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# BIOTECH EXPRESS

*The monthly magazine of Biotechnology*

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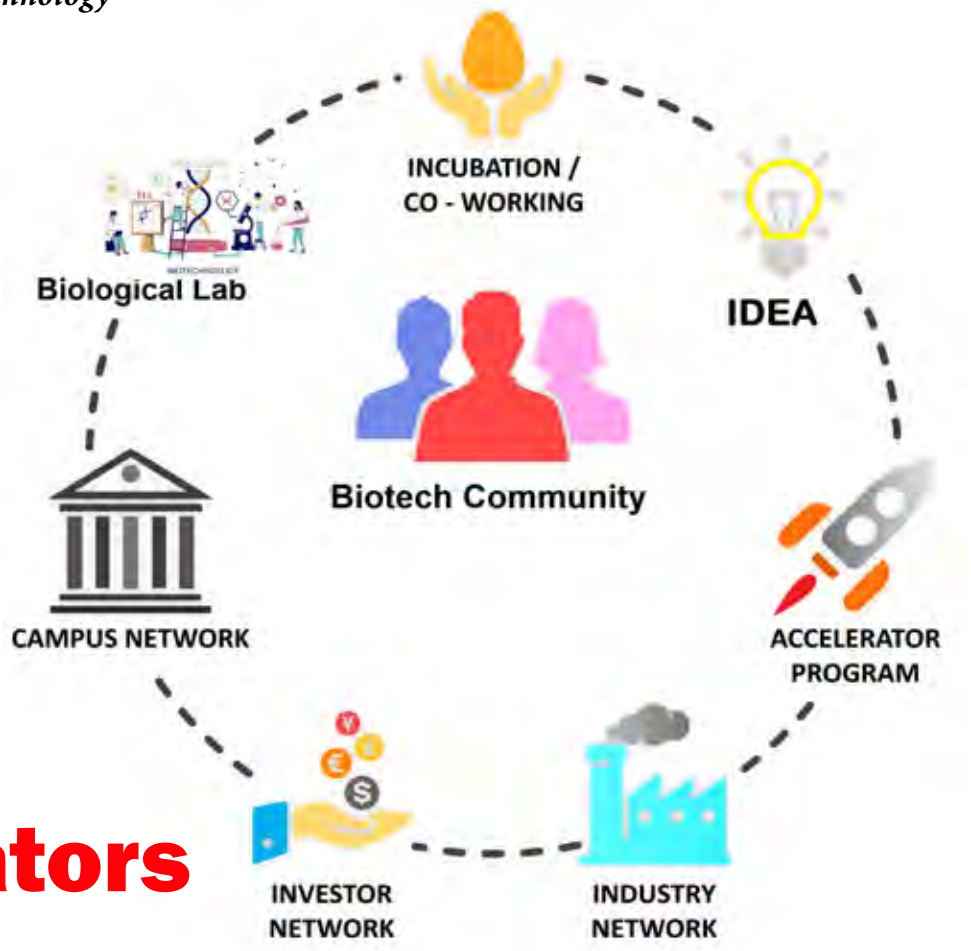
**ASPIRE BioNEST of UoH selected by BIRAC in 2021 as best emerging Bioincubator in the country**

**Reconstitution of the management committee of Federation of Asian Biotech Associations (FABA)**

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# BIOTECH EXPRESS inside...

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BIOTECH EXPRESS

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Dr. Seema P. Upadhye

Managing Editor:
Kamal Pratap Singh

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# From the desk of Editor

Entrepreneurship and startups are only a recent phenomenon in the country. It is only in the last decade and half that people in the country have moved from being job seekers to job creators. Doing a startup is tough and every country sees more failures than success. More often than not an entrepreneur needs to be prepared to face failures and unprecedented hardship.

Having a brilliant idea is different from making that idea a business success. For a startup, it is very important to have mentors who have been through a similar process of starting or have business experience. A great mentor is often what separates success from failure by providing valuable inputs. However, there is no formal mechanism to mentor startups in the country. Every mentoring that happens is on an ad-hoc basis. A startup that has raised funds can count the investors for some form of support.

Government is the single largest enabler for the entrepreneurial ecosystem. Government's role in ease of doing business and helping companies start is vital to ensuring success.

In this and subsequent issues we will discuss various aspects that need discussion around start-up culture in biotechnology in India and welcome suggestions and comments from our readers in this respect so to gather and disseminate different opinions from diverse background of people involved in this field.

Dr. Seema P. Upadhye

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**From the very first issue, Biotech Express team has been delivering what's best for Biosciences community. The audience of this magazine includes students, researchers, faculties and executives of highly prestigious organizations of India. In year 2016, BEM has made new editorial Board combining experience of eminent Advisory Board Members who have been into Award winning Research and head prestigious Administrative positions.**

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# Editorial

# Bioincubators in India

by Kamal Pratap Singh


The entrepreneurial process starts with challenges of working with the unknown and building resources for survival. Several micro and macro level factors including the personality and attitudes of the entrepreneur, identification and creation of opportunities, regulatory frameworks and market conditions, presence of other startups, cultural makeup of the location, access to trained talent, technology, market, finance and mentors influence the success (or failure) of a young enterprise.

The Government of India and State Governments are making efforts to promote biotechnology activities in the country by setting up biotechnology parks, incubators as well as pilot projects through public private partnership to promote this lucrative business that has seen impact after COVID-19 biological pandemic.

There are many various schemes for start-ups which are funded by the following organization either independently or in collaboration. We are not going in detail here, the full information can be accessed on the respective websites or from offices of these organizations.

1. **AIM** Atal Innovation Mission, NITI Aayog, Government of India
2. **DARE** Department of Agricultural Research and Education, Ministry of Agriculture and Farmers Welfare, Government of India
3. **DBT** Department of Biotechnology, Ministry of Science and Technology, Government of India
4. **DoS** Department of Space, Government of India
5. **DSIR** Department of Scientific and Industrial Research, Ministry of Science and Technology, Government of India

6. **DST** Department of Science & Technology, Ministry of Science and Technology, Government of India
7. **MDoNER** Ministry of Development of North Eastern Region, Government of India
8. **MEITY** Ministry of Electronics and Information Technology, Government of India
9. **MoD** MoFPI Ministry of Food Processing Industries, Government of India
10. **MoSDE** Ministry of Skill Development and Entrepreneurship, Government of India
11. **MoT** Ministry of Tourism, Government of India
12. **MSME** Ministry of Micro, Small and Medium Enterprises, Government of India

The following fiscal initiatives have been taken-up by the Government to foster start-up ecosystem in the country:

i. Credit Guarantee Fund for Startups

ii. ii. Tax Exemption on Capital Gains

iii. iii. Tax Exemption to Startups for 3 years

iv. iv. Tax Exemption on Investments above Fair Market Value

The Department of Biotechnology has established Biotechnology Parks/Incubators across the country to translate research into products and services by providing necessary infrastructure support. These Biotechnology Parks offer facilities to Scientists, and Small and Medium sized Enterprises (SMEs) for technology incubation, technology demonstration and pilot plant studies for accelerated commercial development of Biotechnology. These Parks are successfully accelerating the commercialization of new technologies, nurturing and maintaining emerging ventures and assisting new enterprises to forge appropriate linkages with other stakeholders of biotechnology sector including academia and Government. The Department has

TABLE 1: List of BioIncubators in India

| | | |
|---|---|---|
| 1 | a-IDEA, Centre For Agri Innovation | ICAR – NAARM, Rajendranagar, Hyderabad-30, Telangana |
| 2 | VentureStudio | Ahmedabad University, Gujarat |
| 3 | Andhra Pradesh MedTech Zone Limited AMTZ | AMTZ Campus, Andhra Pradesh |
| 4 | Association for Bio-inspired Leaders and Entrepreneurs (Sastra TBI) | Tamil Nadu |
| 5 | NCL-IIT (BHU)Incubation Center | Malaviya Centre for Innovation, Incubation & Entrepreneurship, Varanasi – Uttar Pradesh |
| 6 | BioNEST BITS BIRAC | BITS Pilani K K Birla Goa Campus |
| 7 | Bio-incubation at C-CAMP | NCBS-TIFR, GKVK, Bangalore |
| 8 | Bangalore Bioinnovation Centre | Electronics City Phase 1, Bangalore |
| 9 | BBB - BSC BioNEST Bio-Incubator/Regional Center for Biotechnology | Faridabad, Haryana |
| 10 | Biotech Park Lucknow | Lucknow, Uttar Pradesh |
| 11 | Bio360 – Life Science Park, | PROPOSED |
| 12 | Bio Pharma-IT Park | Information Not Available |
| 13 | Bioriidl | Somaiya Vidyavihar, Mumbai |
| 14 | Clean Energy International Incubation Center | Rohini, New Delhi |
| 15 | Crescent Innovation and Incubation Council | B. S. Abdur Rahman Crescent Institute Of Science And Technology, Urapakkam, Chennai, Tamil Nadu |
| 16 | CSIR-Indian Institute of Toxicology Research | CSIR - IITR, Lucknow |
| 17 | Delhi Pharmaceutical Science Research University | New Delhi |

| | | |
|---|---|---|
| 18 | Entrepreneurship Development Center | Venture Center, Innovation Park, Pune |
| 19 | Foundation for Innovation and Technology Transfer (FITT) | Indian Institute of Technology, Delhi |
| 20 | Golden Jubilee Women Biotech Park, Chennai | Kanchipuram |
| 21 | Healthcare Technology Innovation Center, IIT Madras | Taramani, Tamil Nadu |
| 22 | Hyderabad Eye Institute BioNEST MedTech Incubator at LVPEI | L V Prasad Eye Institute, Hyderabad, Telangana |
| 23 | IIHR, Bangalore | ICAR-IIHR, Bengaluru |
| 24 | IIITH-Foundation | Hyderabad, Telangana |
| 25 | IIT Kanpur | Bioincubator SIDBI Innovation & Incubation Centre IIT Kanpur |
| 26 | IITM Bio-Incubator | Taramani, Chennai |
| 27 | IKP Knowledge Park | Secunderabad, Telangana |
| 28 | IKP-EDEN, Bangalore | Bangalore |
| 29 | Indian Agricultural Research Institute, New Delhi | Indian Agricultural Research Institute, New Delhi |
| 30 | Indigram Labs Foundation | Mohan Cooperative Industrial Estate, New Delhi |
| 31 | Institute of Advanced Study in Science and Technology, Guwahati | Guwahati, Assam |
| 32 | DBT- Institute of Bioresources and Sustainable Development | Imphal, Manipur |
| 33 | International Crops Research Institute-ICRISAT | Telangana |
| 34 | KIIT Technology Business Incubator | KIIT University, Orissa |
| 35 | Mazumdar Shaw Medical Foundation | Bangalore |
| 36 | Incubation Centre @ Mizoram University | Mizoram Univeristy, Aizawl |
| 37 | NIPER Ahmedabad | Gujarat |
| 38 | NIPER-Guwahati | NIPER Guwahati, Changsari, Assam |
| 39 | Panjab University, Chandigarh | Panjab University, Chandigarh |
| 40 | Punjab Biotechnology Incubator (PBTI) | Mohali, Punjab |
| 41 | PERD Center, Ahmedabad | B. V. Patel Pharmaceutical Education and Research Development (PERD) Centre, Ahmedabad, Gujarat |
| 42 | PSG-STEP, Coimbatore | Coimbatore, Tamil Nadu |
| 43 | SBTIC, Hyderabad | Hyderabad, Telangana State |
| 44 | SINE, IIT Bombay | Powai, Mumbai |
| 45 | SRI PADMAVATI MAHILA VISVAVIDYALAYAM | SSIIE-TBI, Tirupati |
| 46 | Sri Ramachandra Institute for Higher Education and Research | Porur, Chennai - Tamil Nadu |
| 47 | SRISTI Innovation BIRAC's BioNest Project | Gandhinagar, Gujarat |
| 48 | Veterinary incubation foundation at TANUVAS | Chennai |
| 49 | TIEDS, IIT Roorkee | IIT Roorkee, Uttarakhand |
| 50 | University of Delhi Bioincubator | University of Delhi |
| 51 | ASPIRE-BioNEST University of Hyderabad | University of Hyderabad |
| 52 | Vellore Institute of Technology-Technology Business Incubator (VITTBI) | Vellore, Tamil Nadu |
| 53 | TICEL Bio Park Ltd | Taramani Road Taramani Chennai |

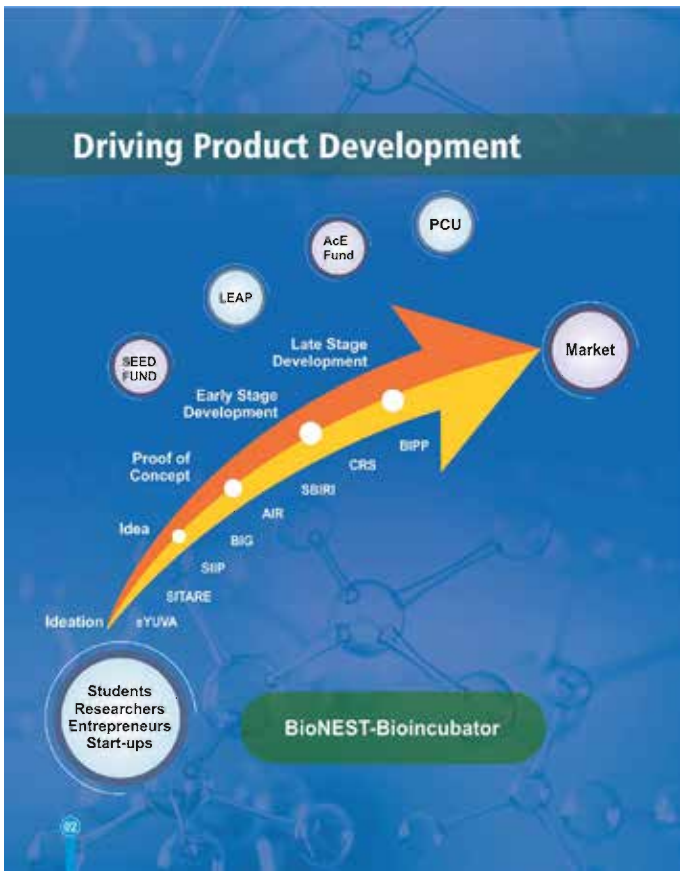
| | | |
|---|---|---|
| 54 | International Biotech Park | Pune – Maharashtra |
| 55 | KINFRA Hi-Tech Park, Kalamaserry | Ernakulam, Kerala |
| 56 | MITCON Consultancy & Engineering Services Ltd | Shivajinagar, Pune |
| 57 | Gujarat Akruti TCG Biotech Ltd. (GATBL) | MIDC , Andheri (E), Mumbai |
| 58 | Guwahati Biotech Park | IIT Guwahati |
| 59 | Punjab Biotechnology Incubator (PBTI) | Mohali, Punjab, |
| 60 | SAVLI BIO-INCUBATOR/ Akruti Biotech Park | Vadodara - Gujarat, |
| 61 | RAMKY PHARMA CITY (INDIA) LTD. | Visakhapatnam, Andhra Pradesh |

come up with 'National Biotechnology Parks Scheme' in which it is proposed to create an ecosystem to absorb the start-ups which have graduated from the incubators and give them a platform for further scaling up their R&D activities in collaboration with the state government and industry.

Several international India-specific Grand Challenges i.e. Wellcome Trust, Bill & Melinda Gates Foundation, Lockheed Martin Corporation, Grand Challenges Canada and bilateral/multi-lateral programmes with other countries also support innovative technology development in India.

**Bio-NEST** was launched by BIRAC (a DBT entity) with a vision that focused on fostering the biotech innovation ecosystem in the country. Unlike start ups in the IT sector, enterprising ideas in the biotech sector need incubation support of a different kind where they need a landing space to test their ideas, run their operations, have access to high end instrumentations and locate in a place where they connect with other start ups and mentors. Bio-NEST program provides support to establish bio-incubators either as a standalone entity or as a part of the academia. Through Bio-NEST, BIRAC has supported more than **55** bio-incubators.

