivo expansion of clinical grade Natural Killer cells without feeder layers in stage III-IV cancer patients, post-chemotherapy and radiation. |
| 2nd meeting of ACTO; Miyazaki, Japan, 2011 | Strategies for addressing stand-alone corneal epithelial and endothelial diseases using in vitro expanded cells using Nano scaffolds and polymers. |
| 15th ICID; Bangkok, Thailand, 2012. | Control of airborne pathogens in hospital and laboratory environments by continuous spraying of an alcohol-free disinfectant: Clinister. |
| Biotech 2012, ILBS; New Delhi, India, 2012 | Immune Cells, intricacies and co-existing potentials in tackling cancers and viruses. |
| Intl. con. on Angiogenesis; Chennai, India, 2012 | Constructive angiogenesis in regenerative medicine and destructive angiogenesis in cancer; commonalities and clues to learn. |
| Indian Society of Oncology; Delhi,India, 2012 | Autologous NK cell based Immune Enhancement Therapy (AIET) for Cancer. Conference on Innovations in Oncology - Targeted therapies and Cancer. |
| 5th ARMS; Toronto, Canada, 2012 | Stem Cell Transplantation in India. Keynote Lecture |
| 1st National Stem Cell Congress; Malaysia, 2012 | Cell based therapies for Spinal Cord Injury. |
| ACTRO 2013; Bangalore, India, 2013 | Personalized treatment for cancer using autologous immune cells. |
| 34th SICOT Orthopedic World Conference; Hyderabad, India, 2013 | In vitro expansion of chondrocytes in a three dimensional manner using a hybrid approach; our experience with human and animal cartilage tissues. |
| 34th Congress of the SIU;Glasgow, UK, 2014 | A novel cell based therapy using Buccal epithelium Expanded and Encapsulated in Scaffold(BEES-HAUS) - Hybrid Approach to treat Urethral Stricture. |
| 7th Intl. Sym.; Okayama University, Japan, 2014 | Recent Progress in Cancer Biology through Multidisciplinary Mode - Keynote Lecture. |
| Russian Ophthalmic Forum, Moscow Russia, Sep 2015 | Corneal Endothelial Precursor Based Approach in Treating Bullous Keratopathy employing Nano-materials and Polymers; From Bench to Bedside |
| National Scientific Medical Center, Astana, Kazakhstan, Nov 2015 | Cell based therapies coming of age |
| Kazakh Research Inst. of Eye Diseases; Kazakhstan, Nov 2015 | Stem cell based applications in Oncology, Ophthalmology, Orthopaedics, Urology and Cosmetology. |
| Vinmec International Hospital, Hanoi, Vietnam. Jan 2016 | Autologous Immune Enhancement Therapy (AIET) for Cancer |
| ATRO -2016, Bengaluru, India, Jan 2016 | Autologous NK cell and T cell combination in treating cancer & cell therapy regulations in Japan |
| 22nd Annual Meet; ISCT 2016, Singapore, May 2016 | In Vivo Challenges in Regenerating Corneal Endothelium, Using Corneal Endothelial Precursors, taken from Discarded Human Corneas. |
| 17th Annual Sym. of HMDMRA, Japan, Dec 2016 | Cell based therapies for Cornea: Our accomplishments and the Future |
| Annual Meeting of JACGM, Japan, Dec 2016 | Importance of mRNA Evaluation in in vitro cultured Corneal Endothelial Precursors and Chondrocytes to adjudge the suitability for transplantation |
| The 16th Congress of the JSRM, Japan, Mar 2017 | Regenerating Corneal Endothelium using Precursors from Discarded Corneas |
| RMCR#4 Tokyo, Japan, Jun 2017 | An overview of Regenerative Medicine Scenario in India & our 12-year experience of Indo-Japan bridging |
| 11th ARMS UoT, Toronto, Canada, Apr 2018 | Novel solutions in Regenerative Medicine through inter-disciplinary interaction among institutes in Japan and India. |
| II Intl. Conference of Cardiologists Kazakhstan, May 2018 | Clinical application of autologous BMMNCs in patients with terminal stage of heart failure and our study of futuristic cell therapy in myocardial regeneration |
| 12th ARMS UoT, Toronto, Canada, Apr 2019 | In vitro Expansion of Articular Chondrocytes Derived from Aged Patients with Osteoarthritis using a Thermo-Reversible Polymer Scaffold |
| 72nd Annual Meeting of the JSCB Japan, June 2020 | Enhanced miRNA140 expression in cultured human chondrocytes using a Thermo-reversible Gelation Polymer (TGP) scaffold that retains Hyaluronic acid. |
| The 19th Congress of the JSRM, Japan Mar 2020 | Articular Chondrocytes from aged patients with Osteoarthritis, expressing pluripotency in 3D In vitro culture using a polymer scaffold. Poster Presentation |
| Interdis. Science and Engg. in Health Systems Japan, Jan 2020 | Journey of NCRM on bridging scientists and clinicians of India and Japan for developing cell therapy solutions in RM |
| 40th Congress of SIU 2020. Oct 2020 | A Novel Buccal Tissue Transportation and 3D Cell Culture System using a Polymer Scaffold for Cell Therapy Application in Urethral Stricture |
| British Society of Gerontology 50th annual Conf, 2021 | Reversal of Senescence Associated B-Galactosidase (SA-ßGal) expression of human chondrocytes, in-vitro cultured in a novel 3D scaffold platform. |
| Developmental disorders, 2021 | Improvement of behaviour and sleep pattern in children with autism spectrum disorder along with serum melatonin and alpha-synuclein after Beta-glucan supplementation in a pilot clinical study. |
| BSDB/Genetics Society Annual Spring Meeting. 2021 | Plasticity of In Vitro Tissue Engineered Human Chondrocytes in a 3D platform reflected in terms of an increased averagetissue telomere length due to increase of progenitors, compared to conventional 2D culture. |
| 20th Congress of the Japanese Society for Regenerative Medicine. 2021 | Autologous buccal mucosal cell therapy for male urethral stricture yielding successful engraftment of cells encapsulated in Thermo-reversible gelation polymer scaffold in an animal study. |

