



# THE BIOTALK MAGAZINE

biotech for everyone

*June 2020 Issue*

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We are a team of Biotech engineers united by our goal to build a Biotechnology community. We want to be a bridge between students, scholars, professors and the industry. We are looking for dots in our community to connect; join us in this initiative to set the right path for our future scientists and engineers!

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# WHAT'S NEW?

## COVID-19 IN A NUTSHELL

### *Recent therapies and treatment options*

Currently biotechnology has gained popularity due to recent advances in genetic engineering or recombinant DNA technology, that has proved its potential in altering life forms. Among the smaller organism's microbes such as bacteria and viruses have been found to be both beneficial as well as dangerous.

To elaborate on this, I wish to share some recent theories and discoveries related to SARS-CoV-2.

It was in late December 2019 when Wuhan city of China reported the outbreak of most pathogenic and contagious disease called COVID-19 caused by the coronavirus SARS-CoV-2. In the earlier decade of this century two more similar diseases called SARS and MERS were reported to affect millions of people in the world. It was found that both the outbreaks were caused by coronavirus strains SARS-CoV and MERS-CoV respectively. Both these diseases were reported to have their emergence in animals and cause had severe morbidity rate. In January 2020, World Health Organisation declared SARS-CoV-2 as a pandemic, that rapidly spread into the whole worldwide. The traces of emergence of this virus were tracked to Wuhan's seafood market where the virus is assumed to have jumped from bats to humans and ultimately causing human-to-human transmission. Viruses are non-living entity outside the host body. But once they enter the host (humans in case of SARS-CoV-2) body they directly enter into the cells, where they use the host cell machinery to replicate and multiply. Once several copies of viral particles are formed inside the cell, they come out by lysis of the cell membrane, making millions of copies of viruses. SARS-Cov-2 possess single-stranded RNA as its genetic material. This virus attaches to the ACE2 receptor of host cells with the help of spike protein present on its surface.

Scientists have been working on development of vaccine of the novel coronavirus but this process still has a long way to go. However, repurposing of the existing anti-viral drugs has shown some promise as therapeutic approach.

Chloroquine and hydroxychloroquine have been used as prophylactic drug for malaria. These drugs have been found to directly target the ACE2 receptor on the host cells and blocks the entry of virus into the cells. However, the rigorous customization of the dosage and severe side effects associated with their administration limits its utility for treatment of COVID-19.

On the other hand, anti-viral drug, Remdesivir had shown positive anti-viral activity in diseases such as Ebola, SARS and MERS. It is a nucleotide analogue that blocks the viral nucleotide synthesis and stops viral replication. But its clinical trials with COVID-19 patients has caused severe side effects and did not display its utility as treatment option.

Lopinavir-ritonavir (Kaletra) is a viral protease inhibitor which inhibits viral 3CLpro or PLpro proteases. This drug has been successfully tried for the treatment of HIV-AIDS. But has been found to be non-effective in patients with severe coronavirus infection.

Ivermectin, an anti-parasitic drug used against HIV-1 virus has been reported to target importin proteins which are responsible for nuclear import. The clinical trials of this drug for novel coronavirus infections are still ongoing.

Other than repurposing of drugs, several other therapeutic options are also under trials for treatment of COVID-19.

Plasma therapy, is a concept put forward by Sunney Xie, the director of Beijing Advanced Innovation Centre for Genomics at Peking University in the year 2020, this therapeutic approach deals with collection of plasma from the blood of patients who have recently recovered from COVID-19 infection. The plasma of such individuals contains antibodies against the SARS-CoV-2 virus and its injection into the body of an infected individual improves its immunity to fight against the viral load at infected site.

One upcoming therapeutic idea about the use mesenchymal stem cells (MSCs) has gained pace after few researchers discussed their inherent property of anti-inflammation and immunomodulation. MSCs have been known to exhibit immunomodulatory properties and reduce the maturation of cytotoxic T-cells and B-cells. If we look at the pathophysiology of COVID-19, we can find that as soon as the virus reaches the lungs, the immune system cells get activated and try to kill the virus. This in turn results in secretion of large number of cytokines at the site of infection. This cytokine storm, eventually results in extensive inflammation ultimately leading to lung fibrosis. This makes the process of breathing difficult and creates pneumonia like conditions. Intravenous injection of MSCs carries them to lungs, where MSCs act by secreting anti-inflammatory cytokines and reduce the lung inflammation.

There are several vaccines which are under clinical development. Recently, a company reported developing a vaccine candidate against COVID-19, they termed this vaccine candidate as mRNA-1273, this vaccine uses synthetic lipid nanoparticles to carry mRNA-1273 as template, it is been certainly believed that this vaccine would train immune system to recognise SARS-CoV-2 S protein, as this protein is used by the virus to bind and enter the host cell. Also, a joint collaboration of University of Oxford and AstraZeneca developed a recombinant vaccine named AZD1222 in

which they engineered a chimpanzee adenovirus to carry DNA for spike antigen, as this approach would build a strong memory B cell and T cell responses.

Thus, several trials are still required to guarantee the success of any therapeutic strategy against COVID-19. Scientist have been extensively working to develop vaccine to combat chances of such outbreaks in future.

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## **ENDOGENIC RETROVIRUSES IN ONCOLOGY**

### *A perspective on detection*

Cancer is one of the deadliest diseases we face today, but it is far from a modern occurrence. Egyptian papyrus scrolls suggest that cancer dates back to 1500BC; in fact the Egyptians could differentiate between benign and malignant tumors, and had surgical procedures for surface tumors that are similar to the ones we have today. Years of research have only begun to scratch the surface of the vast and intricate mechanisms that go to work to awaken this life threatening beast; it is safe to say that the more we unearth, the more we are in the dark. When approximately 10 million people around the globe succumb to cancer annually, it becomes important to elucidate the causative factors. Hence it was estimated that nearly 1/5<sup>th</sup> of all cancers in humans have an underlying infectious etiology.

Retroviruses are a class of viruses that possess genetic material in the form of RNA, which when infects a host cell is converted to DNA by enzyme reverse transcriptase. This DNA now gets integrated into the host cell DNA (integrase), where it is transcribed and translated to produce virions. Now this piece of viral DNA usually exits the host DNA, but if it loses the *env* gene (possibly by mutation), it loses the ability to infect new cells and stays as a part of host DNA indefinitely without being transcribed. When the cell divides, this viral DNA is also distributed to the daughter cells. If this occurs in germ cells and is inherited generation after generation, it is known as an endogenous retrovirus (ERV). The anomaly can later trigger changes in cell cycle and eventually lead to the formation of a carcinogenic cell.

To identify ERVs, it seems like we only have to scan the genome for a particular viral sequence; after all ERVs are recognized by their similarity in genomic structure with all retroviruses,

typically consisting of a *gag*, *pro*, *pol* and *env* genes flanked by two long-terminal repeats (LTRs). However, as simple as it sounds, it is quite difficult. First of all the viral DNA represents a very minute fraction of the total cell DNA, even if the viral DNA has duplicated many times. Also, viruses have an astonishing variety in their sequences, making viral family classification a complicated process. Add to that their propensity to mutate rapidly. Therefore, any method for identifying presence of this ERV must fulfill the following conditions:

- (1) It should be able to function with a broad spectrum i.e. should function regardless of point mutations and minor differences in nucleotide code; and
- (2) The ERV fraction must be quantitatively larger than the native DNA fraction, either by increasing the target ERV sequences or by reducing the native DNA fraction, the latter of which is not feasible for the case of ERV since it is integrated DNA.

Let us assume we have a system or procedure for successfully extracting total cellular DNA from the cells of a sample tissue such as blood, including treatment with mild detergent, protease and RNase to remove lipid, protein and RNA fractions of the cell, yielding pure DNA. This DNA is then amplified via techniques like PCR in case the sample volume is too small. Then the resultant multiple copies of total cell DNA are diluted, mixed with enzymes like DNA polymerase and its required cofactors like magnesium, iron etc. forming the sample solution. This sample solution can then be distributed to multiple wells through microchannels, using positive/negative pressure systems in an enclosed chamber. Now these wells will have clear plastic walls on two opposite sides, and can be a part of a card system as shown in the figure 1.