**ASPIRE** - A Scheme for Promotion of Innovation, Rural Industries and Entrepreneurship Govt. of India, Ministry of MSME. ASPIRE- was launched to set up a network of technology centres and to set up incubation centres to accelarate enterpreneurship and also to promote startups for innovation in agro industry. The main objectives of the scheme are to Create new jobs and reduce unemployment; Promote entrepreneurship culture in India; Grassroots economic development at district level; Facilitate innovative business solution for un-met social needs and Promote innovation to further strengthen the competitiveness of MSME sector. 80 Livelihood business incubators (2014-2016) to be set up by NSIC, KVIC or Coir Board or any other Institution/agency of GoI/State Govt. on its own or by any of the agency/Scheme for promotion of Innovation, Entrepreneurship and Agro-Industry organisation of the M/o MSME, one-time grant of 100% of cost of Plant & Machinery other than the land and infrastructure or an amount up to Rs.100 lakhs whichever is less to be provided. In case of incubation centres to be set up under PPP mode with NSIC, KVIC or Coir Board or any other Institution/agency of GoI/State Govt., one- time grant of 50% of cost of Plant & Machinery other than the land and infrastructure or Rs.50.00 lakhs, whichever is less to be provided.



# PRESS RELEASE


## ASPIRE-BioNEST at University of Hyderabad, "The Best Emerging Bioincubator" in India

**ASPIRE-BioNEST has been recently selected as "The Best Emerging Bioincubator in the country", announced in the valedictory function of Global BioIndia 2021.**

Global BioIndia is a biannual conference conducted by Biotechnology Industry Research Assistance Council (BIRAC), DBT, Govt. of India, in the presence of Hon'ble Vice President Sri M. Venkaiah Naidu and Hon'ble Minister of Science & Technology, Dr. Harsh Vardhan. Incidentally, ASPIRE BioNEST has celebrated its third foundation day on 2nd March 2021.

ASPIRE BioNEST is a Life Sciences incubator, set-up with the support of BIRAC in 2018, by renowned Biochemist Prof. G. Padmanaban of Indian Institute of Science, Bangalore – who applauded it "By Far, The Best Bio-incubator". BioNEST is located on the 3rd floor of the School of Life Sciences at University of Hyderabad.

University of Hyderabad (UoH), established in 1974, has been recognised recently as the Institute of Eminence. Moving forward, the UoH is endeavouring to create an enabling and vibrant ecosystem for translating part of its research into novel, innovative and commercially viable technologies, products and services. Towards this, as a first measure, the University had created over 40000 sft sophisticated plug and play incubation space organised in three independent incubation centres (ICs) under a not-for-profit section 8 company named "Association for Scientific Pursuits for Innovative

ASPIRE - BioNEST
University of Hyderabad

Research Enterprises (ASPIRE)". These ICs viz. ASPIRE-TBI (supported by DST), ASPIRE-TIDE (supported by MEITy) and ASPIRE-BioNEST (supported by BIRAC/DBT) are equipped with state of the art instrumentation infrastructure covering almost all the major areas of research in the campus. ASPIRE manages all incubation and innovation activities in the campus and has been recognized by Department of Scientific and Industrial Research (DSIR) certification, independent Institutional Bio Safety committee (IBSC).

ASPIRE BioNEST, formed as a knowledge-based incubator, nurtures innovation and entrepreneurship in scaling technologies of Agriculture, Biotechnology, Healthcare, Pharmaceutical, and allied areas. ASPIRE BioNEST is a deep science incubator with 20000 sft dedicated plug-and-play laboratory space equipped with modern instrumentation to perform any research in Life Sciences. Presently, there are 26 incubatees and ASPIRE BioNEST offers incubation services mainly to the start-ups

**"ASPIRE-BioNEST incubation center provides an ideal infrastructure and supporting system enabling startup companies to establish and succeed in their ventures. Interested startups may contact all around the year in the office of BioNEST UoH".**

who are actively working to address the pressing needs like medical requirements, environment protection, agricultural innovations, human wellness, animal ethics etc. ASPIRE BioNEST also encourages and supports young budding individual entrepreneurs through bench space incubation. For selecting start-ups for incubation, ASPIRE BioNEST follows stringent selection criteria with the help of a Project Appraisal Committee that mainly focuses on novelty, feasibility, commercial potential, social impact, scalability and economic viability of ideas. The facility has been recognized by Department of Scientific & Industrial Research and at least 10 competitive grants have been bagged by its start-ups. ASPIRE BioNEST provides its facilities to start-up entrepreneurs at a minimal charge (License fee), to meet the operational expense of the facility. Revenues generated through operations & services are utilised for improving the facilities so as to cater the increasing needs of the start-ups. Some portion of the revenues are spent for student awareness programmes and workshops to encourage new ideas and translating them into technologies through Pre-Incubation programme.

ASPIRE BioNEST equipped with the best in the class equipment where most of the Lifesciences research can be performed. The facility has culture rooms to handle Microbiology and Animal cell culture experiments, a BSL-2 lab to conduct research on pathogenic organisms. The common instrumentation facility is capable of handling complete upstream and downstream processing of biotechnological products. ASPIRE BioNEST also established a bioreactor facility in association with Scigenics Biotech Pvt. Ltd. ASPIRE BioNEST arranges interactive meetings with invited notable speakers and different subject matter experts to improve the domain specific knowledge, under the fond memory of Dr. Yellapragada Subbarao (Dr. YSR), great Indian Innovative Scientist. On this occasion ASPIRE felicitates the best publications that has innovative research component with Dr. YSR gold medal and a cash prize.

ASPIRE BioNEST has so far guided its incubatees successfully for at least 10 competitive grants like BIRAC BIG. Within one year of establishment, it stood in 6$^{th}$ place nationwide for any incubator (2018-19), surveyed by Biospectrum magazine. At least 10 patents have been filed by incubating start-ups, ASPIRE BioNEST has become BIRAC BIG Associate partner, has also received enhanced grant from BIRAC.

## LIST OF INCUBATEES at ASPIRE BioNEST of UoH

| S. No. | Company Name |
|---|---|
| Currently Incubated | |
| 1 | Mark Therapeutics Pvt. Ltd. |
| 2 | Algen Biotech Pvt. Ltd. |
| 3 | 30M Genomics Pvt. Ltd |
| 4 | Provis Biolabs Pvt. Ltd. |
| 5 | Albus Ecoprojects Pvt. Ltd. |
| 6 | Avulas CEG Pvt. Ltd. |
| 7 | Bycus Therapeutics Pvt. Ltd. |
| 8 | Reagene Innovations Pvt. Ltd. |
| 9 | Vydya Biotech Pvt. Ltd. |
| 10 | Lazuline Biotech Pvt. Ltd. |
| 11 | UR Advance therapeutics |
| 12 | Green Eco Life sciences |
| 13 | Bionsys life sciences Pvt. Ltd. |
| 14 | Hexanoyl Life Sciences Pvt. Ltd. |
| 15 | Onceoseek Bio Pvt. Ltd. |
| 16 | Convergent Bio Systems Pvt. Ltd. |
| 17 | YMC India Pvt. Ltd. |
| 18 | Vectrogen Biologicals Pvt. Ltd. |
| 19 | Grus Grade Pvt. Ltd. |
| 20 | Avyantra Health Technologies Pvt. Ltd. |
| 21 | Panaceja Biotherapeutics Pvt. Ltd. |
| 22 | Phosyn Fuels LLP |
| 23 | Dr. Usha Kumari |
| 24 | Mr Vydyanath Narsimha |
| 25 | Varient Genomics Pvt. Ltd. |
| 26 | Dr. Amitava Mazumder |
| Graduated | |
| 27 | Innov Accel Health Care Pvt. Ltd. |
| 28 | Novick Bio Pvt. Ltd. |
| 29 | Sri Bioaesthetics Pvt. Ltd. |
| 30 | Sasyaved research labs LLP |
| 31 | Terra Scientfics Pvt. Ltd. |
| 32 | Vins Bioproducts Pvt. Ltd. |
| 33 | Therazymes India Pvt. Ltd |
| 34 | K J B Diagnostics |


The award is the result of excellent scientific infrastructure, nurturing ecosystem, mentoring, support in grant proposals & business plan preparation etc. provided for the start-ups. The infrastructure attracts diverse range of deep-tech start-ups from different domains of life sciences and scientific net worth of the start-ups also helped in attaining the best position. On his remarks, the Vice Chancellor Prof. Appa Rao Podile, expressed his happiness and mentioned that this recognition is the result of collective efforts made by the team members of BioNEST, Dr. Sreedhara R. Voleti, (CEO), Dr. Anil Kondreddy (COO) and the mentors Prof. P. Reddanna, Dr. D. Yogeswara Rao, Prof. GS Prasad.

Prof. Podile, also added that this would have not been possible without the contribution from the incubating start- ups and generous funding support from the BIRAC. The incubator is currently headed by Prof. S. Rajagopal, who is also a full time Professor at School of Life Sciences, University of Hyderabad.

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**Prof. G.S. Prasad, University of Hyderabad**

# BIOSTART-UP

# Reagene Biosciences received Emerging start-up award recognition for 3D bioprinting start-up incubated at University of Hyderabad's ASPIRE-BioNEST Incubation Center

ReaGene Biosciences (https://www.reagenebiosciences.com/) a group company of start-up ReaGene Innovations Pvt Ltd incubated at Aspire-BioNEST University of Hyderabad (**Received the best Emerging bio-incubator 2021 award from BIRAC)** was identified as an emerging start-up company by an independent jury panel of ChemTech- Biopharma conference 2021.

The award was in recognition of the unique 3D models being developed by the group companies. These models are focused on discovery of new products for high value unmet diseases such as sepsis and COVID-19. To date, majority of preclinical research is conducted in animals for both efficacy and toxicity, however, proved to be poorly translated to clinical outcomes. There is a strong need for better translational models to improve clinical translation and decrease clinical attrition rates. Currently used in vitro human single-cell static models do not mimic human physiology, cell-cell and organ-organ communications those play important role in drug efficacy and toxicity in humans *in vivo*.

ReaGene mission is to build proprietary Humanized 3D tools containing multiple cell types of different organs to allow communications of different cell types and organs. These models represent closest to human *in vivo* condition recapitulating human physiology to measure efficacy and toxicity simultaneously and make informed decisions on clinical liabilities before moving drugs into clinical trials. These models are much superior to organoids and spheroids to mimic human physiology and communications.

The founders of ReaGene, Dr. Uday Saxena an alumnus of the University of Hyderabad and Dr. Subrahmanyam Vangala expressed their happiness at the recognition and are hopeful that these proprietary disruptive 3D bio printing platforms will revolutionize drug discovery research in India and rest of the world. Both founders

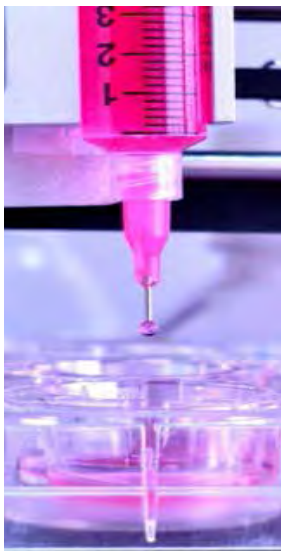
each have nearly 30 years of extensive experience in big pharma companies including Pfizer, Wyeth, JNJ, Purdue Pharma and Reddy Labs in innovative drug discovery and drug development research.

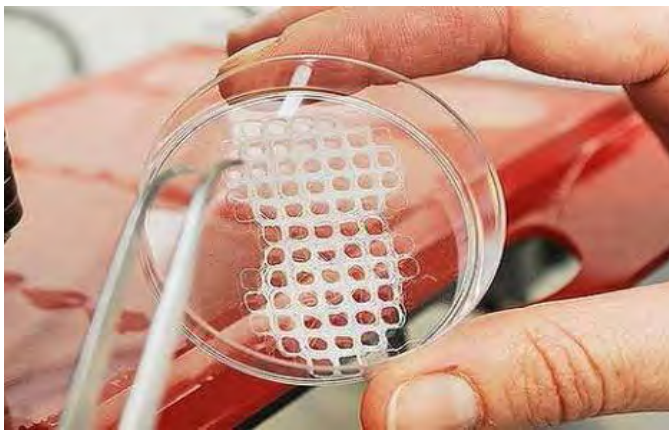
Dr. Uday Saxena

Dr. Subrahmanyam Vangala

ReaGene has ongoing collaborations with Tech Mahindra, Issar Pharma, ProdigY on Sepsis and COVID projects using human vascular 3D lung model. Their larger mission is to apply these tools to elucidate disease pathways, identify novel drug targets, biomarkers, and discover novel drugs or repurpose other drugs on market. In 2019, ReaGene Biosciences was awarded prestigious "Promising Entrepreneurs of India" by Economic Times of India. ReaGene will continue to conduct Bench to Bedside cutting edge innovative research to help patients in India and rest of the world.

Photos: Steps in **3D Printing Tissues for Research**





# PRESS RELEASE

# RECONSTITUTION OF THE MANAGEMENT COMMITTEE OF FEDERATION OF ASIAN BIOTECH ASSOCIATIONS (FABA)

10th March 2021

FEDERATION OF ASIAN BIOTECH ASSOCIATIONS (FABA), announced the reconstitution of the Management Committee of the FABA through a proper election process as a custom for every two years, for the years 2021 and 2022. The committee has representatives from the academy, industry, and Government bodies, with the president from one of the Asian member countries, , this time it is the turn of Bangladesh.The following is the newly reconstituted Management Committee:

Dr. Asadulghani, ICDDR, Bangladesh (President),

Prof. P. Reddanna, University of Hyderabad (Executive President),

Dr. P. Ratnakar, Tech Mahindra (Secretary General),

Dr. Suresh Pothani, ICMR – NARF (Rtd) (Executive Secretary),

**Executive Members**

Dr. Suresh Poosala, Oncoseek Bio Pvt. Ltd., (EC member),

Dr. Markandeya Gorantla, ATGC (EC member),

Dr. Raman Sundaram, ICAR - IIRR (EC member),

Dr. Uday Saxena, ReaGene Innovations (EC member),

Prof. Vijay Kumar Kutala, Nizam's Institute of Medical Sciences (EC member),

Dr. V. Ramanathan, Rallis India Pvt. Ltd. (EC member),

Dr. S. Harinarayana Rao, CDFD R(td.) (EC member),

Dr. Ajith V Kamath, Pandoram Technologies (EC member),

Dr. Ramesh Sonti, CSIR -CCMB (EC member),

Dr. Jagadeesh Gandla, DARE to Start, Germany (EC member),

Ms. Sreedevi Devireddy, SR Innovation Exchange (EC member),

Dr. Ravikrishnan, RCC Labs India Pvt. Ltd. (EC member).

Dr. D. Sambashiva, Nizam College, Osmania University (Treasurer).

The recent last committee meeting held virtually on 10th February 2021 and the following resolutions were taken:

1. The committee appreciated the entire team of the previous committee, specifically by the President, Dr. Anand Govindaluri from Singapore and Dr. Vijaykumar from NIMS, for their pioneering contributions to conduct various activities including the conduct of "International Conference on Supply Chain Challenges in COVID-19 Vaccines: Indian Imperative" and enrolling the corporate and institutional members.

2. To revitalize the FABA chapters in the member countries to enhance their participation in FABA and FABA Academy activities.

3. To rename the "FABA Special Award" in honor of Dr. BS Bajaj, the founder of FABA, and rename it as "Dr. BS Bajaj memorial FABA Award".

***"Dr. BS Bajaj memorial FABA Award" was presented to Dr. Balram Bhargava in recognition of his contributions during the COVID -19 pandemic in the country in the annual event of FABA i.e. BioAsia 2021, on 22nd and 23rd February 2021. It is to emphasize that the ICMR, under the able leadership of Dr. Balram, played an important role in coordinating Government efforts effectively against COVID- 19 pandemic, apart from collaborating with vaccine manufactures to bring out the COVID -19 vaccine in a record period of time.***

According to Prof. Reddanna, Executive President (FABA), "FABA promotes and safeguards the overall interests of Biotechnology as science, profession, industry or trade by coordinating with research professionals, entrepreneurs, industries and academic institutions in various Asian Countries. He also said that FABA promotes collaboration between academia and industries engaged in Biotechnology among the member countries in Asia."

**About FABA**

Federation of Asian Biotech Associations (FABA), established in 2005, is a non-profitorganisation registered under the Indian Societies Act, 1860. It is created to provide a global platform for the development of biotechnology across the globe, particularly in Asian countries. The mission of FABA is to promote innovation and entrepreneurship in the biotech industry, academia, and healthcare sector.For more than 15 years, FABA has been fostering collaboration between academia, industry, and government, thus promoting investments in biotechnology and related fields. FABA also facilitates cross-border trade in terms of export, outsourcing of services, products, and other related activities. FABA sponsors study and business teams in member countries and invites individuals, experts, scientists, and similar delegations from member countries and across the world.