# NCRM NICHE 2021 ABSTRACTS

## Plenary Lecture *on Stem Cells & Regenerative Medicine*

**Prof. Timothy J. Kieffer**
**University of British Columbia, Vancouver, Canada**

**PASRM 2021-001**

### Progress Towards a Stem Cell Based Therapy for Diabetes

Diabetes results from insufficient production of the hormone insulin from beta cells in pancreatic islets. Islet transplantation can replace the lost beta cells in patients but is limited by the scarcity of available donor organs. Our aim is to differentiate pluripotent stem cells into functional islets that can serve as an unlimited source for transplantation to treat diabetes. We have investigated the therapeutic potential of pancreatic endoderm cells derived from human embryonic stem cells. Several weeks following transplant into diabetic rodents, these cells mature and secrete sufficient human insulin, in a regulated manner, to reverse diabetes. In rats, we observed inconsistent survival of pancreatic endoderm cells implanted subcutaneously in macroencapsulation devices designed to be immunoprotective via use of a cell impermeable layer, but this was rectified by the addition of portals designed to enable direct capillary vascular permeation into the device interior. In contrast both device types supported cell survival, differentiation and function in mice, with more rapid C-peptide release and better glucose tolerance observed using the devices containing portals. Kidney capsule grafts often contained ductal cells and cysts, whereas cells implanted subcutaneously within macroencapsulation devices differentiated predominantly to endocrine cells. In collaboration with Aspect Biosystems, we are also exploring the feasibility of using 3D bioprinting as an approach to both contain implanted islet cells and protect them from immune attack. As part of a ViaCyte clinical trial (clinicaltrial.gov identifier: NCT03163511), we investigated the safety and efficacy of pancreatic endoderm cells implanted in non-immunoprotective macroencapsulation devices for the treatment of patients with type 1 diabetes and hypoglycemic unawareness. Patients underwent subcutaneous implant of cell products combined with an immunosuppressive regimen. After implant, patients had increased fasting C-peptide levels, increased glucose-responsive C-peptide levels, and developed mixed meal-stimulated C-peptide secretion. Patients had reduced insulin requirements, increased time in target blood glucose range, and improved hypoglycemic awareness. Explanted grafts contained cells with a mature beta cell phenotype that were immunoreactive for insulin, islet amyloid polypeptide, and MAFA. Collectively, these findings support future investigation into optimizing cell therapies for diabetes.