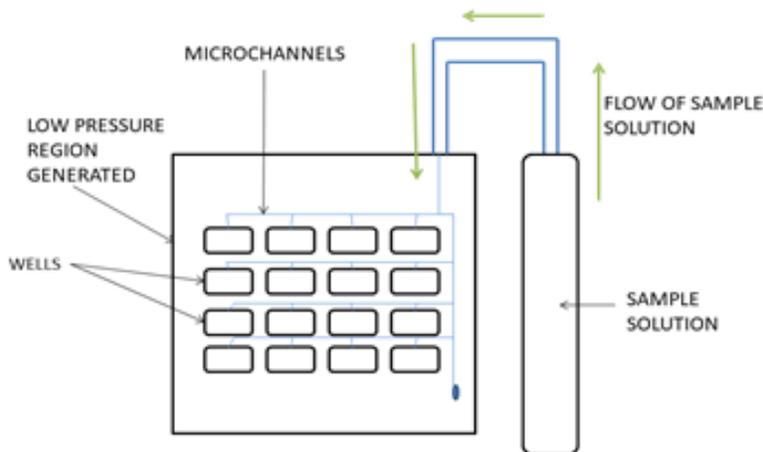


Figure 1 Card System

Each well contains four different primers, specifically designed to identify and subsequently amplify a particular retroviral oncogene. Instead of using PCR for DNA amplification, I would suggest we use loop mediated isothermal amplification or LAMP, a technique that requires

shorter amount of time to produce more copies of a sequence. The added advantage is that we would require a single incubation temperature, removing the requirement of a thermocycler.

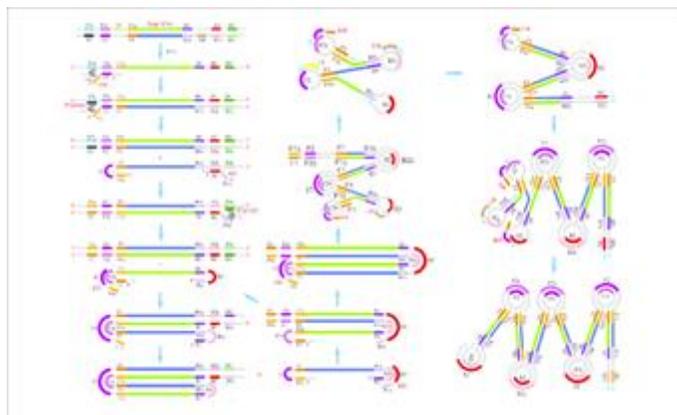


Figure 2 LAMP Schematic

LAMP technique (schematic given in figure 2) causes amplification of the target sequence, leading to an increase in turbidity of solution in that particular well, and allowing us the simplest of detection techniques i.e. optical density (OD) detection and comparison using spectrophotometric analysis. This will identify which well has high OD and hence, since we have designed the primers, which retroviral oncogene is present. Designing of the primers here is the most important task and a huge investment, but the returns on it seem to be quite profitable considering the economy of the remainder of the procedure. This rapid technique would for sure revolutionize how we treat cancer, and can be a huge step in personalized treatment for cancer patients, leading to more number of victories in this raging war against the disease.

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## WHOLE GENOME SEQUENCING OF BACTERIAL GENOMES

The human genome project kickstarted Biotechnology research all over again. Opening doors for genome editing and sequencing in humans, it reinvented Biotechnology as a field people could look up to. One such concept introduced was WGS.

Whole genome sequencing (WGS) can be defined as the process of determining the complete DNA sequence of an organism's genome at one single time. As straightforward as this sounds, this

should not be confused with DNA profiling as profiling only determines the likelihood of a genetic material coming from an individual or a group of individuals. Even in the presence of traditional gene sequencing methods such as Sanger's Sequencing, the WGS has taken over a wide arena of research and development in various fields.

Talking about the basics, sequencing of a bacteria can be done using the general principle of typing of bacteria. Typing and sub-typing allows the differentiation of bacteria beyond species and sub-species level. The typing of bacteria can be divided into two broad categories as follows:

A] **Phenotypic:** characterization of bacteria based on expressed traits.

[e.g.: microbial fermentation, antimicrobial resistance, etc.]

B] **Genotypic:** characterization of bacteria based on genetic content.

There are two types of genotyping methods as follows –

1. **Band based:** The general principle of this method is to obtain DNA in bands. These bands can be produced either by amplification PCR or by cutting with restriction enzymes. Finally, the DNA obtained are run on gel electrophoresis and separated based on their sizes.
2. **Sequence based:** The DNA fragments can be sequenced either by PCR or using WGS. It is possible to analyze SNPs using this typing method.

Choosing the most appropriate method for typing is completely dependent on the purpose and the expected results.

### **Scientist at Work!**

The DNA is cut into several fragments using the restriction enzymes after which ligate adapters are attached onto the DNA fragments. These adapters consist of amplification primers and sequencing primers. If one run contains more than one sample then the adapter should involve a barcode. This barcode is specific to each sample and thus it is possible to involve more samples in a single run. The amplification of these DNA fragments takes place producing more copies of the fragment DNA and then the samples are ready to be sequenced.

The sequence data obtained is stored in FASTA format. However, the data obtained after sequencing is not available in FASTA format as we only get certain reads that are also termed as **raw reads**. These raw reads can be obtained as Single end reads (unidirectional) or Paired end reads. These paired end reads have insert size which fills the gap between the pair. This insert size

only includes the reads + fragment gap and adaptors are not included. The insert size can vary from as small as 300bp to the large 1200bp. The insert size mainly depends upon the sequencing technologies. The raw reads are obtained in the FASTQ format (FASTQ= FASTA + Quality Scores).

As more than one sample is run at a time, splitting and clipping data is done using barcodes in the FASTQ format. Usually, de-multiplexing is done by the sequencer itself. The next step is to trim the reads as certain reads of waste content are present. After these processes, it is necessary to form an assembly of the DNA fragments. When assembly is done without the reference genome, it is termed as **de novo assembly**. We use it when we majorly want to find the gene or any genetic markers that are present. It uses the De Bruijn Graph theory which merges reads to form a longer DNA sequence that we call **Contigs**. The format for contigs is FASTA. Good contigs are the ones that are large enough and contain the genes/genetic markers that one is looking for. N50 is the 50% of the total size of the contigs and is best to be considered for further analysis.

When assembly is done using a reference genome, it is termed as Mapping to a reference genome. It is usually used to detect point mutations. This de novo assembly/ mapping to a reference is done using bioinformatics tools. We use a web-based tool as they are platform independent, require little computer resources and can be done everywhere although it requires a lot of patience. Various assemblers of the Centre for Genomic Epidemiology (CGE) are used for this purpose.

For e.g.: Assembler – Newbler (Overlap Layout Consensus)

- 454
- Ion Torrent

Assembler – Velvet (De Bruijn Graph)

- Illumina
- ABI Solid (color spaced)

## **The Future Of WGS**

As there are many advances in the techniques and tools used in sequencing and efforts to make these tests affordable, there will be a huge impact on the clinical laboratories and companies that give access to genetic information. This technology will be available to the common and many will feel free to get their genomes sequenced. The development of whole genome sequencing will pave way for many more branches of genomics such as metagenomics, reproductive health, DNA analysis for forensics, agrigenomics, etc. Medical assistance related to rare diseases can be

suggested by physicians by analyzing the genome sequencing reports and the healthcare sector will benefit.

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## **BREAST CANCER TUMOR MICRO-ENVIRONMENT (TME) AND CANCER-ASSOCIATED FIBROBLASTS (CAFs)**

Cancer is the second leading cause of death worldwide; its treatment is mainly done with the help of surgery, radiotherapy, chemotherapy, and immunotherapy- these used separately or in combination. The tumor is not just a mass of malignant cells, it comprises of cellular and non-cellular parts with continuous interaction with the nearby environment. Apart from malignant cells, the tumor micro-environment (TME) has cancer-associated fibroblasts (CAFs), neuroendocrine cells, adipocytes, immune and inflammatory cells, blood vessels, lymphatic vessels, and extracellular Matrix (ECM). All these play a significant role during tumor development and metastasis. If these various components are necessary for TME, an alteration might retard tumor development and progression. Research at individual components of TME might help to map better therapies for cancer.

Cancer-associated fibroblasts (CAFs):- CAFs are stroma cells that secrete extracellular matrix (ECM) components. These are associated with progression, invasion and physical remodeling of ECM of the tumor; and is found in abundant amounts in case of breast cancer. CAFs have different RNA and protein expression than their counterparts present in healthy tissues. They produce metalloproteinases that promote metastasis and invasion, and increased expression of genes related to morphogenesis and development has also been seen. It has pro and anti-tumor effects but in the case of breast cancer takes the side of the tumor and helps in the tumor development.