For more information about the Federation of Asian Biotech Associations, visit: **http://biofaba.org.in/**

**About FABA Academy** FABA academy is a special wing under FABA organization that focuses on grooming the students of the Universities in all the member countries and make them "Future-ready". FABA academy prepares the students by providing skill development programs that give them the opportunities in the Pharma and Biotech industries. The academy also provides career guidance workshops and webinars to enlighten young minds with all the available options in the job market. The FABA academy also brings awareness and guidance, among the student community, in the core values behind innovation and entrepreneurship. All this is achieved by conducting webinars, workshops, distinguished lectures, and hands-on training onvarious topics of relevance to the industry, under the supervision of experts from the academy and industry.

For more information about the Federation of Asian Biotech Associations, visit: (**http://biofaba.org.in/faba-academy.html**)

# Guest Article

# Bio-Nylon: The Lucrative Plastic Business

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Nylon is the commercial name for a kind of polyamide thermoplastic. The Polyamide nylon has varying supremacy that makes it an ideal candidate for a wide range of applications. It was first developed in the mid-1930s and the global nylon market is expected to grow at a compound annual growth rate of 6.2% from 2018 to 2025 to reach USD 41.1 billion by 2025[6]. Polyamides, better known under the generic name nylons, are a major class of engineering plastics and they are produced *via* polycondensation of a diacid and a diamine, or ring-opening polymerization of a lactam (a cyclic compound with an amide group) (Fig.1). The backbone of nylon is characterized by recurring units (−CO−NH−) of diamines and dicarboxylic acids that may contain different numbers of carbon atoms rendering varying material properties [2].

Polyamides are named after the number of carbon atoms of each of the monomers, in which the first number corresponds with the diamine and the second with the diacid. Nylon comes in four main grades of polyamide nylon: nylon 66, 11, 12 and 46[5]. Due to the various advantages (Table1), the nylon market is segmented into automobiles, electrical and electronics, engineering plastics, textile, and others. Automotive held the largest market share in 2019; The Asia Pacific was the dominant regional segment occupying over 42.95% of the revenue share in 2019 followed by Europe and North America.

Every year polymers constitute a major fraction of industrial petrochemicals. However, during the current decade, bio-based processes from renewable resources have come into a priority (Fig.2.), as they open routes to value-added chemicals and supreme materials.

Biopolymers produced from renewable raw materials provide an environmentally friendly alternative to conventional petroleum-based polymers and exhibit new interesting properties, such as low water uptake,

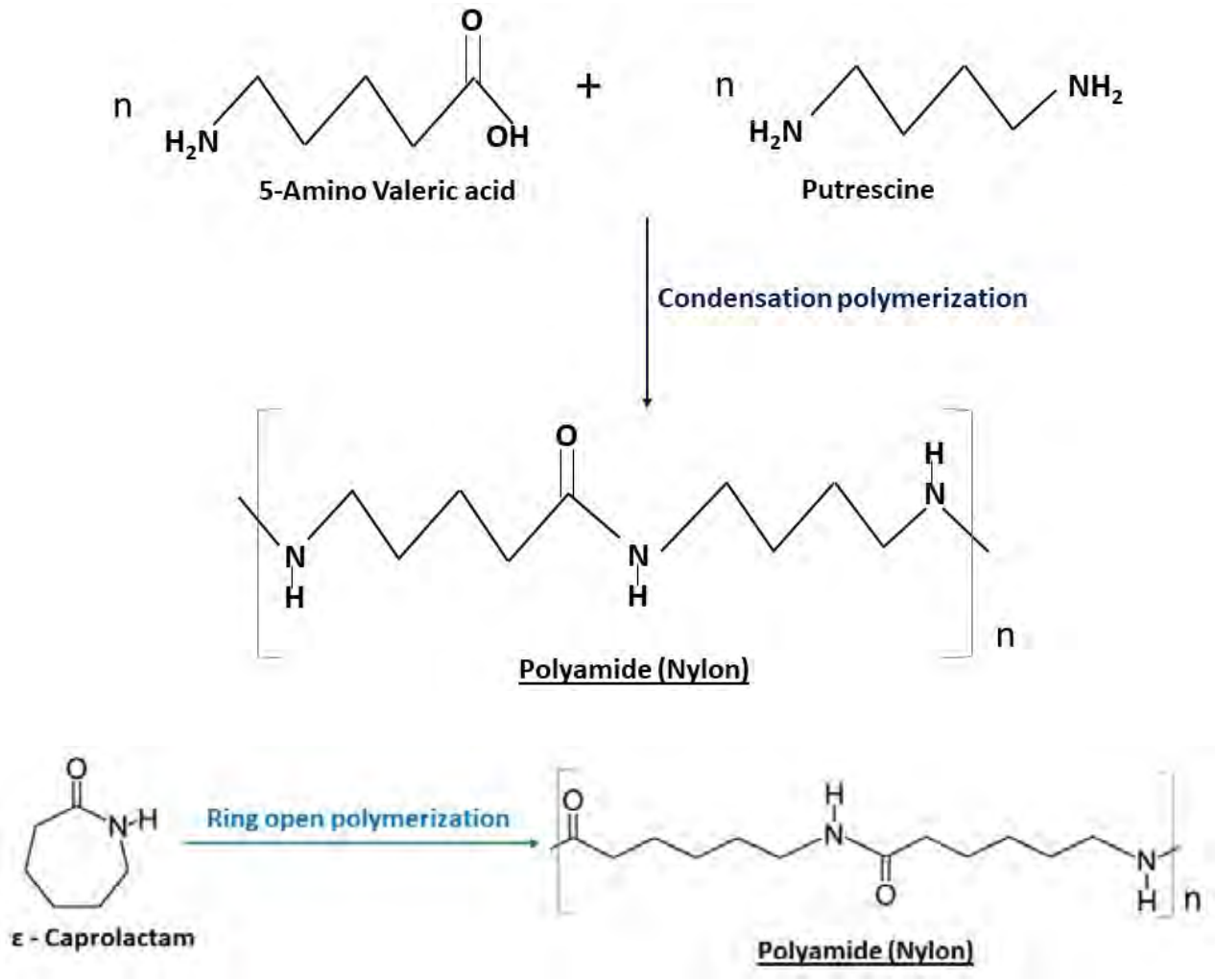


**Fig.1.** Chemical reactions leading to polyamide synthesis

high mechanical resistance, high melting point, and crystallization rate[1]. Vegetable oils derived from non-edible plants are good alternative chemical feedstock due to their specific reactivity and biocompatibility[2]. They are vastly used for durable biothermoplastics, such as biopolyamides which have huge demand as they show promising mechanical and thermal properties.

***The global polyamide market was valued at USD 25.14 Billion in 2016 and is projected to reach USD 30.76 Billion by 2021, at a CAGR of 4.1% from 2016 to 2021.***

The growth in the polyamide market is driven by the polyamide 6 and polyamide 66 segments due to their usage in a wide range of products across several industries. The bio-based and specialty polyamide type segment is projected to be the fastest-growing type segment of the polyamide market from 2016 to 2021. The demand for organic materials is expected to rise globally due to the rise in prices of petrochemical-based raw materials. Bio-based polyamides are a high-quality alternative to substitute petro-based materials and some of the leading industries involved in bio-based polymers and chemicals are shown in Table 2

Bio-polyamides are synthesized from monomers or comonomers, which belong to amino acid, cyclic amide

| Advantages | Disadvantages | Applications |
|---|---|---|
| High Abrasion Resistance : Higher levels of resistance to wear by mechanical action<br><br>Good Thermal Resistance : Special grades of nylon can have a melting point of almost 300°C<br><br>Good Fatigue Resistance : This makes it ideal for components in constant cyclic motion like gears<br><br>High Machineability : Cast billets can be machined into various components that would be too costly to cast into intricate shapes<br><br>Noise Dampening: Nylon is a very effective noise dampener | Water Absorption: Water absorbed results in lower mechanical properties. Nylon 6/12 is specially formulated to resist moisture absorption<br><br>Chemical Resistance: Nylon has low resistance to strong bases and acids<br><br>High Shrinkage: High percentages of shrinkage in cast applications | Electronic equipment, fabrics, food packaging, and home furnishing. Moreover, because of their excellent biocompatibility, nylons are used in medical applications including arthroplasty, implants, molecular medicines, and tissue culture. |

**Table.1**. Properties and applications of Nylon

(lactam), dicarboxylic acid, and diamine families. Three main groups of monomers for the production of biopolyamides are (i) diamines and diacids undergoing polycondensation, where both monomers and only diacid come from renewable feedstock, (ii) amino-carboxylic acids capable for polycondensation and (iii) lactams transformed into polyamides via ring-opening polymerization. Table 3 shows some of those monomers and the raw material used.

Monomers used in biopolyamides synthesis can be obtained partially or fully from biomass [2]. Currently, biomass-derived monomers with the highest industrial meaning for the synthesis of biopolyamides are 11-aminoundecanoic acid, 1, 8-octanedicarboxylic acid, 1, 10-decanediamine, adipic acid, caprolactam and 1, 4-butanediamine.

The main source of bio-based monomers for polyamides is castor oil, which makes up 40–60% of the castor bean. Fatty acids present in vegetable oils can be converted by simple reactions into suitable bifunctional monomers for the production of polyamides by a simple polycondensation process. Among the most known biomonomers are 11-aminoundecanoic acid and sebacic acid produced by conversion of ricinoleic acid derived from castor oil. Typically, raw castor oil is hydrolyzed to give ricinoleic acid, which is then converted to sebacic acid in a reaction with potassium or sodium hydroxide at high temperature [12]. The 1,12-dodecanedioic is most often prepared from petrochemical butadiene, but potentially it can be obtained by an x-oxidation process of lauric acid catalyzed by yeast strain. Undecane-1, 11-dicarboxylic acid and 11-aminoundecanoic acid were also reported as potential monomers [12].

Bio-polyamides, e.g., 1, 5-diaminopentane (cadaverine), pentamethylenediamine, or tetramethylenediamine, are naturally occurring substances or they can be produced by microbial biosynthesis (e.g., by decarboxylation of amino acids (lysine, ornithine)[11,17] and polymerization with substances from microbial fermentation (such as succinate)[15]. Monomers used in biopolyamides synthesis can be obtained partially or fully from biomass. Currently, biomass-derived monomers with the highest industrial meaning for the synthesis of biopolyamides are 11-aminoundecanoic acid, 1,8-octanedicarboxylic acid, 1, 10-decanediamine, adipic acid, caprolactam and 1,4-butanediamine *etc* [9,10].

A large number of the polyamide monomers can be

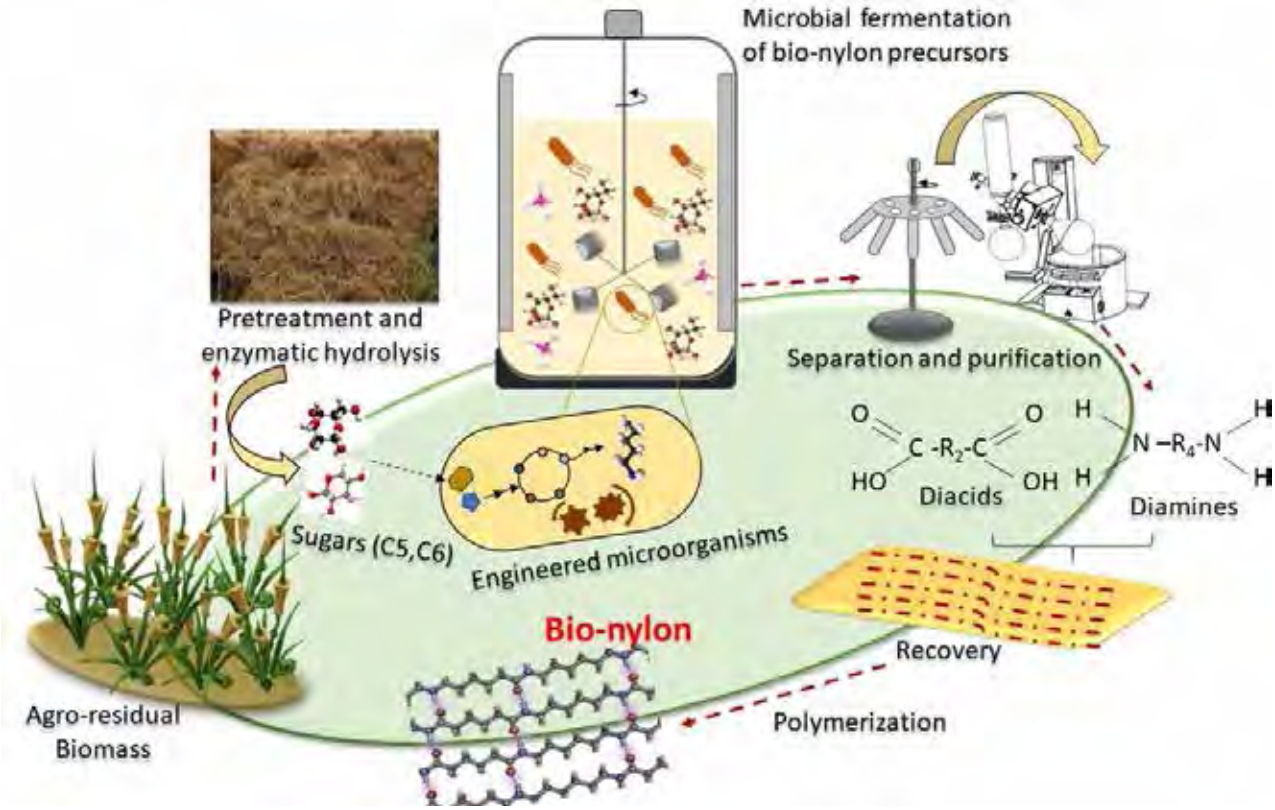


**Fig.2.** A Schematic view for Bionylon synthesis from Agroresidues

| | Global Company | Priority areas |
|---|---|---|
| 1 | Genomatica (San Diego) | Intends to develop enzymatic Industrial pathways for the production of the chemical building blocks hexamethylenediamine, adipic acid and caprolactam. Use of engineered microorganisms to ferment plant sugars to produce caprolactam, and therefore nylon, in a 100% renewable way. |
| 2 | Braskem, Brazil | Active in the production of bioethanol, bioethylene and the bioplastics that can be produced from them |
| 3 | Novamont, Italy | Biorefinary mode of approach , value added chemcials along with biofuel |
| 4 | DSM, Netherlands | Uses biotechnology for many purposes such as semisynthetic penicillins, second generation biofuels, biotechnological pathway to produce caprolactam from lysine and bionylon from castor oil. |
| 5 | Wageningen UR Netherlands | Production of caprolactam, pipecolic acid and other precursors to nylons through modified plants and microorganisms. |
| 6 | Rennovia, USA | Production of biobased adipic acid ( a precursor to caprolactam). |
| 7 | Verdezyne , USA | developed a yeast that can produce adipic acid from vegetable oils and sugars in a single step |

**Table 2**. Global companies ventured into bio nylon

| Monomers | Raw material |
|---|---|
| **Amino acids and lactams** | |
| ε-Caprolactam | Crude Oil |
| 11-aminoundecanoic acid | Castor oil |
| Laurolactam | Butadiene |
| **Diacids** | |
| Adipic acid | Crude oil |
| Sebacic acid (decanedioic acid) | Castor oil |
| 1,12 Dodecanedioic acid | Butadiene , lauric acid (via yeast fermentation) |
| Undecane-1,11-dicarboxylic acid | |
| Terephthalic acid | Crude oil |
| Isophthalic acid | Crude oil |
| **Diamines** | |
| Tetramethylenediamine (putrescine) | Crude oil , biomass |
| Hexamethylenediamine (HMD) | Crude oil |
| Trimethyl Hexamethylenediamine (TMD) | Crude oil |
| m-xylylenediamine (MXD): | Crude oil |
| 1,5-pentanediamine (cadaverine) (PMD): | Crude oil , biomass |
| 1,9-diaminononane: | Crude oil |

**Table. 3**. Monomers of Polyamides and the prominent raw material

produced, in principle, by bio-based routes, which led to the availability of a variety of different polyamides with excellent properties. *Corynebacterium glutamicum* in which the L-homoserine dehydrogenase gene (hom) was replaced by the L-lysine decarboxylase gene (cadA) of *Escherichia coli* showed great potential for the production of the glutamate-derived diamine putrescine, a monomeric compound of polyamides. So far, putrescine has been produced using engineered *E. coli* and *C. glutamicum*. Putrescine was also produced from alternative carbon sources such as crude glycerol[13] biomass hydrolysates[14] , amino sugars and juices *etc.* In one of the recent studies, the methylotrophic and thermophilic bacterium *Bacillus methanolicus* was engineered for the production of the platform chemical cadaverine (1, 5-diaminopentane) from methanol[7]. This was achieved by the heterologous expression of the *E. coli* genes *cadA* and *ldcC* encoding two different lysine decarboxylase enzymes, and by increasing the overall L-lysine production levels in this host.