**Prof. Kazutoshi Mori**
**Kyoto University, Japan**

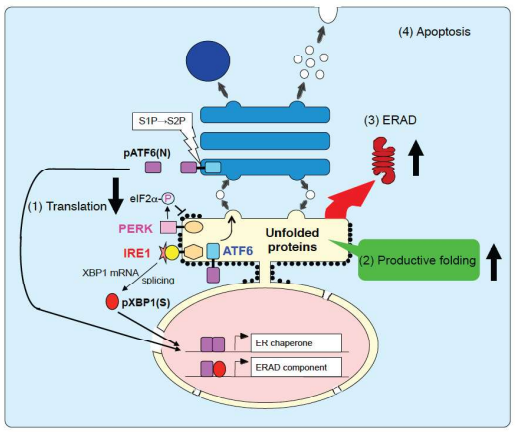
**PASRM 2021-002**

### Dynamics of Function and Regulation of the Endoplasmic Reticulum

The endoplasmic reticulum (ER), where newly synthesized secretory and transmembrane proteins are folded and assembled, has the ability to discriminate folded proteins from unfolded proteins and controls the quality of synthesized proteins. Only correctly folded molecules are allowed to move along the secretory pathway, whereas unfolded proteins are retained in the ER.

The ER contains a number of molecular chaperones and folding enzymes (ER chaperones hereafter), which assist productive folding of proteins, and therefore newly synthesized proteins usually gain correct tertiary and quaternary structures quite efficiently. Yet unfolded or misfolded proteins even after assistance of ER chaperones are retrotranslocated back to the cytosol, ubiquitinated and degraded by the proteasome. This disposal system is called ER-associated degradation (ERAD). Thus, the quality of proteins in the ER is ensured by two distinct mechanisms, productive folding and ERAD, which have opposite directions.

Under a variety of conditions collectively termed ER stress, however, unfolded or misfolded proteins accumulate in the ER, which in turn activates ER stress response or Unfolded Protein Response (UPR). The UPR is mediated by transmembrane proteins in the ER, and three ER stress sensors/transducers, namely IRE1, PERK and ATF6, operates ubiquitously in mammals. Thanks to these signaling pathways, (1) translation is generally attenuated to decrease the burden on the folding machinery; (2) transcription of ER chaperones is induced to augment folding capacity; and (3) transcription of components of ERAD machinery is induced to enhance degradation capacity, leading to maintenance of the homeostasis of the ER. If ER stress sustains, (4) cells undergo to apoptosis.




I will talk on the mechanism, evolution, and physiological importance of the UPR and ERAD as well as its involvement in development and progression of various diseases.

# NCRM NICHE 2021 ABSTRACTS

## Inter-Disciplinary Conclave (IDC)

## IDC Key-note Lecture

**Prof. Dr. Gary A Levy**
**Toronto General Hospital Research Institute (TGHRI), Canada.**

**PASRM 2021-003**

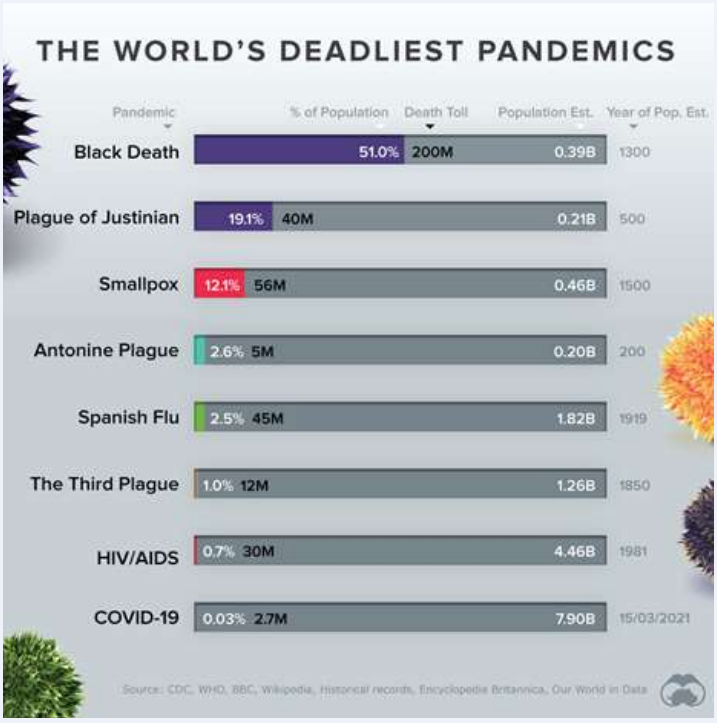
### Lessons learnt from pandemics of the past and present & critical areas of research to face future pandemics