Origin of CAFs: – The source of CAF is not clear. As suggested by some studies, it is derived from more than one source. Emerging evidence suggests that it is a “cell state” rather than a cell type, for instance, we have grouped the immune system cells as immune cells because of their work to protect the body from any kind of harm while comprising of different type of cells. Likewise CAFs are cells having similar phenotypes with some subtypes. Due to the heterogeneous nature of CAFs, several studies conducted to trace its origin have different hypotheses-cancer stem cells (CSCs), pericytes, epithelial cells, endothelial cells, mesenchymal stem cells (MSCs), adipocytes, tissue fibroblasts, and bone marrow stem cells.

Markers used to identify CAFs: – During the passport making process, you may be asked about any sign or mark present on your body for identity purposes, likewise cells also possess biomarkers through which they are identified and classified. In case of CAFs there are no clearly established markers in existence, but some markers used to identify are over-expression of  $\alpha$ -smooth muscle actin ( $\alpha$ -SMA), fibroblast specific protein 1 (FSP-1) and fibroblast activation protein (FAP) as well as by their spindle shape.

Current progress in CAF research: – Being humans we are inquisitive species. Questions on CAFs development the mechanism of CAFs has been fascinating scientists for quite a while. As a result a lot of research is going on worldwide and every day the scientific community is achieving new milestones. There are certain mechanisms by which a transition can take place; such a mechanism is described by a group of scientists- Cangkra and their colleagues- in which cancerous cell releases Activin A that induce CAF phenotype in fibroblast via downregulation of p53 and upregulation of mDia2. Scientists working at the Medical University of Lodz Poland reported another mechanism for the development of CAFs- the endothelial-to-mesenchymal transition (EndMT) where tubulin- $\beta$ 3 upregulation and its phosphorylation might lead to the development of CAFs. The killing of CAFs is possible by Ligustilide and also shows an antitumor effect on breast cancer with reduced chemotherapy resistance.

A team of scientists from China have determined the role of the complement system during breast cancer metastasis which occurs via C3a-C3aR signaling that modulates the CAFs function; they found PI3K/AKT signaling being an integral part of C3a-C3aR signaling which ultimately activates CAFs. Exosomes secreted by CAFs are loaded with proteins, lipids, and non-coding microRNAs such as miR-181d-5p that can affect the TME. MicroRNA miR-181d-5p secreted by CAFs have been seen as a promoter in various functions such as EMT, proliferation, invasion, migration, and an apoptotic inhibitor in breast cancer cell lines by CDX2 and HOXA5 reduction as reported in “Molecular Therapy-Nucleic Acids” published on 6 Mar 2020. Researchers from Hacettepe University School of Medicine of Turkey found that CAFs of breast cancer origin can trans-differentiate the monocytes into M2-like Macrophages which in turn suppresses the immune system by using the PD-1 axis, CAFs have been seen promoting EMT, invasion, and metastasis by inducing M2 Macrophages. CAFs also promotes stemness in Breast cancer cells by maintaining the cancer stem cell (CSC).

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# RESEARCH CORNER

## ANALYSIS OF DIFFERENTIATION POTENTIAL OF MESENCHYMAL STEM CELLS ISOLATED FROM WHARTON'S JELLY

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### INTRODUCTION

#### **Mesenchymal stem cells**

Mesenchymal stem cells(MSC),a progressive subtype of adult stem cells, hold immense prospective for regenerative medicine because of their capability of self-renewal and differentiation into tissue-specific cells such as osteoblasts, chondrocytes and adipocytes[1].MSCs organize tissue development ,maintenance and repair and are of massive use for musculoskeletal regenerative therapies to treat age-related orthopedic degenerative diseases and other clinical conditions like treatment of autoimmune diseases[2].

#### **Umbilical cord Wharton's jelly:**

The umbilical cord comprise of two arteries and one vein surrounded by the layer of mucoid connective tissues known as Wharton's Jelly(WJ).WJ is rich in stromal fibroblast cells and mucoid tissues; it has a network of glycoprotein microfibrils and collagen fibrils. WJ is mostly a hydrated gel composed of hyaluronic acid(abundant glycosaminoglycan).It is reported that stromal cells available in WJ are multipotent in nature when cultured in appropriate conditions and hence can differentiate into various cell lineages.The flow cytometric analysis study showed that the cells harvested from umbilical cord WJ when expanded in vitro expressed certain matrix receptors and integrin markers which suggested stromal cells of WJ are MSCs[3].

### **DIFFERENTIATION POTENTIAL OF WJ MSCs:**

#### **CHONDROGENIC DIFFERENTIATION**

Cartilage is a specialized connective tissue having poor regeneration and self-renewal property in-vivo. Traumatic injury or autoimmune processes are one of the main causes of cartilage damage and degeneration, for which new hope comes from tissue engineering using stem cells that undergo chondrocyte-like differentiation. Analysis of the chondrogenic potential of the WJ-MSCs showed that they have the multipotential capacity and their chondrogenic capacity could be useful for future cell therapy in articular diseases. Wang et al demonstrated that seeding density of WJ-MSCs in poly-glycolic acid(PGA) scaffolds in the presence of chondrogenic medium had important effects on their chondrogenic potential.[4]

#### **ADIPOGENIC DIFFERENTIATION**

Adipogenic differentiation of MSCs is stimulated by the incubation of MSCs in a medium containing 3-isobutyl-1-methyl xanthine, insulin, indomethacin, triiodothyronine, Asc-2-P, basic FGF, and the glucocorticoid dexamethasone. The differentiation of MSCs into adipocytes results in the accumulation of lipids in intracellular vacuoles.[5]

## **MATERIALS AND METHODS:**

### **SAMPLE COLLECTION AND PROCESSING**

Appropriate ethical clearance was taken from concerned authority. Five umbilical cords were collected from a screened caesarean patient, after getting written consent. The collected samples were then processed under sterile conditions in Bio-safety cabinet. In presence of PBS (Phosphate-Buffered Saline), the cords were cut into small pieces of 2-3mm size after removing all blood vessels.

### **EXPLANT CULTURE**

The cord pieces were cultured in culture plates with 3ml complete culture medium (CCM) containing DMEM (Dulbecco's Minimal Essential Medium), FBS (Fetal Bovine Serum) and antibiotics (penicillin, streptomycin, gentamicin, fungizone).

The plates were placed in CO<sub>2</sub> incubator at 37°C and 5% CO<sub>2</sub> content.

After subsequent subculture, cell counting was done to estimate number of viable cells.

### **CHONDROGENIC DIFFERENTIATION**

The cultured cells were further cultured in chondrogenesis media for about 14 days, followed by staining with Alcian Blue stain and observed under light microscope.

### **ADIPOGENIC DIFFERENTIATION**

Again, the cells were cultured in Adipogenesis Differentiation Medium for about 7 days, followed by staining with Oil Red O stain and observed under fluorescent microscope.

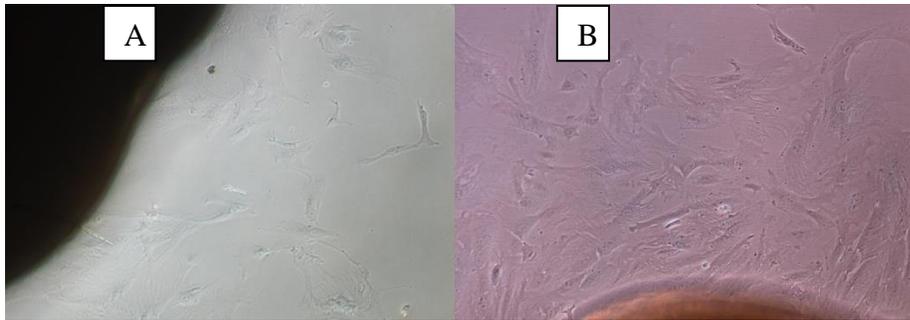
## **RESULTS:**

### **SAMPLE COLLECTION AND PROCESSING**



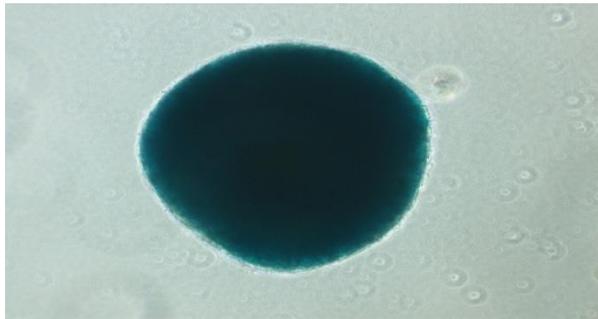
**Figure1:** Collection of cord in falcon containing transport media followed by chopping cords into pieces.