A new metabolic pathway for the production of 5-aminovalerate (5AVA) from l-lysine *via* cadaverine as an intermediate was also established [8] and this three-step-pathway comprises l-lysine decarboxylase (*LdcC*), putrescine transaminase (*PatA*) and γ-aminobutyraldehyde dehydrogenase (*PatD*). Upon expression of *ldcC*, *patA* and *patD* from *E. coli* in *C. glutamicum* wild type, production of 5AVA was achieved for the synthesis of cadaverine from glucose by fermentation. Moreover, 5AVA production from the alternative feedstocks such as starch, glucosamine, xylose and arabinose was also established. Thus, a large number of the polyamide monomers can be produced, in principle, by bio-based routes, which led to the availability of a variety of different polyamides (Table 4) with excellent properties.

To summarize, nylon polymers have found significant commercial applications in fabric /fibers, molded parts for cars, electrical equipment, food packaging and medical devices. Sustainable technologies of extraction and synthesis of a variety of biomass-derived chemicals and monomers of polymers are reported in the recent past and the development of bio-based feedstock is rudimentary for the future progress in bioplastic production and is considered

| Poly amides | Monomer and Raw material | Remarks |
|---|---|---|
| *Polyamide 11* | Monomer is 11-amino-undecanoic acid (C11), a derivative of castor oil | Fully biobased, high quality, commercialized under the brand name Rilsan® |
| *Polyamide 6,6* *& polyamide 6* | Polyamide 6,6 from hexanediamine (C6) and adipic acid (C6) & polyamide 6 (from caprolactam (C6) | Widely used applications |
| Polyamide 4,6 | Produced by polycondensation of butanediamine (C4) and adipic acid (C6). | An engineering plastic with a high crystallinity and melting point. Commercialized under the brand name Stanyl® |
| Polyamide 6,10 | Monomers are heanediamine (C6) and Sebacic acid (C10). castor oil as raw material for the diacid | Engineering plastic for niche markets. Many companies like Dupont, BASF were commercialized it Partially biobased |
| Poly amide 5.10 PA5.4, | From petrochemical monomers | First, systems metabolic engineering of *Corynebacterium glutamicum* was used to create an effective microbial cell factory for the production of diaminopentane as the polymer building block and also open up green routes to production of these novel bio-nylons, co-polymerized with sebacic acid from natural castor oil and succinic acid from microbial fermentation |
| *Polyamide 10,10* | Obtained via the polymerization of decanediamine (C10) and sebacic acid (C10). Castor oil as raw material. | 99 % biobased material<br>The material is commercially produced under the brand names Grilamid® 1S, and TEGOLON® ECO 10-10 |
| Polyamide 4,10 | Produced by the polymerization of butanediamine (C4) and sebacic acid (C10). | Biobased and Commercialized as EcoPaXX |

**Table 4**. Leading polyamides reported in the literature

a unique and fast-evolving field of chemical technology. The need for sustainable, bio-based approaches to material precursors is an area of business attraction. Through carefully drafted fermentation processes, industrial biotechnology rather called white biotechnology can make many wonders. It has been demonstrated by the researchers that using a synthetic biology approach and with genetically engineered microorganisms it is possible to produce many of the monomers of the polyamides from biomass-derived sugars including the abundantly present pentose sugar Xylose of the biomass and it is an economic opportunity for the industries to look in to. The real challenge is of the translation step, how all these laboratory studies can be successfully converted to the commercial scale. Many of the new biotechnological processes combine an enzymatic catalytic step with one or more chemo-catalytic steps and is popularly known as green chemistry which helps to derive new pathways that did not exist and is a tremendous opportunity.

## References

1. Anh Q. D. Nguyen, Jens Schneider , Gajendar Komati Reddy and Volker F. Wendisch,

Fermentative Production of the Diamine Putrescine: System Metabolic Engineering of *Corynebacterium glutamicum, Metabolites,* 2015 (*5)* , 211-231

2. Gregory von Abendroth , Oskar Zelder , Christoph Wittmann From zero to hero – Production of bio-based nylon from renewable resources using engineered *Corynebacterium glutamicum*, Metabolic Engineering 2014 (25) 113–123

3. Guillaume L, Jouanneau J, Briffaudd T. Polyamide, composition comprising such a polyamide and their uses. 2011, US Patent 20110189419 A1

4. Hong SH, Kim JS, Lee SY, In YH, Choi SS, Rih JK, Kim CH, Jeomg H, Hur CG, Kim JJ. The genome sequence of the capnophilic rumen bacterium *Mannheimia succiniciproducens*. Nat Biotechnol. 2004, (22), 1275–81

5. https://matmatch.com/learn/material/polyamide-nylon

6. https://www.gminsights.com/industry-analysis/biobased-and-synthetic-polyamides-market

7. Ingemar Nærdal, Johannes Pfeifenschneider Trygve Brautaset and Volker F. Wendisch, Methanol-based cadaverine production by genetically engineered *Bacillus methanolicus* strains, *Microbial Biotechnology 2015,(8),* 342–350

8. João M.P. Jorge , Fernando Pérez-García , Volker F. Wendisch (2017) A new metabolic route for the fermentative production of 5-aminovalerate from glucose and alternative carbon sources , Bioresource Technology 2017**(** 245), 1701-1709

9. Jong An Lee, Jung Ho Ahn, Inho Kim, Sheng Li, and Sang Yup Lee*, Synthesis, Characterization, and Application of Fully Biobased and Biodegradable Nylon-4, 4 and -5, 4, ACS Sustainable Chem. Eng. 2020 (8), 5604−5614

10. Kind S, Wittmann C. Bio-based production of the platform chemical 1, 5-diaminopentane. Appl Microbiol Biotechnol 2011(91), 1287–96.

11. Kind S , Neubauer S, Becker J, Yamamoto M , Völkert M , Mimitsuka T ,Sawai H, Hatsu M, and Yamada K , Metabolic Engineering of *Corynebacterium glutamicum* for Cadaverine Fermentation, Biosci. Biotechnol. Biochem. 2007, 71 (9), 2130–2135.

12. Lu W, Ness JE, Xie W, Zhang X, Minshull J, Gross RA. Biosynthesis of monomers for plastics from renewable oils. J Am Chem Soc. 2010 (132):15451–5

13. Meiswinkel, T.M.; Rittmann, D.; Lindner, S.N.; Wendisch, V.F. Crude glycerol-based production of amino acids and putrescine by *Corynebacterium glutamicum*. *Bioresour. Technol.* 2013, (*145),* 254–258.

14. Meiswinkel, T.M.; Gopinath, V.; Lindner, S.N.; Nampoothiri, K.M.; Wendisch, V.F. Accelerated pentose utilization by *Corynebacterium glutamicum* for accelerated production of lysine, glutamate, ornithine and putrescine. *Microb. Biotechnol.* 2013 (*6*), 131–140.

15. Oh IJ, Kim DH, Oh EK, Lee SY, Lee J. Optimization and scale-up of succinic acid production by Mannheimia succiniciproducens LPK7. J Microbiol Biotechnol. 2009; 19:167–71.

16. Ranganathan S, Kumar R, Maniktala V. On the mechanism and synthetic applications of the thermal and alkaline degradation of c-18 castor oil. Tetrahedron. 1984(40)1167–78.

17. Stefanie Kind , Steffi Neubauer, Judith Becker, Motonori Yamamoto , Martin Völkert ,Takashi Mimitsuka ,Hideki Sawai, Masahiro Hatsu, and Katsushige Yamada , Metabolic Engineering of *Corynebacterium glutamicum* for Cadaverine Fermentation, Biosci. Biotechnol. Biochem. 71 (9), 2130–2135, 2007

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# Review Article

# Cross reactivity and neutralization: SARS-CoV-2 triggers antibodies from previous coronavirus infections

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## ABSTRACT

With the Introduction of COVID-19 vaccine to the world, Proteomic studies of SARS-CoV-2 revealed that some regions are conserved from other human coronaviruses(CoVs) which leads to cross-recognition by the humoral immune response. Epitopes that are conserved among SARS-like coronaviruses are attractive targets for design of cross-reactive vaccines and therapeutics. The cross-reactivity of the antibodies can neutralise the SARS-CoV-2 strains on the basis of the conserved epitope regions in the structure. Considering the conservation a study found few sites of S2 subunit of Spike protein in SARS CoV 2 that have significant cross reactivity as well as cross neutralization and hence can be the potential contestant for a vaccine that will provide a broad and faster immunization. These epitopes show potential for cross-neutralization and hence can serve as the potential base for immunization and therapeutic development against SARS-CoV-2 and it's strains.

## INTRODUCTION

The Coronaviridea family is a group of RNA viruses infecting a wide range of organisms including vertebrates. It consists of the largest known RNA viruses ranging from 25-32kb with virions of diameter 118-140nm [1]. The family can be divided into two subfamilies, the *Coronavirinae* and the *Torovirinae* on the basis of their nucleocapsid. The *coronavirinae* subfamily can be further divided into four genera, α, β, ɣ and δ[2]. All family member follow the same mRNA synthesis strategy in which the complex polymerase leaps or transfers from one region of the prototype to a more distant region.The high rate of RNA recombination that occurs during genome replication may explain the need for the polymerase complex to dissociate from the template[1].Various member of this family infect a broad range of vertebrate, reflecting symptoms from common cold to severe fatal illnesses diseases such as MERS, SARS, the recent pandemic COVID-19[3]. The COVID-19 pandemic originated from Wuhan, China was a result of an outbreak caused by an enveloped, single-stranded positive-sense RNA virus known as SARS-CoV-2 which

belonged to the group 2 of the betacoronavirus of the Coronaviridea family(subfamily *coronaviridea*)[4,5]. SARS-CoV-2 is one of the members of the humans infecting CoV family, belonging to the same lineage of viruses that cause SARS. Before 2019, six human infecting virus of CoV family namely CoV 229E (HCoV-229E), HCoV-NL63, HCoV-OC43, HCoV-HKU1, SARS-CoV, and MERS-CoV were known, but being genetically mutated the novel Coronavirus SARS-CoV-2 spread as a pandemic resulting in severe to mild upper respiratory tract infections and very high death toll[6]. Closely relating the genome of SARS-COV-2 with that of the other members of the CoV family indicates that the sequence coding for the spike protein (1273 amino acids) has 27 amino acids substitution, receptor-binding area (RBD) has six of these substitutions and six more are in the underlying subdomain (SD)[7]. Phylogenetic analysis of the SARS-CoV-2 revealed that it is 88% similar to that of SARS-like CoVs (bat-SL-CoVZC45 and bat-SL-CoVZXC21) in bats. It is also genetically similar to SARS-CoV and MERS-CoV nearly 79% and 50% respectively[8].

# SARS-CoV-2 Structure

## S GLYCOPROTEIN

S Protein is abundant, clove shaped, type-I viral transmembrane, multifunctional proteins having three segments: a single-pass transmembrane, ectodomain and an intracellular tail[15]. The S protein ectodomain contains S1 subunit, having a receptor-binding domain(RBD), along with a membrane fusion subunit (S2). In the initial step of viral infection the RBD on the S proteins recognise the host-cell receptor, the binding interaction between the host receptor and spike protein is the critical factor determining the cross-species transmission and host range. Coronavirus that infects humans (like HCoV-229E) recognises hAPN (human aminopeptidase N ) along with a wide variety of host receptors [15,16], and ACE2(angiotensin-converting enzyme 2) is recognized by SARS-CoV. Since S protein is common among all the corona family members, hence it is the major target for eliciting antibodies[15].

## M PROTEIN

The structure of M Protein includes three domains - Amino terminus domain(outside the virion), Transmembrane domain, and Carboxyl terminus domain(inside the virion) [17]. The membrane proteinM protein) gives the defined shape - by M-M interaction - to the envelope along with being the most abundant protein of the virion [18]. Coronavirus M proteins maintain structural similarity along different genera despite the high diversity in amino acid content [17]. Studies of genome composition and divergence of SARS CoV-2 revealed the amino acid composition of M protein is the same as that of SARS CoV [19].

## E PROTEIN

The smallest structural protein of coronavirus - E protein - also has three domains similar to M protein. Amino terminal of E protein is hydrophilic and the transmembrane domain is hydrophobic in nature [20]. Along with functioning as viroporin(integral membrane polypeptide ion channel) it also plays a role in pathogenesis, assembly and release of virus [21, 22].

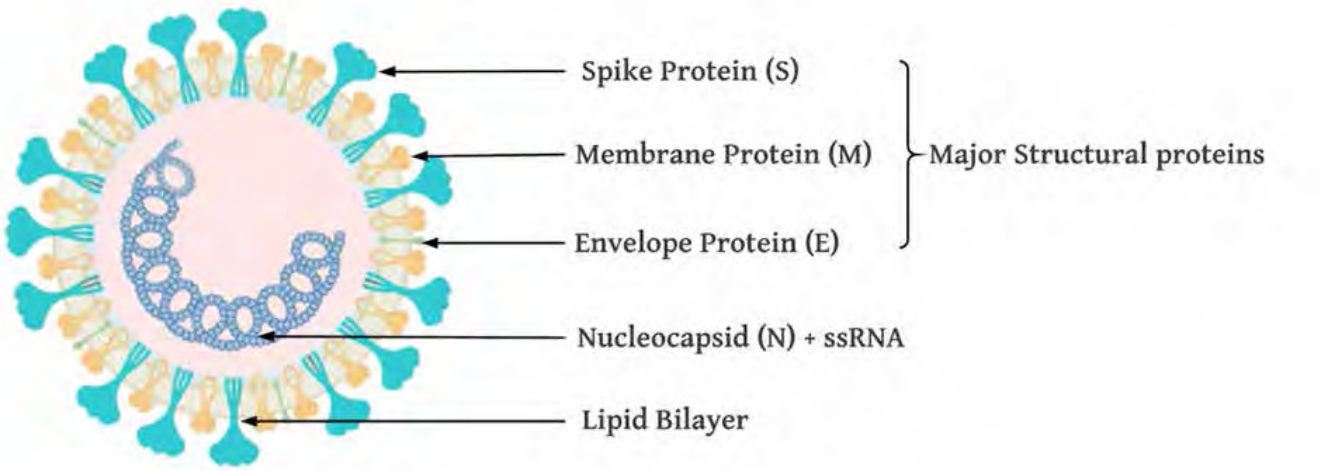


Fig-01: SARS-CoV-2 structure

Absence/inactivation of this protein in coronavirus cause morphological and tropism change which in turn alters the virulence [23]. Similar to M protein the amino acid composition is the same in both SARS CoV and SARS CoV-2 [19].

## N PROTEIN

Likewise other two proteins - M protein and E protein - structure of N protein also have three domains, namely, a NTD, a linker-region(LKR - binds to RNA) and the last Carboxy terminal domain [24]. The linker-region is rochin Serine and Arginine hence also called SR domain [25]. In terms of function N protein serves as multipurpose protein. It has a role in complex formation with the viral genome along with enhancing the transcription efficacy of viruses. It also helps M protein interaction while assembly of the virion[26,27]. In comparison with SARS CoV five amino acid mutations were found - two in IDR(intrinsically dispersed region; position 25 and 26), one in each domain(NTD-position 103, LKR-position 217 and CTD-position 334) [19].

## PUBLIC EPITOPES BETWEEN SARS-CoV-2 AND OTHER CORONAVIRUS STRAINS

SARS-CoV and MERS-CoV have the highest predicted SARS-CoV-2 epitopes, with individuals more commonly affected with 229E, HKU1, NL63 and OC43. 112 single peptides of 794 (14%) predicted SARS-CoV-2 epitopes, shared with four common coronaviruses with high sequence similarity. Of the 112, 21 (794; 2.6%) peptides had precise matches of SARS-CoV-2 and 36 (794; 4.5%, 794: 6.9%), had one and two mismatches respectively[28].