### Important lessons learned from COVID 19.

1. Pandemics are important world problems that largely affect large densely populated urban centers. Research is needed to develop strategies to manage infections in large population centers.
2. The loss of an established early warning system delayed recognition of COVID 19 as a world-wide problem.
3. Once the potential threat was recognized , delay of declaring a pandemic and establishment of appropriate containment strategies led to more severe and extensive disease worldwide.
4. Lack of pandemic preparedness led to high rates morbidity and mortality not only for COVID patients but also to patients with other health care needs(cancer,transplant)
5. High rates of co morbities especially obesity, diabetes and cardiovascular disease led to high rates of mortality in COVID infected patients.
6. Media contributed to public anxiety and stress by giving inaccurate data about COVID 19 including incidence, severity and susceptibility to COVID 19; measures to take to limit transmission; effectiveness of therapeutics and vaccines.

### Introduction:

A pandemic is defined as "an epidemic occurring worldwide, or over a very wide area, crossing international boundaries and usually affecting a large number of people". The classical definition includes nothing about population immunity, virology or disease severity. There have been a number of world pandemics which have resulted in high morbidity and mortality.




### The Covid 19 Pandemic :

For the third time, a zoonotic coronavirus has crossed species to infect humans. The outbreaks were caused by the pathogenic human respiratory coronaviruses (severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV) and COVID-19 which all caused severe respiratory disease. All of these Coronaviruses are related to bat coronaviruses. Whereas SARS and MERS were highly lethal even in younger patients with mortality rates of 20-30%, COVID-19 has a mortality of approximately 2-3% affecting mainly elderly and debilitated patients who have other c -morbidities. To date over 1 million people worldwide have died of COVID-19.. Much is known about COVID-19 including its complete genomic sequence, its cellular receptor (human angiotensin converting enzyme 2 ) which explains why it causes mainly lower respiratory tract infection. Mutations readily occur because coronaviruses have error prone RNA dependent polymerases, making mutations and recombinant events frequent. The recently documented delta variant of COVID 19 is highly infectious and may even cause disease in younger individuals.

### Present Strategies to control pandemics:

For any serious infectious disease there are four main strategies to control/prevent spread:

- Containment
- Mitigation
- Treatment
- Eradication

# NCRM NICHE 2021 ABSTRACTS

## Inter-Disciplinary Conclave (IDC)
## IDC Key-note Lecture

### *Important Areas of Clinical, Social and Basic Research to Pursue Going Forward:*

1. Need for early warning systems for detection of potential pandemics
2. Need to understand mechanisms and potential for zoonotic infections.
3. Need for development of rapid , simple and accurate tests to diagnosis infections
4. Need for new therapeutic drugs to manage infections
5. Need better vaccines to protect against infectious agents
6. Need strategies to inform the public and gain their trust

The presence of Canada's Global Public Health Intelligence Network (GPHIN) proved invaluable for detection of past infectious outbreaks. GPHIN developed algorithms to comb through news reports from around the world, while analysts scrutinized clues on social media, internet blogs, hospital data, financial reports, and by talking to medical sources on the ground. For example, an unusual fluctuation in hog futures in one country might suggest a hidden outbreak of swine flu. The World Health Organization relied on GPHIN for 20 per cent of its epidemiological intelligence and dissolution of GPHIN was a major loss to pandemic preparedness.

Easy to employ laboratory confirmatory tests are essential to track and contain infections. Use of these diagnostic tests will allow understanding of the cause, route of transmission, infectivity rate and morbidity and mortality associated with the infectious agent will determine whether personal, local, regional or national quarantine measures are needed .

Once a pandemic is declared, all efforts must be made to control the spread and mitigate its impact in to reduce incidence, morbidity and mortality and impact using standard public health measures. There is an urgent need for world health agencies to better use the digital word to capture and disseminate information.

As part of pandemic preparedness, discussions must include how to assign and expand access of medical resources including hospital resources (beds, equipment, personnel personal protective equipment (PPE)) and develop and approve new therapeutic agents. There is clearly a need for animal models to study and develop new classes of anti infective and anti inflammatory drugs. The ability to develop effective vaccines such as messenger RNA vaccines for COVID 19 has been a major advance to limit the consequences of COVID 19 and an example of how public private partnerships can be harnessed. There is still a need for more effective vaccines.

Health professionals and news agencies have an important role in transmitting accurate data to the public so they can make informed decisions. This will help in implementing policies which have both social and economic consequences. Lack of appropriate messaging can contribute to public resistance to institution of health care policies.