### **WHARTON'S JELLY CELLS ISOLATED BY EXPLANT METHOD**



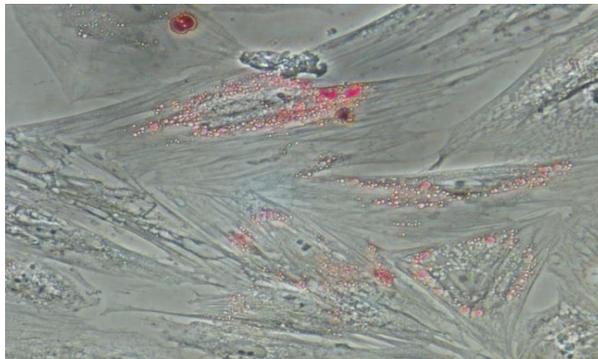
**Figure2:** A. Cells start migrating after 7-9days of Explant culture;B. Cells were long spindle shaped with prominent nuclei.

### **CHONDROGENIC DIFFERENTIATION**



**Figure3:** Blue stained spheroid cell mass indicating chondrogenic differentiation.

### **ADIPOGENIC DIFFERENTIATION**



**Figure4:** Oil Red O stained lipid vacuoles indicating adipogenic differentiation.

### **DISCUSSION**

Stem cells are exclusively used in regenerative medicine and tissue engineering. Wharton's Jelly and hUC-MSCs are hopeful tools for disease treatment with effective stem cell potency [6]. In our laboratory we used an explant method to isolate MSC from umbilical cord tissue. This method is economical, easy and produces a large number of cells on some passages. After isolation and appropriate in-vitro expansion, the WJ-MSCs were differentiated towards adipocytes and chondrocytes. Expected results were observed, thereby proving their differentiation potential.

### **CONCLUSION:**

Wharton's Jelly, the gelatinous tissue within the umbilical cord presents a unique cell population displaying the stemness phenotype known as MSCs. We used an explant method to isolate MSCs from 5 cord samples; the cells were migrated from isolation; showed to proliferate extensively and get adherent to culture plates with clonogenic property. Further, we differentiated the isolated WJ-MSCs towards chondrocytes (micromass culture) and adipocytes to prove the lineage differentiation potential of MSCs.

## REFERENCES

1. Wang D, Zhang H, Liang J, Li X, Feng X, Wang H, et al. *Allogeneic mesenchymal stem cell transplantation in severe and refractory systemic lupus erythematosus: 4 years of experience*. Cell Transplant 2013; 22:2267-77.
2. El-Jawhari JJ, El-Sherbiny YM, Jones EA, McGonagle D. *Mesenchymal stem cells, Autoimmunity and rheumatoid arthritis*. QJM 2014; 107:505-14.
3. Hwai-Shi-Wang et al "Mesenchymal Stem Cell in the Wharton's Jelly of Human umbilical cord" Stem Cells, Vol 2, pp.1330-1337, 2004.
4. Halleux C, Sottile V, Gasser JA, Seuwen K. *Multi-lineage potential of human mesenchymal stem cells following clonal expansion*. J Musculoskelet Neuronal Interact 2001; 2:71-6.
5. Gimble JM, Morgan C, Kelly K, Wu X, Dandapani V, Wang CS, et al. *Bone morphogenetic proteins inhibit adipocyte differentiation by bone marrow stromal cells*. J Cell Biochem 1995; 58:393-402.
6. La Rocca, G. Connecting the dots: The promises of wharton's jelly stem cells for tissue repair and regeneration. *Open Tissue Eng. Regen. Med. J.* 2011, 4, 3-5.

# OPINIONS

## SARS-CoV-2: WHAT AFTER THE VACCINE?

*People are emotionally torn apart by the coronavirus. No one is sure who is to be blamed for such a pandemic yet a bold and emotional Rohit Singh puts forth his views on the pandemic and its aftereffects.*

Thought we were invincible, invigorating the military might and advancement in technology no one had a clue, humanity will be deterred by a parasite- Coronavirus seems worse than the Spanish flu. There are no effective drugs or vaccines to treat this killer flu strain nor any medical or media infrastructure to spread awareness. This invisible virus threatens nations with long twilight months of sickness, recession, and health-care systems overwhelmed to its maximum capacity. It has already taken more than 400,000 lives in just 6 months and the count is on since we live in a more globalized world than ever before it becomes difficult to contain the virus in one place.

It is obvious who is responsible, the Communist Party of China could have contained the virus in the region, but they deliberately let this epidemic to become a global pandemic. The travel restriction could have been made mandatory for their citizens and they could have more transparent to the world in sharing the information, although bashing would not serve any purpose one must be held accountable. The world order will not be the same as before the spark for self-dependence has ignited leading to deglobalization. Countries will try to become more reliant on their local supply chain, rather depending on other countries for essential goods. The new cold war between the Supply Chain Giant and the Super Power called The Great Decoupling, will initiate more aggressively. The power struggle will prevail, such pandemic will be the new normal for this world, proxy wars will be more frequent. Countries will be aligned to serve their common interests; some will benefit while some will collapse. This ghastly race could cause severe casualties that no one can imagine, hunger and poverty will be a corollary. Arms and technology race will strive for new heights to superpose one's supremacy and dominance on others.

“The global economy is expected to suffer a loss of 5.5-8.8\$ trillion due to the Coronavirus pandemic”, says Asian Development Bank (ABD), which is equivalent to two-three times India's GDP. The shock has uniquely raised the capital and liquidity risks in both the real economy and financial systems simultaneously. The liquidity problem hampers credit intermediation and investments, on the other hand, healthy households, and companies face severe cash-flow problems. The capital problem shuts the credit channels, which damages capital formation. The damaged household and company balance sheets cripple and have a significant effect on growth. It seems a speed bump in economic growth, but it is not that simple, it will have a long-lasting effect. The International Labour Organisation (ILO) estimates more than 25 million job losses due

to coronavirus. The Tourism, Aviation, Hospitality, Sports league, Abroad education industry will have stunted growth for the next 2 years, other sectors will underperform and many companies may file for bankruptcy if the government fails to provide fiscal stimulus in their respective economy.

But every cloud has a silver lining, Coronavirus has not only increased our social consciousness for the environment but during the lockdown we learned the importance of work from home, which could significantly reduce the stress on resources and help companies in increasing their profit. The practicing of social distancing norms has made us more disciplined. We have improved our culinary skills, yoga and meditation have become routine and we spend more time with our family. The sky is clean, the air is pure, the rivers are tidy and nature is thriving. It is evident we can change the course of humanity and its future through our actions if we are determined to incorporate good practices. Soon the importance of upgrading existing medical infrastructure to combat future pandemics will be prioritized by the policymakers. We would witness an exponential growth in the funds for medical research and the pharmaceutical sector.

Humanity has faced daunting situations in the past but remained victorious. Coronavirus has made us realize the importance of preparation for an epidemic, although it will be expensive but cause a lesser dent on our economies in such a crisis. The world must prepare because it will not be the last pandemic to hamper millions of lives, but there would be such many more incidences in the future. Biotechnology has great potentials in combating such attacks and providing a one-point solution. Two basic aspects biotech can provide, is the speedy research and large-scale manufacturing of vaccine. Over the last decade, technology such as DNA sequencing, DNA synthesis, Genetic engineering, Immunoinformatic has become more advance and economically viable, which can play a crucial role in developing a vaccine against Coronavirus. The best example is the biotech start-up Moderna Therapeutics, which has successfully developed an mRNA vaccine against SARS-CoV-2 and is under its first clinical trial. The mRNA vaccines do not rely on any kind of lab culturing or bioreactors, it can be synthesized using chemical methods. The mRNA is easy to pack into a delivery vehicle having a chemical structure called lipid nanoparticles, which boosts the uptake of the vaccines in our body. Thus, it is potentially faster, safer, and cheaper than any other type of vaccine, certainly designed and manufactured more quickly during new pandemics.

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## QUALITY CONTROL- BUILDING THE RATIONALE

Quality control is a “fault finding exercise”. It is not only about identifying the fault, but indeed implementing this fault-finding exercise in your scientific practice with the right perspective. Which means that when you find a fault through the quality control analytical procedure you have a reason to be happy that the product not reaching the market and the patient population in such a state. On the other hand, finding a fault in the product is a part of your quality control testing and if you feel anxious about it or rather nervous about it then we need to rethink about the rationale of the quality control methods.