## ACE2 INDEPENDENT RECEPTORS IN VIRAL PATHOGENESIS

It's already known that both SARS-CoV-2 and SARS-CoV use hACE2 receptors for the viral entry in the host cell [29,30], however lectins and vimentin

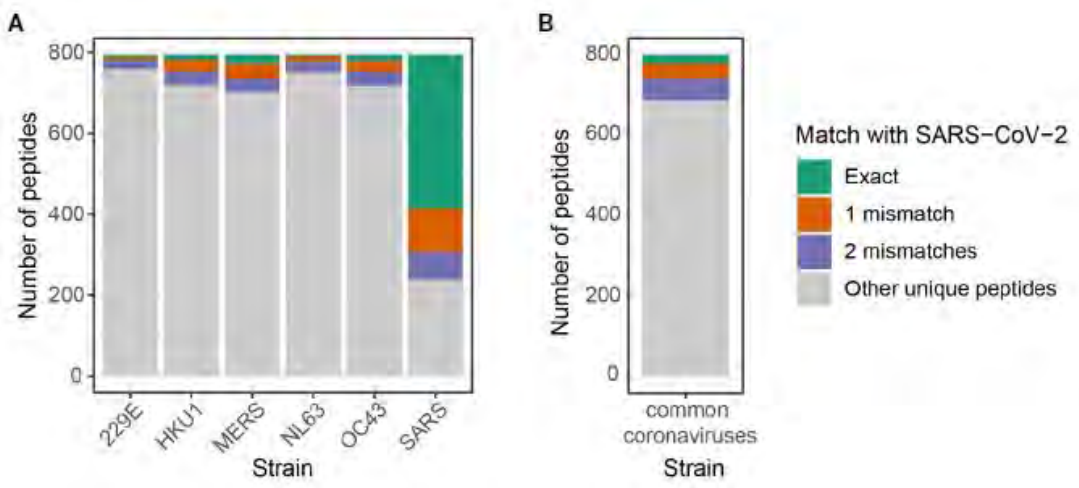


Fig-02: Number of shared predicted epitopes between SARS-CoV-2 and other coronavirus strains by allowing up to two mismatches. (A) Map of public peptides out of 794 SARS-CoV-2 predicted epitopes expanded by allowing up to two amino acids difference.

Note that it includes duplicated peptides that may be shared across coronavirus strains, i.e. peptides shared across SARS-CoV-2, SARS-CoV, and MERS-CoV are counted in both SARS and MERS. (B) Unique predicted epitopes from four common coronaviruses, 229E, HKU1, NL63, and OC43, shared with 794 SARSCoV-2 predicted epitopes.

Source: Lee CH, Pinho MP et.al [28]

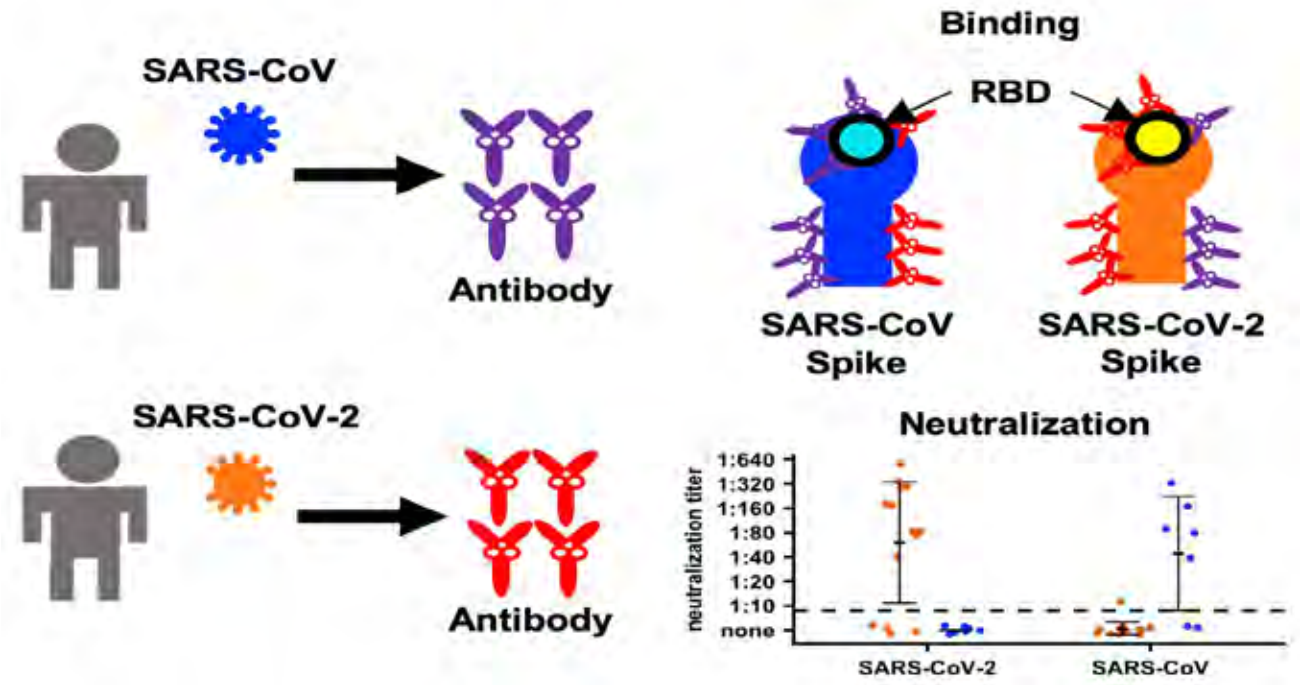


Fig-03: Cross-reactive antigen binding is common between SARSCoV and SARS-CoV-2, Cross-reactive antibody responses target both RBD and non-RBD regions, Cross neutralization of live viruses may be rare between SARS-CoV and SARS-CoV-2 Source: Lv H, Wu NC et.al [36]

are also exploited by SARS-CoV for the cell entry [31,32]. ACE-2 as well as a C-type lectin can be used by SARS-CoV to attack host cells [32]. In contrast some research suggested that mannetic lectins interfere with viral entry, by blocking possible other interactions. SARS-CoV-2 appears to infect various cell types and it is thus fair to speculate about the possibility of an alternative route of viral invasion through separate ACE2-interactions. Because of the relevance of this subject and its huge effects on human lives, future research would need to closely assess if Non-ACE2 interactions in ACE2 are in competition to prevent viral entry or if ACE2-independent interactions have a synergistic influence with ACE2-mediated entry to intensify COVID-19 symptoms.

## CROSS-REACTIVITY BETWEEN CORONAVIRUS AND INFLUENZA VIRUS

A study from Oxford found out that there is minimal potential of cross reactivity between coronavirus, specifically SARS CoV-2, and influenza virus. In this study 4,800+ epitopes from all strains of coronavirus were compared with 1,334 MHC-I influenza virus-derived epitopes [33].

## CROSS REACTIVITY BETWEEN SARS CoV AND SARS CoV-2

According to study done, SARS CoV 2 infected patients showed antibody response towards s-protein and Receptor binding domain(RBD) of S1, on detection of Cross reactivity towards SARS CoV it was seen that cross-reactive antibodies showed response to both RBD and Non-RBD regions. On comparing sequences of SARS CoV and SARS CoV 2, S2 subunits of Spike protein have the highest conservation. Further advancement in studies resulted in the fact that even cross reactivity was significantly high, chances of cross neutralization were rare in the cohort [34]. Considering the conservation a study found two sites, namely HR2 and FP, of S2 subunit of Spike protein in SARS CoV 2 that have significant cross reactivity as well as cross neutralization and hence can be the potential contestant for vaccine that will provide a broad and faster immunization [35]

## CONCLUSION

The SARS-CoV-2 Spike S2 subunit consists of broadly immunogenic epitopes in conserved functional domains, including cross-reactivity with endemic HCoVs. HR2 and FP being conserved, functionally important and immunogenic sites, can elicit cross-reacting antibodies and hence can serve as potential regions for the development of broadly neutralizing responses against CoVs. Spike HR2 and FP sites vaccines may provoke a wide neutralizing spectrum of reactions, may be able more quickly to attract populations of preexisting memory B cells and may be less vulnerable to the viral escape because they have a lower tolerance for the substitution of amino acid. Future research could solve the functioning implications of such cross-reactive antibody responses and the potential impact on an individual's history of sensitivity to endemic CoVs.

## References


1. Payne S. Family Coronaviridae. Viruses. 2017:149–58. doi: 10.1016/B978-0-12-803109-4.00017-9. Epub 2017 Sep 1. PMCID: PMC7149805.

2. Andrew M.Q. King, Michael J. Adams, Eric B. Carstens, Elliot J. Lefkowitz, Virus Taxonomy, Elsevier, 2012, Pages 806-828, ISBN 9780123846846, https://doi.org/10.1016/B978-0-12-384684-6.00068-9.(https://www.sciencedirect.com/science/article/pii/B9780123846846000689)

3. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W, China Novel Coronavirus Investigating and Research Team. 2020. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 382:727–733. https://doi.org/10.1056/NEJMoa2001017.

4. Coronaviridae Study Group of the International Committee on Taxonomy of Viruses. The species Severe acute respiratory syndrome-related coronavirus: classifying 2019-nCoV and naming it SARS-CoV-2. Nat Microbiol. 2020 Apr;5(4):536-544. doi: 10.1038/s41564-020-0695-z. Epub 2020 Mar 2. PMID: 32123347; PMCID: PMC7095448.

5. Zhou P, Yang XL, Wang XG, Hu B, Zhang L, Zhang W, Si HR, Zhu Y, Li B, Huang CL, Chen HD, Chen J, Luo Y, Guo H, Jiang RD, Liu MQ, Chen Y, Shen XR, Wang X, Zheng XS, Zhao K, Chen QJ, Deng F, Liu LL, Yan B, Zhan FX, Wang YY, Xiao GF, Shi ZL. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature. 2020 Mar;579(7798):270-273. doi: 10.1038/s41586-020-2012-7. Epub 2020 Feb 3. PMID: 32015507; PMCID: PMC7095418.

6. Wei X, Li X, Cui J. 2020. Evolutionary perspectives on novel coronaviruses identified in pneumonia cases in China. Natl Sci Rev 7:239–242. https://doi.org/10.1093/nsr/nwaa009.

7. Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, Meng J, Zhu Z, Zhang Z, Wang J, Sheng J, Quan L, Xia Z, Tan W, Cheng G, Jiang T. 2020. Genome composition and divergence of the novel coronavirus (2019-nCoV) originating in China. Cell Host Microbe 27:325–328. https://doi.org/10.1016/j.chom.2020.02.001.

8. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, Wang W, Song H, Huang B, Zhu N, Bi Y, Ma X, Zhan F, Wang L, Hu T, Zhou H, Hu Z, Zhou W, Zhao L, Chen J, Meng Y, Wang J, Lin Y, Yuan J, Xie Z, Ma J, Liu WJ, Wang D, Xu W, Holmes EC, Gao GF, Wu G, Chen W, Shi W, Tan W. 2020. Genomic characterization and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet 395:565–574. https://doi.org/10.1016/S0140-6736(20)30251-8.

9. Lan J, Ge J, Yu J, Shan S, Zhou H, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature. 2020;581: 215–220. 10.1038/s41586-020-2180-5

10. Hofmann H, Pohlmann S. Cellular entry of the SARS coronavirus. Trends Microbiol. 2004;12: 466–472. 10.1016/j.tim.2004.08.008

11. Vennema H, Godeke GJ, Rossen JW, Voorhout WF, Horzinek MC, et al. Nucleocapsid-independent assembly of coronavirus-like

particles by co-expression of viral envelope protein genes. EMBO J. 1996;15: 2020–2028. 10.1002/j.1460-2075.1996.tb00553.x

12. Siu YL, Teoh KT, Lo J, Chan CM, Kien F, et al. The M, E, and N structural proteins of the severe acute respiratory syndrome coronavirus are required for efficient assembly, trafficking, and release of virus-like particles. J Virol. 2008;82: 11318–11330. 10.1128/JVI.01052-08

13. Gao Y, Yan L, Huang Y, Liu F, Zhao Y, et al. Structure of the RNA-dependent RNA polymerase from COVID-19 virus. Science. 2020;368: 779–782. 10.1126/science.abb7498

14. Snijder EJ, Decroly E, Ziebuhr J. The Nonstructural Proteins Directing Coronavirus RNA Synthesis and Processing. Adv Virus Res. 2016;96: 59–126. 10.1016/bs.aivir.2016.08.008

15. Mittal A, Manjunath K, Ranjan RK, Kaushik S, Kumar S, Verma V. COVID-19 pandemic: Insights into structure, function, and hACE2 receptor recognition by SARS-CoV-2. PLoS Pathog. 2020 Aug 21;16(8):e1008762. doi: 10.1371/journal.ppat.1008762. PMID: 32822426; PMCID: PMC7444525.

16. Wentworth DE, Holmes KV. Molecular determinants of species specificity in the coronavirus receptor aminopeptidase N (CD13): influence of N-linked glycosylation. J Virol. 2001; 75: 9741–9752. https://doi. org/10.1128/JVI.75.20.9741-9752.2001 PMID: 11559807

17. Arndt, A. L., Larson, B. J., & Hogue, B. G. (2010). A conserved domain in the coronavirus membrane protein tail is important for virus assembly. *Journal of virology*, *84*(21), 11418-11428.

18. Nal, B., Chan, C., Kien, F., Siu, L., Tse, J., Chu, K., ... & Altmeyer, R. (2005). Differential maturation and subcellular localization of severe acute respiratory syndrome coronavirus surface proteins S, M and E. *Journal of general virology*, *86*(5), 1423-1434.

19. Neuman, B. W., Kiss, G., Kunding, A. H., Bhella, D., Baksh, M. F., Connelly, S., ... & Buchmeier, M. J. (2011). A structural analysis of M protein in coronavirus assembly and morphology. *Journal of structural biology*, *174*(1), 11-22.

20. Schoeman, D., & Fielding, B. C. (2019). Coronavirus envelope protein: current knowledge. *Virology journal*, *16*(1), 1-22.

21. Nieto-Torres, J. L., DeDiego, M. L., Verdiá-Báguena, C., Jimenez-Guardeño, J. M., Regla-Nava, J. A., Fernandez-Delgado, R., ... & Enjuanes, L. (2014). Severe acute respiratory syndrome coronavirus envelope protein ion channel activity promotes virus fitness and pathogenesis. *PLoS Pathog*, *10*(5), e1004077.

22. Pervushin, K., Tan, E., Parthasarathy, K., Lin, X., Jiang, F. L., Yu, D., ... & Torres, J. (2009). Structure and inhibition of the SARS coronavirus envelope protein ion channel. *PLoS Pathog*, *5*(7), e1000511.

23. DeDiego, M. L., Álvarez, E., Almazán, F., Rejas, M. T., Lamirande, E., Roberts, A., ... & Enjuanes, L. (2007). A severe acute respiratory syndrome coronavirus that lacks the E gene is attenuated in vitro and in vivo. *Journal of virology*, *81*(4), 1701-1713.

24. McBride, R., Van Zyl, M., & Fielding, B. C. (2014). The coronavirus nucleocapsid is a multifunctional protein. *Viruses*, *6*(8), 2991-3018.

25. Hurst, K. R., Koetzner, C. A., & Masters, P. S. (2009). Identification of in vivo-interacting domains of the murine coronavirus nucleocapsid protein. *Journal of virology*, *83*(14), 7221-7234.

26. Chang, C. K., Sue, S. C., Yu, T. H., Hsieh, C. M., Tsai, C. K., Chiang, Y. C., ... & Huang, T. H. (2006). Modular organization of SARS coronavirus nucleocapsid protein. *Journal of biomedical science*, *13*(1), 59-72.

27. Sheikh, A., Al-Taher, A., Al-Nazawi, M., Al-Mubarak, A. I., & Kandeel, M. (2020). Analysis of preferred codon usage in the coronavi-

rus N genes and their implications for genome evolution and vaccine design. *Journal of virological methods*, *277*, 113806.

28. Lee CH, Pinho MP, Buckley PR, Woodhouse IB, Ogg G, Simmons A, Napolitani G, Koohy H. Potential CD8+ T Cell Cross-Reactivity Against SARS-CoV-2 Conferred by Other Coronavirus Strains. Front Immunol. 2020 Nov 5;11:579480. Doi: 10.3389/fimmu.2020.579480. PMID: 33250893; PMCID: PMC7676914.

29. Li F. Structure, Function, and Evolution of Coronavirus Spike Proteins. Annu Rev Virol. 2016; 3: 237–261. https://doi.org/10.1146/annurev-virology-110615-042301 PMID: 27578435

30. Hoffmann M, Kleine-Weber H, Schroeder S, Kruger N, Herrler T, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020; 181: 271–280 e278. https://doi.org/10.1016/j.cell.2020.02.052 PMID: 32142651

31. Yu YT, Chien SC, Chen IY, Lai CT, Tsay YG, et al. Surface vimentin is critical for the cell entry of SARSCoV. J Biomed Sci. 2016; 23: 14. https://doi.org/10.1186/s12929-016-0234-7 PMID: 26801988

32. Jeffers SA, Tusell SM, Gillim-Ross L, Hemmila EM, Achenbach JE, et al. CD209L (L-SIGN) is a receptor for severe acute respiratory syndrome coronavirus. Proc Natl Acad Sci U S A. 2004; 101: 15748–15753. https://doi.org/10.1073/pnas.0403812101 PMID: 15496474

33. Lee, C. H., Pinho, M. P., Buckley, P. R., Woodhouse, I. B., Ogg, G., Simmons, A., ... & Koohy, H. (2020). Potential CD8+ T cell cross-reactivity against SARS-CoV-2 conferred by other coronavirus strains. Frontiers in immunology, 11, 2878.