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# Select Oral Presentations on late breaking abstracts with emphasis on COVID-19

**Dr. Stanley Jeremiah**
**Yokohama City University, Japan**

**PASRM 2021-004**

## Pandemic preparedness: Respiratory disinfection to reduce casualties

The COVID-19 pandemic has provided valuable insights on the progression of a point source viral outbreak into a pandemic shedding light on the inadequacy of control measures that we have to limit the spread of respiratory viral outbreaks. It took over one year since the outbreak till the arrival / approval of a specific vaccine to control its spread (Commissioner, 2021). As specific therapeutic or preventive measures for any novel virus take time to develop, get tested and approved; the pathogen of the outbreak would be disseminated widespread during the "wait-time". The outcome of this wait-time could vary from less severe to mass casualties based on the infection fatality rate of the pathogen causing the outbreak. SARS-CoV-2 with a maximum observed infection fatality rate of 1.54% (Ioannidis, 2021) has been considerate as the wait-time has not been severely deleterious to humanity. Future viral outbreaks with a higher infection fatality rate can cause mass casualties if we are not equipped with broad antiviral measure to control the spread and buy us time until specific measures are available. The concept of respiratory disinfection involves in rendering the respiratory tract of a person temporarily sterile to reduce the viral transmission. Disinfecting the respiratory tracts of the subjects in an outbreak zone can limit the spread in that area. Also, scenarios like COVID-19 infected individuals requiring an emergency lifesaving surgical procedure can be tackled with respiratory disinfection to reduce the risk of transmission to healthcare providers. Opening of public gatherings during the pandemic can also be made possible with this concept. Although different agents maybe suitable (Kawana and Kudo, 1999), Silver nanoparticles seem to be an attractive candidate that could considered and evaluated for pandemic preparedness on foreseeing a possible respiratory viral outbreak in the future (Jeremiah et al., 2020).

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**Dr. Tomohiko Kisaka**
**Hiroshima University, Japan.**

**PASRM 2021-005**

## Construction of a decentralized medical device development platform during the COVID-19 pandemic

Hiroshima University has developed Biodesign program in collaboration with Government of India as part of Prefectural medical-related industry cluster formation. In US and India, they have raised the solutions of "value supply chain established in Silicon Valley" and "frugal innovation driven by lean-startup in Emerging Country," respectively. Based on learning from School of International Biodesign in India, we aim to realize frugal innovation by taking technological advantage and reliability of Japan in developing medical devices at affordable price. After launching Fellowship in 2019, we were entrusted with Local Innovation Support Project for regional companies1) and provided academic guidance to manufacturing companies. The COVID-19 pandemic required medical resource optimization. In order to promote medical technology (MedTech) development even under stagnant logistic situation, we proposed "Decentralized Platform among Local Core Institutions" with AMED support. We report our research experience2),3) from the viewpoint of biomedical engineering as an optimal solution promoting MedTech demonstrating resilience.

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# Select Oral Presentations on late breaking abstracts with emphasis on COVID-19

**Dr. K. Raghavan**
**JAICARE, Madurai, India.**

**PASRM 2021-006**

## Two variants of Biological response modifier glucans (BRMG) in Covid-19 pilot study; Follow-up summary

Cytokine storm and Coagulopathy having been implicated as major causes of morbidity and mortality in COVID-19 patients, we conducted a randomized multiple-arm pilot clinical study in 24 RT-PCR positive COVID-19 patients. The Patients were randomly divided into three groups (Gr): Gr. 1 control (n=8); Gr. 2: black yeast Aureobasidium pullulans AFO-202 strain produced beta 1,3-1,6 glucan n (n=8); and Gr. 3, a combination of AFO-202 and N-163 strain produced beta glucan (n=8). The study's preliminary results showed that for thirty days, there was significant control of IL6, D-Dimer and neutrophil to lymphocyte ratio (NLR), a significant increase in lymphocyte to CRP ratio (LCR), leukocyte-CRP ratio (LeCR) and marginal control of ESR in COVID-19 patients. Follow-up study revealed that the patients of Gr-2 and 3 maintained status quo for more than two months without re-infection or morbidities. Gr.1 patients had increase in te levels of the parameters of inflammation after 15 days. CT scores and BReath count for Early prediction of Worsening Covid COurse: BREW-COCO scores showed significant improvement in patients of Gr.2 and 3 thereby confirming the potentials of these beta glucans which are well known food supplements with decades of a track record for safety for their use as an adjunct in the management of COVID-19 and the ensuing long COVID-19 syndrome.