Let us for a while think about an analogy of a mother who is cooking for her family. When the mother is getting to the end of the cooking process, she takes a small portion of the food and tastes the food before it is being served to the family members. She is doing this to ensure that the family members get the exact quality of the food that she is thinking of. If the salt is slightly lesser or the spice is little more, the mother will be relieved to have found that out as a part of her “sampling” and “testing” routine well before the family members could identify and complain of it. Therefore, Good Manufacturing Practices (GMPs), although important, represent only one element in maintaining and improving quality. If product quality is defined as meeting or exceeding customer needs and expectations, then mere compliance with GMPs does not provide assurance of meeting these requirements.

The analytical method for each product is developed systematically and validated extensively to make sure that the method works for the purpose it is developed for. When such method is developed with specificity and sensitivity to the product and is used for testing then it is a positive outcome that the method is able to predict if there is any deviation or fault in the product.

Gone are those days where the makers are not essentially the consumers. Various factors like the increase in population, commoditization of medicinal products, extent of population who suffer lifestyle disorders, frequency of epidemic and pandemic attacks and so has created a very strong demand pressure which in turn has shrunken the demand supply gap. Here time to market plays a vital role both from social and commercial advantage perspectives. In this juncture, adopting cutting-edge technologies takes us closer to the process and will allow us to offer corrective feedback that can influence the ongoing batch itself. Some of the considerations that are relevant to review include:

- a. It is feasible for manufacturers to implement
- b. It contributes to ensuring the safety, quality, or purity of the drug product

c. The value of the contributions or added assurance exceeds the cost in money or other burdens of implementing or continuing the practice

The tools and technologies associated with Process Analytical Technologies (PAT) and Quality by Design (QbD) enable the quality Personnel not only to meet the quality norms set by the regulatory agencies but also to get closer to the process and deliver a product that consistently meet the quality parameters and expectations of the consumers.

*S.Salavadi Easwaran  
Academic Dean  
Biocon Academy*

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## **DARK SIDE OF BIOTECHNOLOGY: BIO-TERRORISM, BIOLOGICAL WARFARE AND BIO-WEAPONS**

Ever heard of one living form killing the other? Many might think of Charles Darwin's theory of "the survival of the fittest" which explains species fighting for their own existence in the natural environment, however, this is not what I am referring to. As the topic itself reveals the word "terror", it is something concerned to deliberate release of micro-organisms and toxins to cause disease and eventually death of animal, plants and humans; prepared and released by terrorists, broadly entitled as "Bioterrorism" or "Biological warfare". Quite fascinating isn't it? This is what brings about the ill use of Biotechnology. Biological weapons are made as site of attraction, which is due to the advantages they offer- high cost efficiency (only \$1 per casualty), access to enormous range of diseases, onerous detection by routine security system, easy transportation and high fatality.

Adoption of Bioweapon is not a modern era novelty. Elementary forms of biological warfare have been exercised since antiquity. Around 300 B.C., in Pre-Christian era, animal cadavers were used by Greeks to contaminate water wells of enemies. During Indian- French war, on the order of British commander Sir Jeffrey Amherst blankets with smallpox virus on it were distributed to obliterate population of Indian tribes opposed to the British. In that era, the possible way of transmission was using infected subjects to contaminate objects, surfaces and consumables to spread infection at the highest pace possible due to minor development in technology and poor knowledge. The onset of germ theory in diseases and advances in microbiological techniques led to a new level of sophistication to theoretical use of bioagents in war. Likewise, recent advances in life sciences and biotechnology have made it quite straightforward to produce bioweapons in large quantities with facilities and expertise available even to extremists and paramilitary groups.

Hard to believe, occurrence of pandemics such as plague, glanders, anthrax, is not a natural phenomenon? But a deliberate release-BIOTERRORISM per say! It is periodically reported that the causative agents of anthrax and glanders disease *Bacillus anthracis* and *Pseudomonas mallei* were inoculated on cattle by Germans before sending them to enemy states. Such bioweapons then became the coherent war weapons. As World War I evidenced large scale use of non-traditional chemical weapons, it was conventional that World war II would see further voluminous use of Bioweapons; the Japanese program aimed to produce Bioweapons. Lieutenant general Ishii established bioweapon research center, Unit 731 to produce numerous bioweapons including *Yersinia pestis*, *Vibrio cholera*, *Neisseria meningitis*, and *Bacillus anthracis* which were tested on prisoners of war. U.S. made its footsteps in era of Bioweapon immediately after the outcome of WW II. A large scale experiment involved propagation of bacterium, *Bacillus subtilis* which resulted in infections, not without consequences in the New York subway. It validated the spread of pathogens from single station was possible due to displacement of air.

A Bioweapon can be more potent pound for pound, than hydrogen bomb. While there are plentiful of pathogens (bacteria, viruses and toxin), only scanty possess the properties to be a bioweapon. Eitzen outlines characteristics that makes bioweapon, a potential bioweapon. Ideally, one should be highly toxic, extremely infectious, stable both in stockpile and dissemination, preferably communicable, easy to grow, develop and produce and constitute difficulty in medical responses. Bioweapons productions uses bio-agents as raw materials including living-organisms primarily micro-organisms such as bacteria, virus, fungi and toxins (of plant and animal origin). These bio-agents are distinguished into three groups:

Category A (easy transmission, high mortality rate),  
Category B (moderate transmission, low mortality rates) and  
Category C (can be genetically-engineered for group transmission).

In 19<sup>th</sup> century first measure against the use of Bioweapon took place during the Hague conference where the document entitled 'laws and duties of war on land' about prohibition on the use of poisoned arms was signed by 24 countries. In 1925, Geneva protocol prohibited use in war of stifle, virulent or another gases and of Bacteriologic techniques of warfare was signed. This treaty only prohibited use of bio-agents as weapons, but not their development and stockpiles. In 1972, Convention on the Prohibition of the Development, Production and Stockpiling of Bacteriological (Biological) and Toxin Weapons and on Their Destruction was signed by over 100 countries but it had several loopholes. Bioterrorist events after ratification of Biological weapon convention have confirmed that the convention doesn't prevent proliferation of biological weapons. Several countries remained to produce and test bio-agents for military purposes. Bioterrorism has made permanent imprints on the world, ones that are hard to erase. Thus, it is recommended to take provident steps to protect against biological warfare and ensure that our responses enhance global security.

## **BIOTECHNOLOGY- A PROMISING CHOICE**

Biotechnology is a rapidly growing sector around the world. It offers a combination of technology and innovative approaches that deal with research and development in the field of sciences. It is responsible for many of the things that make our lives better. The field focuses on the intersection of biology and technology, leading to a vast array of new products that are designed to enrich lives, make day-to-day living easier and make us healthier. From vaccine production to genetic modification, Biotechnology is everywhere. As a result, careers in this field are quite promising for new graduates. This article provides a brief overview of the various options that are available and ensure a promising future in the field of Biotechnology globally.

The broad gauge options include biotech engineering, research, pharmaceutical, microbiology, agriculture, food technology, botany and zoology. I shall point out the further options in each of the above mentioned fields.

- **Biomedical engineering:** It combines engineering and biological expertise to design solutions to problems in biology and medicine. They design biomedical equipment, devices and medical software such as artificial organs, prostheses and diagnostic machines to improve quality and effectiveness of patient healthcare.
- **Biotech engineering:** This study utilizes the study of microorganisms or knowledge of antibiotics and further implement them in various industrial purposes. The knowledge is applicable in areas like agriculture, food sciences and medicine.
- **Biochemist:** These individuals study chemical properties of living things and biological processes such as cell development, cell growth, heredity and disease. They conduct research projects, analysis and synthesis of biomolecules, effects of drugs, hormones and nutrients on tissues and biological processes to develop products and improve human life.
- **Medical scientist:** They conduct clinical research to improve patient health by investigating diseases and prevention methods. They also develop and test medical devices, investigate samples for causes and treatments of toxicity, pathogens and chronic diseases. They also standardize drug potency, doses and methods for mass manufacturing and distribution of drugs and medicinal compounds.
- **Microbiologist:** They study viruses, bacteria and the immune system and conduct research and lab experiments to aid in the diagnosis of infectious illnesses.

- **Process development scientist:** they oversee the manufacturing process in an organization's lab, looking for ways to increase quality and efficiency adhering to standardized protocols.
- **Agricultural engineering:** focuses on crop and soil improvement for betterment of human life.
- **Soil and plant scientist:** these individuals conduct extensive research and analysis on various food crops and vegetables to improve quality, quantity and hence improve human life.
- **Animal scientist**
- **Epidemiologist**
- **Food scientist and technologist**

To prepare a successful career in biotechnology, a thorough and rooted ground work is required.