34. Lv, H., Wu, N. C., Tsang, O. T. Y., Yuan, M., Perera, R. A., Leung, W. S., ... & Mok, C. K. (2020). Cross-reactive antibody response between SARS-CoV-2 and SARS-CoV infections. *Cell reports*, *31*(9), 107725.

35. Ladner, J. T., Henson, S. N., Boyle, A. S., Engelbrektson, A. L., Fink, Z. W., Rahee, F., ... & Altin, J. A. (2021). Epitope-resolved profiling of the SARS-CoV-2 antibody response identifies cross-reactivity with endemic human coronaviruses. *Cell Reports Medicine*, *2*(1), 100189.

36. Lv H, Wu NC, Tsang OT, Yuan M, Perera RAPM, Leung WS, So RTY, Chan JMC, Yip GK, Chik TSH, Wang Y, Choi CYC, Lin Y, Ng WW, Zhao J, Poon LLM, Peiris JSM, Wilson IA, Mok CKP. Cross-reactive Antibody Response between SARS-CoV-2 and SARS-CoV Infections. Cell Rep. 2020 Jun 2;31(9):107725. doi: 10.1016/j.celrep.2020.107725. Epub 2020 May 18. PMID: 33500101.

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# Review Article

# Synthetic Biology: Art and Science of Creating Super plants and Super-humans

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**Abstract:**

Synthetic biology is a new interdisciplinary field of biology which is emerging as a powerful tool which will be able to design, engineer, and synthesize life forms which were never existed before. Synthetic biology firstly involves modification of existing genetic material by incorporating synthetic DNA sequences and/or removing the junk pieces in it or secondly by completely synthesizing a new genome and incorporating it in live cells. The approaches used for engineering synthetic genomes, its methodology are discussed. Furthermore, insights on recent advances, current challenges, governing authorities across nations, and future prospects of synthetic biology has been included in the current article.

Figure *1* Marvel comics super heroes

## Introduction

Since the dawn of human civilization, humans have a strong urge to be superior to the rest of the planet's living things. This urge never stopped; instead, it stayed there for generations, increased enormously with evolution, and still existed in the modern era. In today's world, most developed nations show their power and strength through the means of military and nuclear weapons they possess. The industrial revolution has made such difficult things possible. But wait, what if I tell you that a nation declares itself as a superpower as they have created real-life Superhuman, aka Superman.

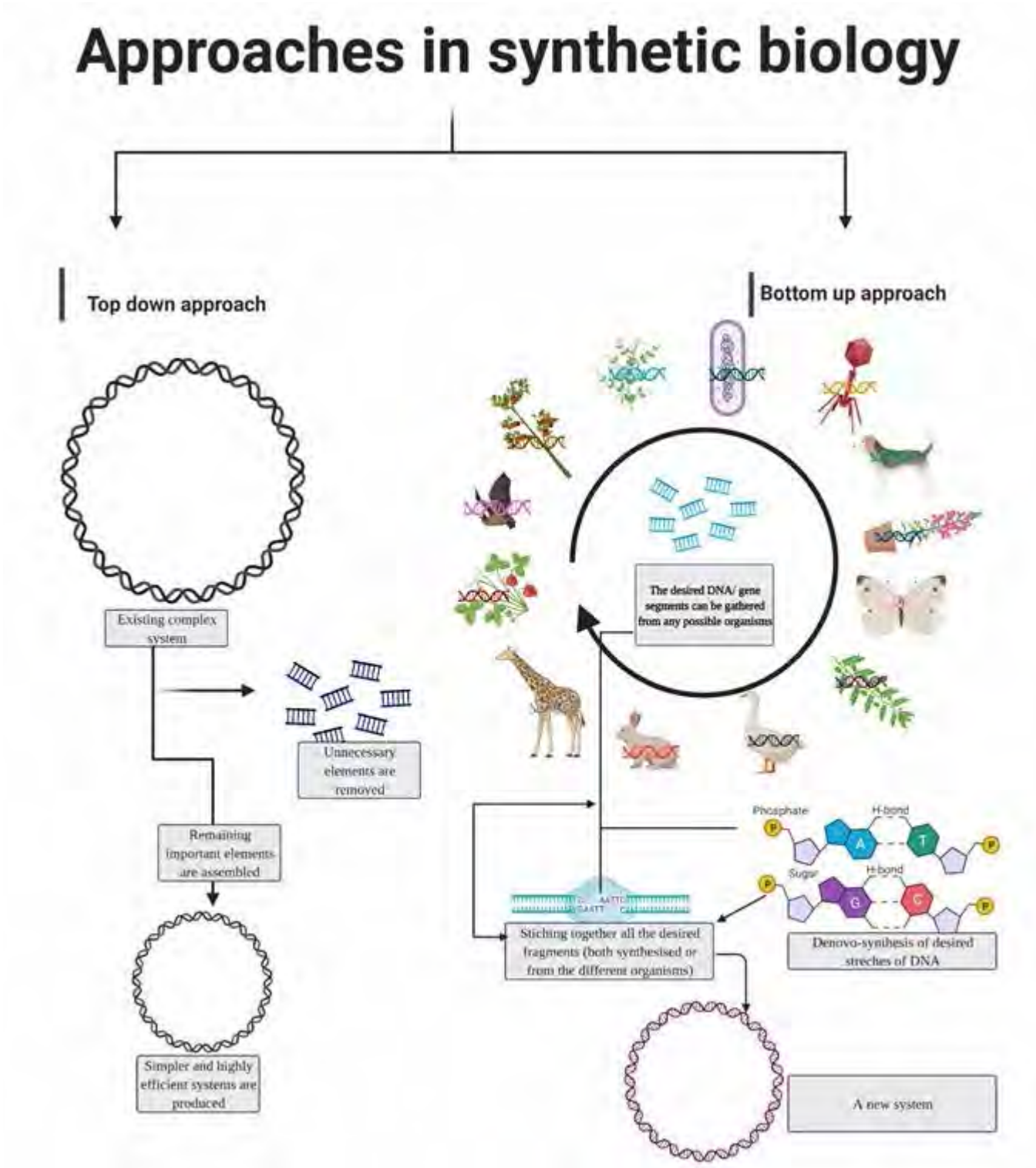



Figure 2 Approaches in synthetic biology (Created with BioRender.com)

Imagine how dramatic (just like Marvel Cinematic Universe) and serious the situation will become. YES, it may be certainly possible with the term SYNTHETIC BIOLOGY. Synthetic Biology is one of the evolving field in science. This new interdisciplinary area involves the application of engineering principles to biology. For most of the people in biology, this discipline serves as a fascinating area, the fictional world of their imagination where they can design/ redesign the ladder and its steps, i.e., DNA.

**What is SYNTHETIC BIOLOGY?** For understanding it clearly, we will simplify the complex meaning behind it. As the name suggests, Synthetic biology simply means artificially made/engineered (synthetic) genomes (life). Basic biology says that all the 2303320living organisms existing are made up of cells controlled by the genetic material inside them. It is called nucleic acids (genetic material/ All the genes present in an organism). These nucleic acids control all the necessary and metabolic activities to carry out the cell's life functions. In synthetic biology, these genes, genetic pathways, and genetic networks are altered or rearranged to produce the desired organism.

Now let's discuss in detail Synthetic genome engineering (SGE), a sub-discipline of synthetic biology; this aims to (re-)design and fabrication of biological entities or components and biological systems that do not already exist on planet earth. It also combines the chemical synthesis of DNA (synthetic DNA) to manufacture cataloged DNA sequences and their assembly into whole new genomes. This creates another question regarding the existing genetic engineering technology and CRISPR technology.

**How a Synthetic genome engineering (SGE) is different from Genetic engineering (Genome editing), there may be a doubt?** Let's clear it, according to the National Institute of Health (NIH), in genome editing, researchers typically use specific techniques and tools to make small but significant changes to the organism's DNA. In contrast, synthetic genome engineering involves long stretches of DNA (genes found in other organisms or be completely novel) to be stitched together to create an artificially synthesized genome. Moreover, synthetic genome engineering facilitates us to make changes throughout the genome, which seems over the limits of genome editing. Only a small stretch of DNA is being manipulated.

There are two approaches for it as explained in Figure 2: 1) Top-down: An older model can be redesigned to make the existing model more efficient (reducing the complexity of the existing system and creating a small-sized system), and the second one is 2) Bottom-up:

A new model can be designed from scratch (individual parts are synthesized and reassembled to create a new system). For SGE, mostly, the bottom-up approach is used.

**Methodology:** When we look for the methodology of synthetic genome engineering, it starts with designing a prototype or blueprint of the genome we wish to engineer using platforms like J. Craig Venter, CEO of Synthetic Genomics Inc. Biostudio. This software enables us to explore four main aspects such as 1) Recoding: it is one of the simplest features which is mostly used for the purpose of recording the codons (3-digit code of amino acids which are building blocks of proteins), designing restriction sites and PCR tags. Next is 2) Modularization: which allows designing the DNA fragment sizes required for the assembly of genome, 3) Add-in: which allows us to add the desired sequences from existing organisms and 4) Simplification: which involves reducing errors and removal of unnecessary genes, sequences and making the model amenable to survival and performance. After this, a trial-and-error analysis is performed to reveal the model's flaws, and necessary actions have been taken.


Figure *3:* J. Craig Venter, CEO of Synthetic Genomics Inc.

**Applications:** So next thing which makes us curious is what has happened/recent advances till the date in this evolving field. One can see the achievements in the picture below: Starting from creating a simple synthetic phage genome to creating complex synthetic true yeast chromosomes, the area has flourished significantly. One of the pioneers of SGE, J. Craig Venter Institute, has excelled in their research. In 2003, they assembled bacteriophage PhiX74 genome (5386 bp long) in about two weeks and later in 2006, they created a completely synthetic genome of a min-

imal bacterium, *Mycoplasma laboratorium*.

Further, they are putting efforts to make it function in a living cell. Another jewel in the crown of synthetic biology was added in 2019 which reveals a microorganism (bacteria *Escherichia coli*) which has modified genome (possibly artificial) and is able to code 59 codons instead of the natural number of 64 codons to encode 20 amino acids.This paradigm shifts from "genome reading" to "genome writing" tells us about humankind's advancements so far.

Interestingly, Dr. Jef Boeke from Johns Hopkins University leads a project called "The Sc2.0 Project" with the team of international collaborators, which is first attempt to design and synthesize a eukaryotic genome- *Saccharomyces cerevisiae*, i.e., our Baker's Yeast, which aims at synthesizing the entire yeast genome, which consists of 16 chromosomes, nearly 6,000 genes and a total of 12 megabases of non-redundant of DNA. They designed the Synthetic Chromosome Recombination and Modification by LoxP-mediated Evolution (SCRaMbLE) system for gene rearrangements. They introduced more than 5,000 LoxP sites (if it is getting hard to understand, Wikipedia is there to help you) so as to introduce desired rearrangements and deletions. They have also introduced neochromosome (a completely new chromosome) having tRNA genes, ditched destabilizing transposons, which makes it stable, removed "junk sequences," which made it leaner, and as already mentioned, introduced SCRaMbLE system, which makes it a built-in inducible diversity generator.

So far, we have talked about the applications of SGE relevant to microbes only, which needs an update and upgrade, so what do you think! Do we have something to talk about on higher organisms? Absolutely yes! Currently, we can find few published examples of synthetic plant biology, which involves the production of synthetic sensors and synthetic metabolic pathways, but the research is still in its initial stages and faces difficulties in creating plant synthetic genome like 1) scarcity of well-characterized and interchangeable parts and modules of plant genome, required for their modeling and assembly, and fine-tuning of synthetic gene networks 2) context-dependency ofbiological parts and modules which makes the synthetic process unpredictable 3) Host-compatibility issues like codon optimization, genetic instability, regulatory incompatibilities and genomic position effects after integration of synthetic devices into a plant can create major malfunction of model.

So what could be looked at as the next step to progress in plant SGE? The answer is Synthetic plastome (genome of a plastid, a type of organelle found in plants) engineering. There are certain advantages in using plastome for synthetic modification, such as the plastome's prokaryotic nature may help in building synthetic circuits in plants. A tiny plastid genome with fewer but important components will be of great value for two reasons:

1) The regulatory network responsible for plastid functioning can be deciphered, and

2) It can be used in biotechnological research by serving as template for engineering plastomes

**Challenges and Future prospects:** Using SGE to create synthetic plastomes can serve as the breakthrough to open a gateway for plant genome engineering. Practically speaking, there is still the lack of availability of well-characterized genetic parts, modules, strictly controlled expression devices, and thorough knowledge of plastid gene expression. As human nature tends to see hope even in the darkest hours, so in the future, this emerging field can be seen as a threshold to alleviate the problems related with biotic and abiotic stresses and to help in increasing the production of food, secondary metabolites, and even completely synthetic life forms. Advancement in technology has paved road for development of new algorithms, various models, and precise softwareswhich will help in better characterization and standardization of the orthogonality of more biological parts and modules, as well as better rational designs. Encouragingly, funding agencies in different countries have started to look into plant synthetic biology projects. We also hope that advances in the field of science and technology will show us the miracles in need of an hour.

Perspective creates a different scenario and differs from person to person. One perspective says whether this technology is safe and raises concerns over bio-terrorism, the environment, and the human race. Whereas, other perspective focuses on advancement

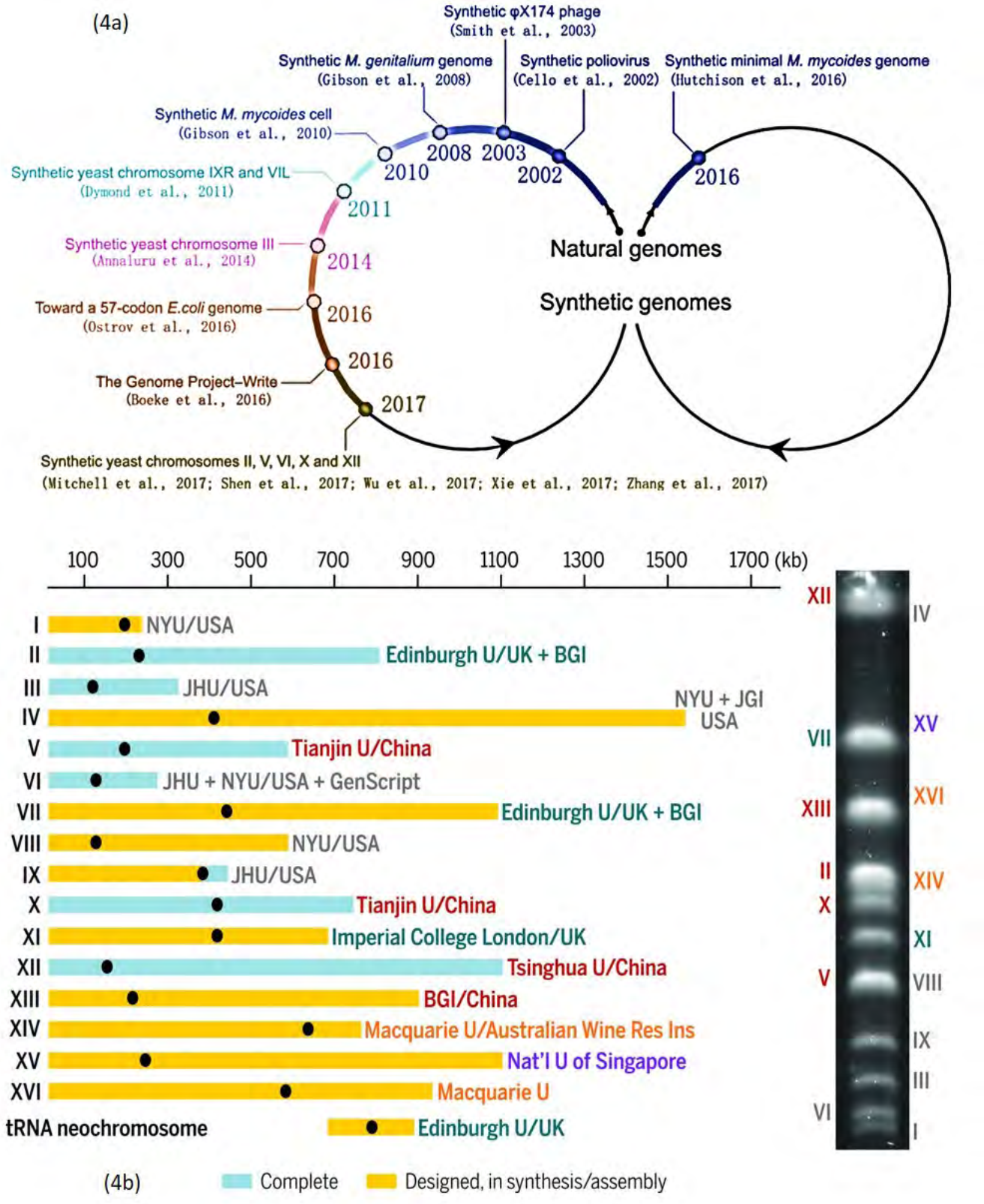



*Figure 4a: Technological advancements in the field of synthetic biology and their milestones;*

*Figure 4b: Sc. 2.0 project; scale on the top indicates chromosome size in kilobase pairs; Roman numerals arranged vertically on left indicates the chromosome numbers; Coloured bars in the middle indicates the size of the chromosome; on extreme right gel picture depicts the various chromosomes separated on the gel on the basis of their size.*

in SGE to fasten the process and creation of meaningful and useful models for the desired output. Still, wherever there are concerns over safety, there need to be governing authorities to control experiments. At the International level, several treaties contain provisions that apply to synthetic biology; these include: -The Convention on Biological Diversity (CBD),-Biological Weapons Convention, -Cartagena Protocol on Biosafety, -Nagoya–Kuala Lumpur Supplementary Protocol on Liability, and -Australia Group Guidelines.