**Dr. K. Ramesh Shankar**
**Lincolnshire Partnership NHS Foundation Trust, United Kingdom.**

**PASRM 2021-007**

## Physician Burnout during COVID-19 Pandemic & Mental Health Support.

The concept of physician burnout has undoubtedly been a ubiquitous challenge that health care professionals have faced even prior to the current pandemic, COVID-19.

When assessing physician burnout, Amanullah et al. noted that it was crucial to use a unifying method to assess burnout and regarded the Maslach Burnout Inventory as the measure of choice (1). Maslach et al. best-defined burnout as a "psychological syndrome characterised by emotional exhaustion, depersonalisation and a sense of reduced accomplishment in day-to-day work" and hence, designed the inventory with the three mentioned components (2) . One such study conducted by Dimitriu et al during the first wave of the pandemic assessed burnout amongst 100 healthcare professionals using the MBI and noted that 76% of the sample reported burnout, which was noted as "superior to studies conducted in normal periods" (3). A recent systematic review categorised further contributing factors to burnout including sleep deprivation, lack of supportive work environments and gender differences (1).

Physician burnout has been deemed as an issue of high importance due to the potential serious consequences of burnout that have previously been reported by Shanafelt et al such as "deterioration in the quality of care" for service users, increase in the use of drugs and alcohol & possible marital and family problems (4). Hence, emerging research illuminates the need for interventions to reduce physician burnout; certain recommendations that have been made include: a formalised burnout reduction programme, online or telephone access to helplines and support programmes through staff wellbeing services (1). In addition, primary preventative methods including training during medical school regarding stress management techniques and pandemic planning could be incorporated for the future.

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# FCQ Elite Presentations

**Jenifer Kiem Aviani and Lily Muflianti**,
*Institut Teknologi Bandung, Indonesia*

**PASRM 2021-008**

**Several scientific findings and theories have been disproven or superseded over time. Discuss on one scientific finding or theory in the field of cell-based therapies or regenerative medicine which has now been disproven or superseded with evidence.**

**Abstract:**

*Aging, Cancer, and Regeneration:*

Aging can be defined as the physiological deterioration in line with the increasing age of an organism. In order to distinguish the aging process from damage that occurs stochastically over time, Benjamin Gompertz described aging as a process leading to an exponential increase in mortality with time. Aging involves series of time processes molecular changes in the somatic tissues.

The first foundation of aging theory was carried out by August Weismman and George William based on evolution perspective. Weismann and William's view had yielded a hypothesis where somatic cells progressively lose the traits of immortal proliferation and regeneration as a result of active selection for increased reproductive fitness. The observation based on evolutionary point of view had resulted in Weismann barrier where multicellular and higher order organisms tend to aged and have limited regeneration capacity, in contrast to immortal regeneration of simple organisms.

Study on urodeles had brought an insight where retention of embryonic traits causes epimorphic regeneration. So that there might be a role of developmental state and regeneration capacity. Repeated injury had resulted in defective regeneration, meaning there is a regeneration capacity. Theory of regeneration capacity is answered through Haflick and Olovnikov's research where cells undergo progressive shortening of terminal DNA sequence teleomeres and its expression will lead to longer lifespan and might resulted in cancer development. Later development of the research and theories had brought insights of molecular mechanisms happened during aging including the importance of Lin28/Let7/Lin 41 pathway, epigenetic control, and senescence-associated secretory phenotype (SASP) which also shared pathway with cancer. Thus, aging and regeneration capacity limitation is an evolutionary strategy to prevent our body from cancer. Based on the old theories, aging and cell development is an irreversible process due to global gene expression changes in every stage of development.

*New Perspective of Aging: the Reverse Process:*

Experiments on somatic cell nuclear transfer (SCNT) on amphibians and the latest was on sheep had brought new insight that the cells might be reprogrammed to become young again. Thus the cell development is reprogrammable. In 2006, Yamanaka and colleagues discovered the anti-aging elixir, the 4 Yamanaka factors Oct4, Sox2, Klf4, c-Myc cocktail, which application could reset cellular damage associated, stress-associated, and senescence associated epigenetic markers in fibroblast. The application had resulted in induced pluripotent stem cells (iPSC) which restored all aged cell telomeres restriction fragment (TRF) length back to or even longer that the embryonic state and completely reset age-related DNA methylation changes. This finding had suspended the theory of irreversible reprogramming and even brings back the cell back to pre-Embryonic Fetal Transition, crossing the barrier by inducing pluripotency.