1. Build an educational foundation- a solid education rooted in science-related coursework is a must.
2. Stay open-minded-since there are too many options, it can be confusing to pin down one option. Keep the blinders off and explore all the areas.
3. Hone your soft skills: while technical skills and scientific knowledge are a baseline, companies now also require you to communicate effectively, engage positively with others, defend your hypotheses, troubleshoot issues and handle conflicts. Companies now need a whole package.
4. Build your professional network: Start early for this attribute. Keep every contact in place and treat as essential. Build meaningful connections with supervisors, colleagues, advisors, professors and industry professionals.
5. Keep learning and adapting: change is the only constant. Hence, up-skilling by earning additional certificates in the discipline, attending conferences and utilizing your network is a way to prepare for dynamic industry.

So here's wishing all the enthusiastic biotech students the very best. I hope this article helps you gain clarity over the subject and the career prospects associated with it.

*Kadambini Alva P.  
Ex-Faculty  
PPSIJC*

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## **DESPERATE TIMES LEADING TO OVER EXAGGERATED MEASURES?**

Since as long as we have known, the biotech industry has been acting like a group of introverted superheroes, working in silence till the world calls out for help. As soon as they are summoned, the industry, or rather bits of it does everything in its power to find a solution as soon as possible

and go back to being its reserved self. However, over a period of time, these rescuers seemed to have developed a hunger for credit and fame and hence have stepped into an unhealthy competition.

In the past few years, there have been several innovative inventions in the field of biotechnology, most of them leading to medical breakthroughs. Although stem cell research and targeted cancer therapies were one of the most alarming advances in the field of medicine, the infamous Theranos start-up project wasn't one of them. In 2003, a Stanford dropout Elizabeth Holmes founded a company called Theranos and claimed to have invented a new ground-breaking technology wherein the medical diagnostic tests which typically require a vial of blood to provide accurate results could be performed using just a pinprick of blood, no more than the amount a glucometer requires.

Predictably, this was perceived as a great opportunity for investors and in no time the company was able to raise \$700 million to carry out the said method of diagnosis for all their clients. In 2015, the company was at its peak when a WSJ journalist did some snooping around and published an article basically alleging that the technology which according to the claim was being used by Theranos was nothing but a big web of lies. Further investigation eventually revealed that the said technology never truly worked and the company had been deceptive about the inefficiency of their technique since the beginning. Not only did they cheat their customers, but also risked numerous lives by providing manipulated and inaccurate results.

The current global crisis has been keeping these industries on their toes, conducting numerous research trials in order to find a vaccine to provide immunity against this novel contagion and bringing life back to normal. The current on-going researches seem more or less encouraging till these companies start playing fastest finger first. At a crucial time like this, the entire world is in a state of vulnerability, waiting for a miraculous vaccine to be created and as unethical as it sounds, some companies maybe using this to their advantage and turning people's hopes into a money-making opportunity.

In May 2020, a biotech company- Moderna Therapeutics announced the success of its trials and claimed the possibility of developing vaccines in bulk by no later than Fall 2020. Unsurprisingly, the stock market went skyrocketing as soon as the news came out, leading to a surge in Moderna's stock price by 30 percent within a matter of hours. After the market closed, the company announced a stock-offering apparently to raise \$1 billion to help with the vaccine development even though no such announcement had been made during the news release regarding the success of their vaccine trials. By the next day, Moderna had still not released any data to back up its claims which could be evaluated by scientists. The lack of scientific information was a cause of concern as people couldn't help but consider the possibility that the claims put out by the company may have been a strategy solely to elevate their stock rate and it was quite plausible that there was

close to no truth in them. Even now Moderna's the development made on the vaccine hasn't been transparently shared with the public. We simply come across vague news report for the sake of keeping Moderna's name alive in the competition.

Such cases set an example that no matter what the depth of the crisis is, we still need to look out for people or establishments who opt for money over ethics or worse, the law. Scientists all over the world have been trying their best to come up with a permanent solution to get rid of Covid-19 or atleast neutralize the effects it has been having on humans across the world since it came into existence. It needs to be understood that there are actual humans working on this and the only thing we can do to protect ourselves from fraud is be patient and trust the process. Hope and desperation can sometimes lead us to believe every little piece of information which brings positive news regardless of its reliability.

*Shailja Rabindra Singh  
Thadomal Shahani Engineering College  
Student*

# INTERVIEW WITH DR. ANUPMA WADAVLIKAR

Dr. Anupma Harshal Wadavlikar is a *high-achieving teacher, mentor who has steered Under Graduate Research*, transforming the teaching learning process through research-based pedagogy. With over seventeen years of experience empowering UG, PG students, brings a thoughtful perspective to the table and is tech savvy. Adept at transforming complex topics into innovative, engaging, and informative stories. Entrepreneurial at heart and a team player recognized for an impassioned approach.

She has been a professor at K.C. College in Mumbai and has been associated with the Department of Biotechnology India for various projects. She currently works as a consultant with Indian Institute of Science Education and Research on the Manav- Human Atlas Project, and has also been Indo-US Foldscope Grant Awardee in 2019.

We were thrilled to interview ma'am for our magazine. Her dynamic contributions to the field of Biotechnology as a professor and scientist truly inspire us. Read her interview where she talks about her ideologies, projects and opportunities for students in the Manav Human Atlas Project!

## **1. The current covid-19 pandemic has got the entire world to a standstill. Are you working on any projects related to coronavirus?**

Not directly in terms of research and development but we did do a short stint for the Department of Biotechnology in the form of a quiz for awareness of students to engage them and the quiz was designed in a format which also helped them to upskill. There was information from CDC and WHO about vaccine development, RT PCR and so on.

## **2. Do you think the scientific community is ready to deal with such a challenge.**

I think there is a gap between what the citizens are getting as information and what the scientific community is actually constructively engaged in research. I feel the government needs to have a front face comprising of a team of scientists who can make the people aware in a simple language about what is going on and what is needed to be done instead of all the myths that are going around.

As students in science we know that vaccine development is a process. If there was no reaction for 30 days, we can't say there won't be no late reaction after 45 days. It is a process that requires a 4 weeks 8 weeks and 12 weeks study, and then there is a dosage study, immunization for children

and so on. We know that this study cannot be speeded up. I believe a lot of niche work is going on.

Some kind of awareness was there, we weren't completely ill prepared, we were slightly prepared for such a pandemic. We didn't though have any SOPs, that is what has left us like this.

### **3. What kind of projects were you working on before the lockdown began?**

I have been initiated as an expert and person engaged in Science Communication and Public Engagement on the Manav platform. Before that I was on the Indo-US Foldscope Grant where we tied up the project with the Northeast region. I did a DNA barcode of plants used in Medicine.

### **4. Are there any opportunities for students?**

Manav is a platform for students. It will give an opportunity to students to annotate papers from their homes. Students will be reading real-time research papers and highlighting important parts of it. The platform will be freely available to all students. They will get an opportunity to interact with scientists, with fellow students as Manav scholars. Your professors and seniors will be expert reviewers for your annotations. You can visit [manav.gov.in](http://manav.gov.in) to join Manav as a student or research scholar.

There are also many webinars on data science and biotechnology that students can access once a part of manav.

### **5. Since you've been in the teaching profession since many years, do you think our education system in Biotechnology is at par with the global standards?**

All teachers give it their own element to upgrade the syllabus. We need to change the way we are executing the syllabus. Am I making my students capable of asking questions? Am I helping them evolve a critical thinking skill? Such questions need to be answered.

### **6. Your research spans various domains of Biotechnology-metagenomics, bioremediation, epidemiology. Do you believe that success in a field like Biotech can be achieved by a broader approach rather than an in-depth approach?**

I feel when we teach Biotechnology, the first line that we write is DNA to RNA to Protein and say this is the central dogma, and every teacher after saying this says the one gene one enzyme hypothesis, and that is when we start narrowing our student's outlook. I think this needs a change. You have to be aware of a lot of topics to decide where you see yourself after 5 years.

## **7. Are there any other opportunities for students to explore?**

Apart from Manav, you can go to <https://indiabioscience.org/> which also comes out with a publication <https://www.biotechnika.org/>, and they have multiple courses, engagements on platforms and activities, workshops on writing research papers and evaluate content.

# EDITORS' PAGE

## *EDITOR'S ARTICLE*

### **BIOTECHNOLOGY INTELLECTUAL PROPERTY DURING A PANDEMIC**

Covid-19 has created an uproar in the world so loud that its screams would be remembered in medical history for years to come. During a pandemic like this, the world has surrendered to innovation and research in the Biotech industry. From pharma giants to prestigious universities to nascent start-ups, everybody is trying to make an impression. At what cost though?