**Conclusion:**As far we have seen SGE, we can truly say … this technology not only enables us to create something new, but to understand the process of how life works, gives the promising opportunity to create crops with high yields, better resistance to pest and diseases, and better adaptability on introduction to new areas as well in case of humans it might allow us to tackle incurable genetic diseases, to know the evolutionary process and can help us to predict the mysteries of genetic material.

So, in the end, we can say that this field challenges the laws of nature. Still, as someone has said, "if we eat GMOs, we may die, but if we do not eat GMOs, then we are definitely gonna die," which might be said in the context of increasing demand and decreasing supply. So, bringing Superplants with unbelievable qualities and comic characters like Superman, Spiderman into reality is not just Stan Lee's job anymore; it can be done by scientific researches too.

**References:**


- Boehm, Christian R. and Ralph Bock. 2019. "Update on DNA Technology Recent Advances and Current Challenges in Synthetic Biology of the Plastid Genetic System and Metabolism." 179 (March):794–802.
- Dymond, Jessica, Jef Boeke, and Chromosome Rearrangement. 2012. "The Saccharomyces Cerevisiae SCRaMbLE System and Genome Minimization © 2012 Landes Bioscience. 2012 Landes Bioscience." 3(3):168–71.
- Kubis, Armin and Arren Bar-even. 2019. "Synthetic Biology Approaches for Improving Photosynthesis." 70(5):1425–33.
- Liu, W. and Stewart Jr, C.N., 2015. Plant synthetic biology. Trends in Plant Science, 20(5), pp.309-317.
- Luo, Zhouqing, Qing Yang, Binan Geng, Shuangying Jiang, Shihui Yang, and Xiaozheng Li. 2018. "Science China."
- Pretorius, I. S. and J. D. Boeke. 2018. "Yeast 2. 0 — connecting the Dots in the Construction of the World's First Functional Synthetic Eukaryotic Genome." (March):1–15.
- Richardson, Sarah M., Leslie A. Mitchell, Giovanni Stracquadanio, Kun Yang, Jessica S. Dymond, James E. Dicarlo, Dongwon Lee, Cheng Lai, Victor Huang, Srinivasan Chandrasegaran, and Yizhi Cai. 2017. "Design of a Synthetic Yeast Genome." 1044(March):1040–44.

# Featured News

Top highlights of
Biotech Industry and Govt


# Some Countries Pause Dosing of AstraZeneca Vaccine Due to Clotting Concerns

March 12, 2021

Multiple countries across Europe and parts of Asia have suspended the use of AstraZeneca's COVID-19 vaccine over fears the medication is leading to the development of blood clots in some patients who have received the medication.

Denmark was first to announce its suspension of the use of AstraZeneca's vaccine until a review of the clotting can be conducted. According to the European Medicines Agency, there have been30 cases of thromboembolic events among five million people who had received the AstraZeneca shot in Europe. Two people in Denmark and Austria, who received the vaccine, died from clotting issues, while a third was hospitalized with pulmonary embolism, BioSpace previously reported.

According to the EMA, the number of thromboembolic events in vaccinated people is no higher than the number seen in the general population. While those kinds of events can be serious, the EMA did not suggest pausing dosing with the AstraZeneca vaccine. The agency said dosing should continue. The Danish Health Authority also said there is no evidence the vaccine is responsible for blood clots. The EMA added that it is reviewing all of the reports of blood clots and will provide an update as it gains more informa-


tion.

The World Health Organization issued a statement that there is no reason to stop using the vaccine because, as of this time, "no causal link has been established," the Washington Post reported. In its announcement this morning, WHO said the AstraZeneca vaccine has been injected millions of times across the globe and no deaths had yet been directly attributed to the medication, Agence France-Presse noted in its report.

"Reports of blood clots received so far are not greater than the number that would have occurred naturally in the vaccinated population," Phil Bryan, vaccines safety lead at Britain's Medicines and Healthcare Products Regulatory told CNBC. "We are keeping this issue under close review but available evidence does not confirm that the vaccine is the cause. People should still go and get their COVID-19 vaccine when asked to do so."

An AstraZeneca spokesperson said "the safety of the vaccines has been extensively studied in Phase III clinical trials and peer-reviewed data confirms the vaccine is generally well-tolerated."

Despite those assurances from the regulatory agencies, countries across Europe, including Denmark, Norway and Iceland, as well as Thailand in Asia, suspended the use of specific batches of the vaccine developed by AstraZeneca and Oxford University, or completely paused using that medication citing the potential adverse events. Austria and Italy are among those nations that have said that they will stop using certain batches of the vaccine as a precautionary measure, CNBC reported. The countries are waiting for reports on the vaccine's safety before resuming the use of AstraZeneca's drug.


# BioAsia 2021 saw over 31,000 participants

February 12, 2021

BioAsia concluded with a huge participation from industry, government and general public. The 18th edition of the annual flagship event of Government of Telangana, witnessed the participation of around 31,450 participants representing 72 countries. More than 60 high profile speakers participated in this summit.

The FABA Special Award was presented to Dr Balram Bhargava, secretary to Government of India, Department of Health Research, Ministry of Health & Family Welfare & Director-General, Indian Council of Medical Research for his exemplary contributions to medicine and healthcare. He was felicitated for spearheading the fight against Covid-19 in India and also commencing several marquee projects such as India-Stanford Biodesign programme, c-GMP Centre for Excellence for Stem Cell Studies, Society for Less Investigative Medicine (SLIM) and many more.

During the valedictory session of BioAsia 2020, Jayesh Ranjan, principal secretary, Industries and IT, Government of Telangana said, "Since this edition was virtual and the theme of the event was very contextual to the current scenario, hence, we didn't restrict the conference open only to the life sciences professionals but made these sessions available for the general public without any registration fee. The sessions covering the current situation of vaccines, the impact of Covid-19 on various healthcare services, and the way forward were very extremely well encapsulated by 60 eminent speakers during these two days."

Niti Aayog CEO Amitabh Kant urged industry stakeholders to identify four or five 'moonshots' and assured that the government will go 'all out' to create the right ecosystem for these sectors in terms of incentives and quality infrastructure so that it takes the country to the next level. In technology, a moonshot is an ambitious, ground breaking project undertaken without expectation of near-term profitability.

# Russia Engaging in Anti-Pfizer Disinformation Campaign to Boost Sales of Sputnik Vaccine, U.S. Alleges

March 08, 2021

The Russian government is attempting to cast a negative light on the COVID-19 vaccine developed by Pfizer and BioNTech, as well as other vaccines, in order to boost sales of its own vaccine, Sputnik V, the US government charged.

First reported by The Wall Street Journal, the U.S. Department of State has identified multiple publications that reportedly serve as fronts for Russian intelligence that are involved in the disinformation campaign. According to the report, these publications are raising concerns about the safety and efficacy of the western-developed vaccines. The publications are also suggesting the vaccines were rushed through development and the regulatory process, not only in the United States but in other western countries. The cost of the Western-made vaccines, particularly the mRNA vaccine developed by Pfizer and BioNTech, has also been a focus of Russian disinformation, the government said.

"We can say these outlets are directly linked to Russian intelligence services," an official with the State Department's Global Engagement Center said of the sites behind the disinformation campaign, the Journal reported. "They're all foreign-owned, based outside of the United States. They vary a lot in their reach, their tone, their audience, but they're all part of the Russian propaganda and disinformation ecosystem."

Russia first authorized Sputnik V in August, well ahead of western vaccines. The government granted authorization while the vaccine was still in clinical studies.

The Journal's report pointed to several publications that are allegedly controlled by the SVR, Russia's foreign intelligence service. One publication, New Eastern Outlook and Oriental Review, is aimed at the Middle East, Asia and Africa, and offers comment on the U.S. role in the world. News Front is controlled by the FSB, the successor to the KGB. Another publication, Rebel Inside, is controlled by the GRU, Russia's military intelligence agency.

# Biotech Industry News


## 65% of world's vaccines manufactured in Hyderabad

FEBRUARY **04, 2021**

Almost 65 per cent of all vaccines manufactured in India and exported around the world come from Hyderabad, Bharat Biotech Chairman and Managing Director Dr Kishna Ella said on Monday.

He said that there is no cluster like Hyderabad's Genome Valley anywhere in the world which contributes such huge volumes.

He was speaking after receiving Genome Valley Excellence Award at the inaugural session of Bio Asia 2021, the 18th edition of Asia's biggest life science and healthcare industry conference.

Dr Krishna Ella and Bharat Biotech's Joint Managing Director Suchitra Ella received the award from Telangana's Industry Minister K. T. Rama Rao. Stating that he is honoured to receive the award, Krishna Ella said this award was for all entrepreneurs who contributed to city's growth. He said despite Hyderabad being the largest vaccine manufacturing hub in the world, the city is not getting the recognition while Bengaluru gets too much attention.

**Pointing out that Dr Reddy's and Aurobindo Pharma have joined the vaccine race, he said it is going to be bigger game of vaccines for India and the world.**

He pointed out that besides Bharat Biotech, Biological E, Indian Immunologicals and Shanta Biotech were manufacturing vaccines for domestic market as well as exports.

Krishna Ella, whose firm developed India's first indigenous vaccine for Covid-19, said 'pandemic vaccines and everything in future will come from Hyderabad'.

# Amgen buying Five Prime for $1.9 Billion to Bolster Oncology Portfolio

Mar 04, 2021

Shares of Five Prime Therapeutics were soaring this morning after Amgen announced it was acquiring the company and its Phase III ready anti-FGFR2b antibody bemarituzumab for $1.9 billion in cash. Amgen is eying an expansion of bemarituzumab into multiple oncology indications.


Amgen said the acquisition of Bay Area-based Five Prime and its innovative oncology assets will bolster its own cancer portfolio. Amgen acquired the company for $38 per share. This morning, share prices soared 38% to trade at $37.91 as of 10 a.m. When the transaction is complete, Five Prime will merge with a wholly-owned subsidiary of Amgen.

Five Prime's lead asset bemarituzumab is a first-in-class, Phase III ready anti-FGFR2b antibody. The asset demonstrated statistical significance in a Phase II study in frontline advanced gastric or gastroesophageal junction (GEJ) cancer. All three efficacy endpoints, progression free survival, overall survival and overall response rate, were met, the company announced in November.

Bemarituzumab targets FGFR2b, which has been found to be overexpressed in approximately 30% of patients with non-HER2 positive gastric cancer, as well as other solid tumors. Additional analysis from the Phase II study showed a positive correlation between efficacy and expression of FGFR2b on tumor cells, confirming both the importance of the FGFR2b target and the activity of bemarituzumab against this target. In its announcement this morning, Amgen said that correlation suggests that FGFR2b could play a role in other epithelial cancers, including lung, breast, ovarian and other cancers.

# Bharat's Next-Gen COVID-19 Nasal Vaccine Moving Toward Human Testing

Mar 05, 2021

Days after vaccine-maker Bharat Biotech released interim Phase III efficacy data for a COVID-19 vaccine already in use in India, a pulmonary expert is expressing enthusiasm for the company's next-generation intranasal vaccine on track to enter clinical testing this quarter.

Randeep Guleria, a pulmonologist and Director of the All India Institute of Medical Sciences, New Delhi, said that although children are at less risk for severe COVID-19, they can be infectious, and if approved, a nasal vaccine would boost compliance. "In half-an-

hour, you can vaccinate an entire class," he added.

Nasal vaccines marketed for influenza have been particularly useful for children, although there have been concerns over their efficacy compared to injected vaccines. The new vaccine candidate, BBV154, is delivered with by an engineered chimpanzee adenovirus vector and has been administered in a single dose to rodents and rhesus macaques, but data has not yet been published. The company believes that stimulating a protective effect will be possible given that the nose is the point of entry for SARS-CoV-2.

At least three other companies have launched Phase I trials for intranasal COVID-19 vaccine candidates, the most recent of which is Maryland-based vaccine company Altimmune. Altimmune last month began enrolling up to 180 patients in a Phase I trial for its AdCOVID, also administered with a single dose and delivered via adenovirus.

In January, New York-based Codagenix began testing its COVI-VAC single-dose intranasal candidate in a 48-person Phase I trial in India. The first reported trial was from Chinese company Beijing Wantai Biological Pharmacy Enterprise, which was scheduled to begin enrolling up to 100 patients in November.

# FDA Approves Third Sarepta Treatment For Duchenne Muscular Dystrophy

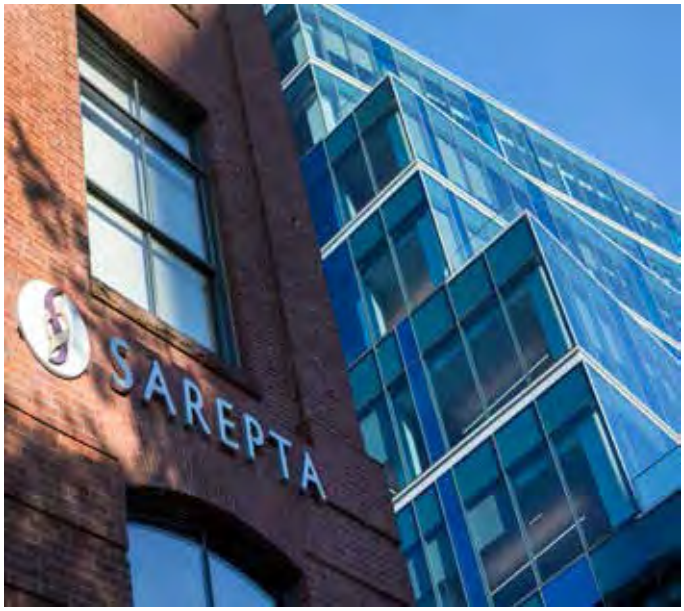
Feb 28, 2021

The U.S. Food and Drug Administration (FDA) approved Sarepta Therapeutics' Amondys 45 (casimersen) for patients with Duchenne muscular dystrophy (DMD) who have a confirmed mutation amenable to exon 45 skipping. Sarepta's two other drugs on the market for DMD are Exondys 51 and Vyondys 53, which are for patients amenable to exon 51 and exon 53 skipping, respectively.

The exon-skipping technology allows for the formation of a truncated form of the dystrophin protein. The dystrophin gene is the largest gene in humans, and as such, is too large for the viral vectors typically used in gene therapy. So Sarepta developed a technique that allows for the gene mutations to be "skipped" which results in a shortened but still functional form of the protein.

On January 7, 2021, the company announced topline results from Part 1 of its Study SRP-9001-201 of a gene therapy, SRP-9001, in 41 DMD patients. The therapy is designed to deliver a micro-dystrophin-encoding gene to muscle tissue. At 12 weeks after treatment compared to baseline, the trial met its primary biological endpoint of micro-dystrophin protein expression.