This phenomenon had brought the hypothesis of Waddington epigenetic landscape of development, aging, and reprogramming. Waddington proposed that genetic and epigenetic influences produced a developmental program of differentiation during development. This visual representation, based on Waddington's epigenetic landscape, illustrates somatic cell differentiation and somatic restriction at critical developmental transitions (PT, EFT, NT, AT) leading to loss of regenerative potential and aging. The transition from germ line-competent naive ES cells to primed ES cells leads to a reduced capacity for germ-line transmission but a retention of replicative immortality and the capacity to differentiate into all somatic cell types. The initiation of ES cell differentiation at the pluripotency transition leads to the production of diverse intermediate progenitors that generally lack telomerase expression. The subsequent differentiation of somatic cells and passage through the embryonic–fetal transition 'hardens' the pathways, reducing plasticity and thereby inhibiting regenerative potential. Induced pluripotent stem cell reprogramming is capable of restoring somatic cells back to either naive or primed immortality.

The reprogramming is not as easy as in theory. Expression of let-7 is the biggest hurdle of pluripotency. Moreover, the reprogramming cocktail also resulted in upregulation of senescence pathways which also share pathway with the cancer development pathway. Full pluripotent iPSC had been studied to cause side effect of development of teratoma. Thus, another safer approach is needed. One of the approach is transient reprograming and induced Tissue Regeneration (iTR) a strategy to achieve partially reprogramed state to reversing the epigenetic state and telomerase without reversion to pluripotency. Control of timing and intervention during transient reprogramming will bring new perspective on safer in vivo reprogramming method.

# FCQ Elite Presentations

**Noora Jabeen and Mizna Nafisa**
*Kasturba Medical College, India*

**PASRM 2021-009**

## Cornea and cartilage are avascular tissues of mammalian body; Compare and contrast the cell-based therapy approach strategies to be considered, based on their nature, function, till date reported outcomes and lessons learned.

### Abstract:

Cornea and cartilage are avascular tissues, yet the regenerative medicine approaches are different for both. Maintaining avascularity in the cornea is crucial to maintain transparency and vision [1]. Whereas in cartilage, avascularity slows down its healing and regeneration. For the restoration of cornea, autologous cells from limbus as well as from other sites are researched. Each of the layers of cornea can be individually regenerated or a self-assembled complete corneal construct can be produced [2]. Recombinant human collagen was proposed to block neovascularization in the cornea and improve visual acuity [3]. Tissue engineering also proposes use of biomaterials and scaffolds that promote indigenous growth of corneal cells. Hence xenoderived [4] and synthetic polymer scaffolds [5] are being commercialized.

Unlike cornea, articular cartilage is constantly under sheer force and dynamic compression. This poses a challenge to morphogenesis and use of regenerated cartilage scaffolds. Cartilage regeneration mainly evolved the use of autologous chondrocyte implantation [6]. The use of bioreactors to mechanically stimulate the chondrocytes is a crucial step in cartilage regeneration that is different from corneal regeneration [7]. The use of lubricants to sustain joint motility is also an added factor [8].

Although Stem cell therapy continues to face many challenges, one of them being the dedifferentiation and loss of "stem like" characteristics of the transplanted cells when expanded in vitro, a lot of advances and breakthroughs continue to occur. Perhaps regenerative medicine is the answer to the setbacks in current modern medicine.

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**Aishwarya Raj and Soham Deepak Jagtap**
*National Institute of Mental Health and Neuro Sciences (NIMHANS), India*

**PASRM 2021-010**

## The terms "Gain of function research" and "Dual use research of concern (DURC)" though are known for long, have recently gained significance, following the SARS-COV-2 outbreak. Narrate with literature evidence, one beneficial outcome and one adverse outcome of them from the pre-Covid era.