Intellectual property has ensured to keep a civilized battle in the pharma field. Incentivizing innovation and valuing multiple years of efforts put by scientists in developing a product, it has been a faithful armor. However, what happens when a crisis like the coronavirus hits the world? Does it pierce through the armor, attacking billions of dollars and years of research?

Five major challenges have come up:

1. Finding a treatment for covid-19 which requires large scale R&D effort- vaccines and drugs
2. Large scale production of diagnostic kits with both high testing accuracy and capability.
3. Sudden and massive burden on hospitals in terms of ICU capacity and ventilators.
4. A need for digital innovation-epidemiology modelling and geospatial data to understand and study the spread of the virus in populations, including tracking of cases and carriers.
5. High demand of medical staff- doctors and nurses- increasing requirement of personal protective equipment- face shields, googles, gloves, sanitizers and so on.

The IP ecosystem actors include:

Big pharma and drug development firms, testing service providers, universities, digital health community developers and IT giants.

In order to comprehend the seriousness of this issue, we need to evaluate povs of the stakeholders, the government and the public.

WHO launched a voluntary covid-19 product pool-to collect patent rights, regulatory test data, and other information that could be shared for developing drugs, vaccines, and diagnostics to combat Covid-19. (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/covid-19-technology-access-pool/solidarity-call-to-action/>).

Their effort to ensure equitable access to essential health technology by removing barriers of intellectual property and facilitate open sharing of knowledge has met with a backlash from the industry and first world countries. “At this point in time, I think it’s nonsense, and... it’s also dangerous. Investing billions to find a solution and, keep in mind, if you have a discovery, we are going to take your (intellectual property), I think, is dangerous.” said Pfizer chief executive Albert Bourla.

Similarly, AstraZeneca (AZN) chief executive Pascal Soriot argued at the forum that intellectual property is “a fundamental part of our industry and if you don’t protect IP, then essentially, there is no incentive for anybody to innovate. What is important is for companies to volunteer to provide their products at no profit, like we’re doing right now in case of a pandemic or crisis, when it’s needed.”

The Medical Patent Pool deals with providing access to drugs of HIV, malaria, TB and now covid-19 to poor countries by ensuring licensing deals already. Companies are clearly opposed by attempts of dismissing IP even during a pandemic. They believe patents provide them with security and incentive to innovate, and sharing years of research on technologies on open access platforms is only going to delay vaccine production. From their end, they are collaborating with each other and universities, trying to optimize the process and focusing thoroughly on combating covid-19.

The government is keen on eliminating this crisis and restoring their economies and people’s lives. Numerous governments are in support of compulsory licensing provisions- to get rid of this IP hindrance. However, as politics and power has always dictated a country’s stance, the affluent nations are hesitant to disregard IP for these are the nations that reside the companies working on the treatment.

What about us though? The public simply wants a solution. Irrespective of who makes it, until a solution is discovered our lives are at a standstill. Whether IP incentivizes this process or compulsory licensing fast-tracks it, the public shall not be economically burdened to avail this insurance.

As a biotechnologist, I understand what happens behind the scenes in the pharma world. The market is brutal and your intellectual property is your only means of survival. However, there is

humanity and understanding between these competitors- they will rescue us. Only question is, at what cost.

*Deepakshi Kasat*

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## FILM REVIEW

### **THE AMAZING SPIDER-MAN**

Besides its contribution to a large number of industries like food, medicine, agriculture, and environment, Biotechnology has also inspired the film industry. The plots of a large number of sci-fi movies are based on various branches of biotechnology where scientists create a super serum giving birth to Captain America, or bring back the dinosaurs in Jurassic Park, or accidentally create a virus which turns everyone into a zombie in Resident Evil. One such movie is ‘The Amazing Spiderman’ starring Andrew Garfield.

The second reboot of this superhero franchise revolves around a familiar plot, Peter Parker is bitten by a genetically-altered spider and gains superhuman strengths. The spider is not the only GMO in this movie as the ‘Lizard’ who is the main villain of this film is a result of cross-species genetics. Dr Curtis Connors wishes to employ the regenerating abilities of a lizard and develops a lizard serum using the facility and resources at Oscorp. But he is forced to skip directly to human trials so the serum can be used as a cure to Norman Osborn’s illness. He self-injects the serum hoping that it would grow his missing arm; he is successful at first but soon transforms into a giant lizard-man.

Even though the chances of a living person mutating into a hybrid creature are very slim, cross-species genetics is a well-explored area. Attempts have been made for making a human-animal hybrid also known as a Chimera (derived from Greek mythology). Human-pig embryos were successfully created at the Salk Institute in California with the intention of growing human organs inside pigs.

With modern gene editing technologies, it is very much possible to insert certain traits from one species to another. This technology has made it possible for researchers to create Avatar-like plants that glow in the dark. Fireflies produce an enzyme called Luciferase that lights them up. The scientists first obtain the piece of the gene responsible for the production of the enzyme Luciferase. They then use genetic engineering to transfer these genes to pieces of plants which then grow into whole plants that glow. Why stop at plants? What if your pet animals could glow in the dark? Well

turns out they already can. Scientists have successfully transferred Jellyfish genes into rabbits, cats, and many other animals which makes them glow in the dark too.

Lizards are the most closely- related animals to humans that can generate entire appendages. The scientists at Arizona State University studied regeneration properties of the Green Anole Lizard and discovered that they turn on at least 326 genes in specific regions of the regenerating tail. Using next-generation technologies they sequenced and found out what genes were required to regrow the lizard tail. They believe that by following this ‘genetic recipe’ and then harnessing those same genes in human cells, regeneration of muscles and cartilages might be possible in the future.

Even though cinema has dramatized our current science, scientists are working towards exploring applications of genetic engineering in humans. Who knows, one day we might come across a human with super sticky fingers and web-shooters.

*Bhairavi Savur*

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## **GET TO WORK!**

*Solve the word search and test your knowledge on hematopoietic cells.*

The process of hematopoiesis involves the differentiation of multipotent cells into blood and immune cells. The multipotent hematopoietic stem cells give rise to many different cell types, including the cells of the immune system and red blood cells.

Find these different cell types in the word search given below based on the following clues:

1. They transport oxygen throughout the body
2. Release histamines necessary for immune response
3. Play a role in the inflammatory response and fight some parasites
4. Help fight bacterial and fungal infections
5. Engulf and digest debris, including bacteria
6. They include T and B cells
7. They help the blood to clot
8. Play role in allergic reactions and their cells release granules filled with chemicals that cause inflammation
9. They process antigen material and present it on the surface to the T cells

10. They originate in the bone marrow and secret large amounts of antigens

H	I	N	P	L	O	D	M	P	P	S	A	E	O
H	S	E	Y	E	T	E	A	H	A	T	A	T	M
M	E	U	E	T	E	N	C	M	E	L	T	Y	P
O	T	T	E	A	I	D	R	O	O	E	T	C	O
I	Y	R	O	L	P	R	O	M	L	T	Y	O	I
S	C	O	S	H	H	I	P	A	L	Y	O	H	R
P	O	P	I	R	L	T	H	S	E	C	A	P	L
C	B	H	N	B	L	I	A	T	C	O	P	M	O
T	M	I	O	H	E	C	G	C	A	R	L	Y	C
I	O	L	P	O	C	C	E	E	M	H	L	L	Y
H	R	P	H	L	C	E	H	L	S	T	I	L	H
A	H	A	I	L	S	L	P	L	A	Y	L	T	M
L	T	H	L	C	T	L	R	D	L	R	L	S	Y
L	I	H	P	O	S	A	B	C	P	E	H	E	B

## REFERENCES

### COVID-19 IN A NUTSHELL: Recent therapies and treatment options

1. Su, S., Wong, G., Shi, W., Liu, J., Lai, A. C. K., Zhou, J., ... Gao, G. F. (2020). *Epidemiology, Genetic Recombination, and Pathogenesis of Coronaviruses*, (January).
2. Kumar, A., Singh, A., Shaikh, A., & Singh, R. (2020). *Diabetes & Metabolic Syndrome: Clinical Research & Reviews Chloroquine and hydroxychloroquine in the treatment of COVID-19 with or without diabetes: A systematic search and a narrative review with a special reference to India and other developing countries*, (January)
3. To, L., & Editor, T. H. E. (2020). *Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro*, (February), 2019–2021. <https://doi.org/10.1038/s41422-020-0282-0>
4. Liu, C., Zhou, Q., Li, Y., Garner, L. V., Watkins, S. P., Carter, L. J., ... Albaiu, D. (2020). *Research and Development on Therapeutic Agents and Vaccines for COVID-19 and Related Human Coronavirus Diseases*. <https://doi.org/10.1021/acscentsci.0c00272>
5. Caly, L., Druce, J. D., Catton, M. G., Jans, D. A., & Wagsta, K. M. (2020). *The FDA-approved drug ivermectin inhibits the replication of SARS-CoV-2 in vitro*, 178(March), 3–<https://doi.org/10.1016/j.antiviral.2020.104787>
6. (<https://www.firstpost.com/health/plasma-therapy-identifying-multiple-antibodies-that-neutralise-covid-19-can-lead-to-better-treatment-8381661.html>)
7. Golchin, A. (2020). *Mesenchymal Stem Cell Therapy for COVID-19: Present or Future*, <https://doi.org/https://doi.org/10.1007/s12015-020-09973-w> *Mesenchymal*
8. Mullard, A. (n.d.). *World Report COVID-19 vaccine development pipeline gears up*. *The Lancet*, 395(10239), 1751–1752. [https://doi.org/10.1016/S0140-6736\(20\)31252-6](https://doi.org/10.1016/S0140-6736(20)31252-6)

### ENDOGENIC RETROVIRUSES IN ONCOLOGY: A perspective on detection

1. Lasse Vinner1, Tobias Mourier1, Jens Friis-Nielsen2, Robert Gniadecki3, Karen Dybkaer4, Jacob Rosenberg5, Jill Levin Langhoff6, David Flores Santa Cruz2, Jannik Fonager7, Jose M. G. Izarzugaza2, Ramneek Gupta2, Thomas Sicheritz-Ponten2, Søren Brunak2, Eske Willerslev1, Lars Peter Nielsen8,9 & Anders Johannes Hansen1. Investigation of Human Cancers for Retrovirus by Low-Stringency Target Enrichment and High-Throughput Sequencing, *Scientific Reports- Nature*, 2015
2. Kassiotis G. Endogenous retroviruses and the development of cancer. *J Immunol*. 2014;192(4):1343-
3. Figure 2: Li, Jing-jian & Xiong, Chao & Liu, Yue & Liang, Jun-song & Zhou, Xing-wen. (2016). Loop-Mediated Isothermal Amplification (LAMP): Emergence As an Alternative Technology for Herbal Medicine Identification. *Frontiers in Plant Science*. 7. 10.3389/fpls.2016.01956.

### BREAST CANCER TUMOR MICRO-ENVIRONMENT (TME) AND CANCER-ASSOCIATED FIBROBLASTS (CAFs)

1. <https://www.who.int/news-room/fact-sheets/detail/cancer> (Accessed on 20/05/2020)
2. <https://www.medicalnewstoday.com/articles/326031> (Accessed on 20/05/2020)
3. Wei, R., Liu, S., Zhang, S., Min, L., & Zhu, S. (2020). Cellular and Extracellular Components in Tumor Microenvironment and Their Application in Early Diagnosis of Cancers. *Analytical cellular pathology (Amsterdam)*, 2020, 6283796. <https://doi.org/10.1155/2020/6283796>
4. Soysal S, D, Tzankov A, Muenst S, E: Role of the Tumor Microenvironment in Breast Cancer. *Pathobiology* 2015;82:142-152. doi: 10.1159/000430499
5. Wu, H., Hao, M., Yeo, S.K. et al. FAK signaling in cancer-associated fibroblasts promotes breast cancer cell migration and metastasis by exosomal miRNAs-mediated intercellular communication. *Oncogene* 39, 2539–2549 (2020). <https://doi.org/10.1038/s41388-020-1162-2>
6. Yael Raz et al. Bone marrow-derived fibroblasts are a functionally distinct stromal cell population in breast cancer. *J Exp Med* 3 December 2018; 215 (12): 3075–3093. doi: <https://doi.org/10.1084/jem.20180818>
7. Eble JA, Gullberg D. What Is the Fuss about Integrins and the Tumor Microenvironment? *Cancers*. 2019; 11(9):1296. doi: <https://doi.org/10.3390/cancers11091296>
8. Ning X, Zhang H, Wang C, Song X. Exosomes released by gastric cancer cells induce transition of pericytes into cancer-associated fibroblasts. *Medical science monitor: international medical journal of experimental and clinical research*. 2018;24:2350.
9. Nair, N., Calle, A.S., Zahra, M.H. et al. A cancer stem cell model as the point of origin of cancer-associated fibroblasts in tumor microenvironment. *Sci Rep* 7, 6838 (2017). <https://doi.org/10.1038/s41598-017-07144-5>
10. Wawro ME et al. Invasive colon cancer cells induce transdifferentiation of endothelium to cancer-associated fibroblasts through microtubules enriched in tubulin-β3. *International journal of molecular sciences*. 2019 Jan;20(1):53. <https://doi.org/10.3390/ijms20010053>
11. Barrett R, Puré E. Cancer-associated fibroblasts: key determinants of tumor immunity and immunotherapy. *Current Opinion in Immunology*. 2020 Jun 1;64:80-7. <https://doi.org/10.1016/j.coi.2020.03.004>
12. Liu T, Zhou L, Li D, Andl T, Zhang Y. Cancer-Associated Fibroblasts Build and Secure the Tumor Microenvironment. *Front Cell Dev Biol*. 2019 Apr 24;7:60. doi: 10.3389/fcell.2019.00060. PMID: 31106200; PMCID: PMC6492564.
13. Wawro M et al. Invasive Colon Cancer Cells Induce Transdifferentiation of Endothelium to Cancer-Associated Fibroblasts through Microtubules Enriched in Tubulin-β3. *International Journal of Molecular Sciences [Internet]*. MDPI AG; 2018 Dec 23;20(1):53. Available from: <http://dx.doi.org/10.3390/ijms20010053>
14. Ma J et al. Ligustilide promotes apoptosis of cancer-associated fibroblasts via the TLR4 pathways. *Food and Chemical Toxicology*. 2020 Jan 1;135:110991. <https://doi.org/10.1016/j.fct.2019.110991>
15. Shu, C., Zha, H., Long, H. et al. C3a-C3aR signaling promotes breast cancer lung metastasis via modulating carcinoma associated fibroblasts. *J Exp Clin Cancer Res* 39, 11 (2020). <https://doi.org/10.1186/s13046-019-1515-2>

16. Wang H, Wei H, Wang J, Li L, Chen A, Li Z. MicroRNA-181d-5p-Containing Exosomes Derived from CAFs Promote EMT by Regulating CDX2/HOXA5 in Breast Cancer. *Molecular Therapy-Nucleic Acids*. 2020 Mar 6;19:654-67. <https://doi.org/10.1016/j.omtn.2019.11.024>.
17. Gok Yavuz, B., Gunaydin, G., Gedik, M.E. et al. Cancer associated fibroblasts sculpt tumour microenvironment by recruiting monocytes and inducing immunosuppressive PD-1+ TAMs. *Sci Rep* 9, 3172 (2019). <https://doi.org/10.1038/s41598-019-39553-z>
18. Prabhu, K.S. et al. Non-Coding RNAs as Regulators and Markers for Targeting of Breast Cancer and Cancer Stem Cells. *Cancers* 2020, 12, 351. <https://doi.org/10.3390/cancers12020351>

### **DARK SIDE OF BIOTECHNOLOGY: BIO-TERRORISM, BIOLOGICAL WARFARE AND BIO-WEAPONS**

1. An Overview on Biological weapons and Bioterrorism, *American Journal of Biomedical Research*, 2017, Vol. 5.
2. Bioweapons and Bioterrorism: A Review of history and Biological agents, *Defense S&T Tech Bull*, 2013.
3. Bioterrorism and Biological warfare, *International Journal of Science and Research*, 2017, Vol. 6.

### **BIOTECHNOLOGY INTELLECTUAL PROPERTY DURING A PANDEMIC**

1. <https://www.iam-media.com/coronavirus/ip-crucial-finding-breakthrough-covid-19-medicines-novartis-policy-head-states>
2. <https://www.statnews.com/pharmalot/2020/05/29/who-covid19-coronavirus-patents/>
3. Crisis-Critical Intellectual Property: Findings from the COVID-19 Pandemic; Frank Tietze et al, 2020.

### **THE AMAZING SPIDER-MAN**

1. <https://www.bbc.com/future/article/20170222-the-uneasy-truth-about-human-animal-hybrid-rids>
2. <https://www.dailymail.co.uk/sciencetech/article-2730005/Could-LIZARDS-key-regrowing-human-limbs-Scientists-identify-genes-needed-regenerate-reptiles-tail-say-recipe-used-humans.html>
3. <https://amazingspiderman.fandom.com>