### Abstract:

Gain of function research involves altering any biological agent to enhance its attributes, while, dual use research concern is one that is beneficial to mankind but can be harmful if misapplied. Public interest in both of these terms have gained heightened attention since the peak of SARS-CoV-2 pandemic. As is any coin, these researches too are dual faced. On the beneficial end, there is a great requirement to be prepared for any sort of global pandemic outbreak. Given the devastating economical and health effects of the pandemic, advanced surveillance and predictions will help in responding to future pandemics. With emerging zoonotic viruses like influenza many of which can be termed as pandemic potential pathogens (PPP), it is a boon to have infection control and/or intervention strategies

ready at hand. So is the identification of high-risk genetic pool before-hand. Such was the need for studies in 2012 with H5N1 virus that was adapted to transmit infection in ferrets through aerosols. At the same time, the risks associated with such studies should not outweigh the benefits; ethical and biosafety concerns being the primary risk. The 2014 incident of accidental anthrax exposure in Center for Disease Control and Prevention, Atlanta, Georgia, if repeated with a study with the modified flu virus, can lead to a grave public health crisis, even causing the next pandemic. Weaponisation of PPPs can herald a new arms race and even bioterrorism. Thus GoFR and DURC are researches that needs to be critically handled like a dual edged sword.

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**Alfred Patisenah and Daisy Ramadhani M.**
*School of Life Sciences and Technology, Indonesia*

**PASRM 2021-011**

**Several scientific findings and theories have been disproven or superseded over time. Discuss on one scientific finding or theory in the field of cell-based therapies or regenerative medicine which has now been disproven or superseded with evidence**

**Abstract:**

*The Rise and Fall of STAP: Somat ic cell reprogramming by external stimuli*

Two decades ago, Vacanti et al. put forth the idea of pluripotent spore like cells existing within adult animal tissues exposed to stress[1]. As plant somatic cells were known to undergo nuclear reprogramming into immature blastema cells upon experiencing drastic environmental stress, this eventually spurred Obokata et al. to investigate the possibility of these pluripotent spore like cells arising from differentiated animal somatic cells[2]. This hypothesis was then tested through pluripotency assessments as well as teratoma and chimera production of somatic cells exposed to low pH treatment, which all produced seemingly successful results[2,3]. The cells were then termed STAP (stimulus-triggered acquisition pluripotency) cells[2]. However, the published papers came under suspicion for experimental misconduct and data manipulation and were finally retracted[4,5]. Internal investigations with genomic analysis showed indications of embryonic stem cells contaminating the STAP cell lines[6]. Attempts to replicate the experiment by several different research institutes also failed to produce pluripotent STAP cells[7]. The failed attempts highlighted the possible errors that could have led to Obokata's result, such as autofluorescence[7]. In conclusion, STAP cells have been successfully disproved, and STAP was regarded as a scientific artifact arising from negligence and misinterpretation of data. This story reminds us of the importance of rigorous research in an attempt to falsify the hypothesis and the careful design and execution of scientific experiments.

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**PASRM 2021-012**

**Several scientific findings and theories have been disproven or superseded over time. Discuss on one scientific finding or theory in the field of cell-based therapies or regenerative medicine which has now been disproven or superseded with evidence**

# FCQ Elite Presentations

**Abstract:**

*Microfracture, Autologous Chondrocyte Implantation (ACI-P and ACI-C) superseded by current generation M-ACI*

The cartilage has very limited tissue regeneration capacity and cartilage defects represent a risk factor for the development of arthritis. Autologous Chondrocyte Implantation (ACI) is a 2-step procedure that has been followed for over 30 years in treating articular cartilage defects. There are 4 grades of severity of cartilage defects as per the International Cartilage Repair Society (ICRS), and ACI is indicated for grades 3 and 4, which affects more than 50% of the cartilage depth and the defects underlying the bone.[1] In Porcine-type I/III collagen membrane (ACI-C), the graft failures are high, while treatment failures and graft hypertrophy in Subsequent Surgical Procedures(SSPs) are high in Periosteal flap ACI (ACI-P). There are no significant changes in the functional outcomes between ACI-P and ACI-C as well.[2] The Matrix-induced Autologous Chondrocyte Implantation (M-ACI), simple less-invasive, and less-extensive procedure produce a higher functional outcome, shows low hypertrophy and the histological outcome showed that cartilage was well integrated with the underlying subchondral bone. It neither requires a watertight seal nor a periosteum cover under which the cultured chondrocytes are usually injected.[3] The technical advantages of M-ACI make it an emerging, fast, suture-free, and less-invasive method in regenerative medicine resulting in ACI-P and ACI-C becoming less relevant in practice.[1]

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*In 2020 and 2021, it is being conducted as a Virtual event due to the ongoing COVID-19 pandemic related travel restrictions.*

*See you all in*

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