However, the trial failed to meet its primary functional endpoint, which was a NSAA total score compared to placebo at 48 weeks. The North Star Ambulatory Assessment (NSAA) is a 17-item scale to measure functional motor abilities in children with DMD who are ambulatory. It is typically used to monitor progression




of the disease and treatment. Although there were improvements, they were not statistically significant. The FDA approved Exondys 51 in 2016 but Sarepta has still not completed the confirmatory study. A confirmatory trial for Amondys 45 is ongoing, with data expected in 2024. Amondys 45 has a price tag that is "at parity" with the other drugs, which are expensive. They are dosed on the basis of the patient's weight, and can run as much as $1 million annually.

# Convalescent Plasma Doesn't Prevent Progression of COVID-19

Mar 04, 2021

Back in the summer of 2019, the U.S. Food and Drug Administration (FDA) authorized convalescent plasma for emergency use in hospitalized patients but said at the time that it needed to review more research data to validate its efficacy.

Early this week, the National Institutes of Health (NIH) stopped a trial it was running on convalescent plasma after an independent review committee found the therapy was providing no clear meaningful benefit for patients with COVID-19 who were treated and released from the ER.

The new trial, termed the Clinical Trial of COVID-19 Convalescent Plasma of Outpatients (C3PO), only included 511 participants out of its 900-participant goal. Overall, the trial was conducted at 47 hospital emergency departments. Patients were included if they had COVID-19 symptoms for a week or less.

On February 25, an independent data and safety monitoring board found that while convalescent plasma was likely safe, it was unlikely to offer any benefit. Researchers from the study have reportedly said they are still waiting until the data are fully analyzed before they can provide direct conclusions on the treatment's effectiveness.

In November of last year, another study from Argentina also found that the use of convalescent plasma offered no clinical benefit, nor did it improve mortality in patients with COVID-19 pneumonia.

In an interview with USA Today, Dr. Simone Glynn, the NIH trial's program scientist, said they "do not see any sign that convalescent plasma had a benefit" in patients at risk for more severe disease.

Daniel Griffin, infectious disease specialist at New York's ProHEALTH Care, added that convalescent plasma, in the setting of COVID-19, doesn't seem to provide a significant impact on mortality and hospitalization rates, two key metrics looked at during the trial.

Currently, more than 180 trials are studying the efficacy and safety of convalescent plasma for COVID-19, including two studies at Johns Hopkins University in Baltimore to investigate whether the therapy reduces the risk of symptom development in people exposed to SARS-CoV-2 and one study from Vanderbilt University to see if plasma reduces severe disease when given to hospitalized patients early in the course of their disease.

# Biotech Research

## Light-emitting tattoo engineered

February 26, 2021

The technology, which uses organic light-emitting diodes (OLEDs), is applied in the same way as water transfer tattoos. That is, the OLEDs are fabricated on to temporary tattoo paper and transferred to a new surface by being pressed on to it and dabbed with water.

The researchers, who described the process in a new paper in the journal Advanced Electronic Materials, say it could be combined with other tattoo electronics to, for instance emit light when an athlete is dehydrated, or when we need to get out of the sun to avoid sunburn. OLEDs could be tattooed on packaging or fruit to signal when a product has passed its expiry date or will soon become inedible, or used for fashion in the form of glowing tattoos.

"In healthcare they could emit light when there is a change in a patient's condition -- or, if the tattoo was turned the other way into the skin, they could potentially be combined with light-sensitive therapies to target cancer cells, for instance.

"Our proof-of-concept study is the first step. Future challenges will include encapsulating the OLEDs as much as possible to stop them from degrading quickly through contact with air, as well as integrating the device with a battery or supercapacitor."

The OLED device the researchers developed is 2.3 micrometres thick in total (less than one 400th of a millimetre) -- about a third of the length of a single red blood cell. It consists of an electroluminescent polymer (a polymer that emits light when an electric field is applied) in between electrodes. An insulating layer is placed in between the electrodes and the commercial tattoo paper.

The light-emitting polymer is 76 nanometres thick (a nanometre is a millionth of a millimetre) and was created using a technique called spin coating, where the

polymer is applied to a substrate which is spun at high speed, producing an extremely thin and even layer. Once they had built the technology, the team applied the tattooable OLEDs, which emitted green light, on to a pane of glass, a plastic bottle, an orange, and paper packaging.

Journal Reference:
Jonathan Barsotti, Alexandros G. Rapidis, Ikue Hirata, Francesco Greco, Franco Cacialli, Virgilio Mattoli. Ultrathin, Ultra-Conformable, and Free-Standing Tattooable Organic Light-Emitting Diodes. Advanced Electronic Materials, 2021; 2001145 DOI: 10.1002/aelm.202001145

# COVID-19 isolation linked to increased domestic violence, researchers suggest

February 27, 2021

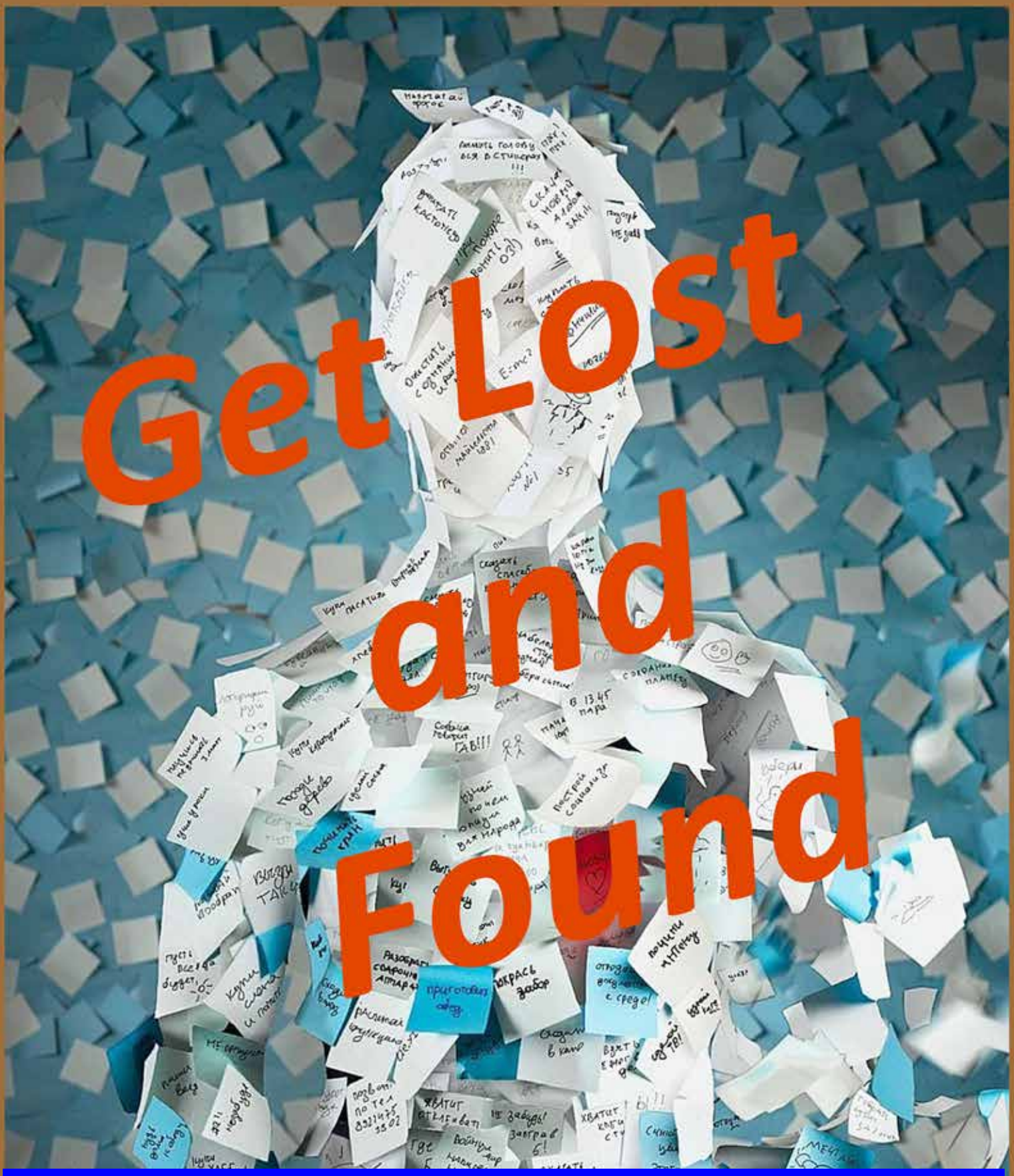
Data collected in surveys of nearly 400 adults for 10 weeks beginning in April 2020 suggest that more services and communication are needed so that even front-line health and food bank workers, for example -- rather than only social workers, doctors and therapists -- can spot the signs and ask clients questions about potential intimate partner violence. They could then help lead victims to resources, said Clare Cannon, assistant professor of social and environmental justice in the Department of Human Ecology and the lead author of the study.

Research participants in the study completed an online survey asking about previous disaster experience, perceived stress, their current situation as it relates to COVID-19, if they experienced intimate partner violence, and what their personal and household demographics were. In all, 374 people completed the survey. Respondents, whose average age was 47, were asked about how COVID-19 had affected them financially and otherwise.

Of the respondents, 39 reported having experienced violence in their relationship, and 74 percent of those people were women. Although only 10 percent of the sample reported experiencing intimate partner violence, the people that had experienced that violence reported more stress than the segment of the sample that had not experienced it. Furthermore, the results show that as perceived stress increased, participants were more likely to end up as victims of violence.

"Importantly," Cannon said, "these data do not suggest causality and there is no way to determine if intimate partner violence was present in those relationships prior to the pandemic. What the data do suggest, however, is that experiencing such violence is related to reporting more exposure to stress." Researchers found that as people find themselves in a more tenuous financial situation due to COVID-19, "there are more things to worry about and subsequently argue about. In many instances, that type of situation leads to an occasion for intimate partner violence," the researchers said. "In our sample's case, as people lost their jobs and suffered financial losses, they also likely increased their worry about eviction," Cannon said. Notably, similar findings linking financial and job loss stresses with increased intimate partner violence were reported in the 2008 recession, Cannon said.

Journal Reference:
Clare E. B. Cannon, Regardt Ferreira, Frederick Buttell, Jennifer First. COVID-19, Intimate Partner Violence, and Communication Ecologies. American Behavioral Scientist, 2021; 000276422199282 DOI: 10.1177/0002764221992826

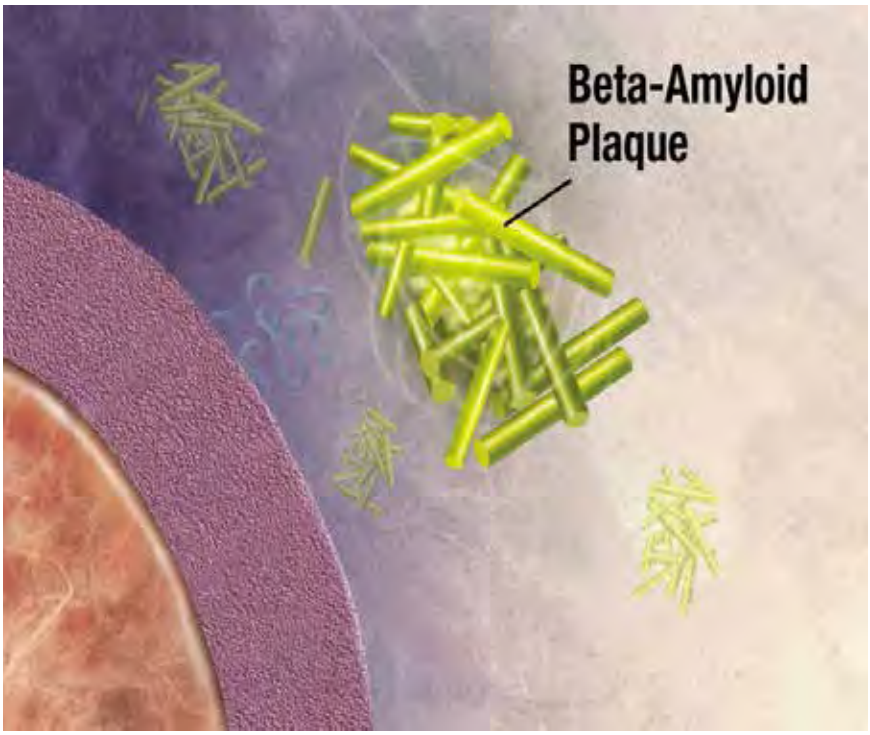



**Biotech Express magazine put forward all the news and articles related to biotechnology in front of its diverse audience. Since Biotechnology is amalgamation of different branches of science, we also try to include updates from several disciplines. This magazine would like to take you near the greatest people from field through interviews which will surely help to carve out the decision process by knowing nitty-gritty of the field.**

# CBD reduces plaque, improves cognition in model of familial Alzheimer's

FEBRUARY 09, 2021

A two-week course of high doses of CBD helps restore the function of two proteins key to reducing the accumulation of beta-amyloid plaque, a hallmark of Alzheimer's disease, and improves cognition in an experimental model of early onset familial Alzheimer's, investigators report.




The proteins TREM2 and IL-33 are important to the ability of the brain's immune cells to literally consume dead cells and other debris like the beta-amyloid plaque that piles up in patients' brains, and levels of both are decreased in Alzheimer's.

The investigators report for the first time that CBD normalizes levels and function, improving cognition as it also reduces levels of the immune protein IL-6, which is associated with the high inflammation levels found in Alzheimer's, says Dr. Babak Baban, immunologist and associate dean for research in the Dental College of Georgia and the study's corresponding author.

"Right now we have two classes of drugs to treat Alzheimer's," says Dr. John Morgan, neurologist and director of the Movement and Memory Disorder Programs in the MCG Department of Neurology. One class increases levels of the neurotransmitter acetylcholine, which also are decreased in Alzheimer's, and another works through the NMDA receptors involved in communication between neurons and important to memory. "But we have nothing that gets to the pathophysiology of the disease," says Morgan, a study coauthor.

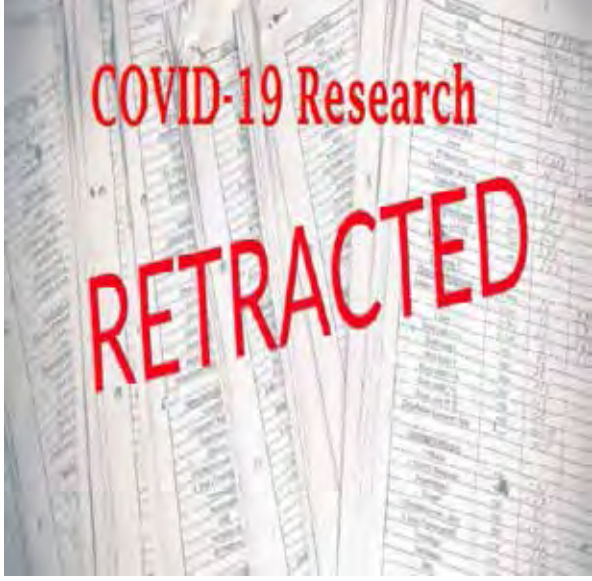
They found CBD appears to normalize levels of IL-33, a protein whose highest expression in humans is normally in the brain, where it helps sound the alarm that there is an invader like the beta-amyloid accumulation.

CBD also improved expression of triggering receptor expressed on myeloid cells 2, or TREM2. Low levels of TREM2 and rare variations in TREM2 are associated with Alzheimer's, and in their mouse model TREM2 and IL-33 were both low.

They found CBD treatment increased levels of IL-33 and TREM2 -- sevenfold and tenfold respectively.

Journal Reference:
Hesam Khodadadi, Évila Lopes Salles, Abbas Jarrahi, Vincenzo Costigliola, MB Khan, Jack C. Yu, John C. Morgan, David C. Hess, Kumar Vaibhav, Krishnan M. Dhandapani, Babak Baban. Cannabidiol Ameliorates Cognitive Function via Regulation of IL-33 and TREM2 Upregulation in a Murine Model of Alzheimer's Disease. Journal of Alzheimer's Disease, 2021; 1 DOI: 10.3233/JAD-210026

# Bio Controversies




## Frontiers Removes Controversial Ivermectin Paper Pre-Publication

March 2, 2021

**T**he editors of Frontiers in Pharmacology have taken down an article about the use of the antiparasitic drug ivermectin in COVID-19 patients. The paper, which was written by members of an organization called the Front Line COVID-19 Critical Care Alliance (FLCCC), had been provisionally accepted and posted in abstract form by the journal in January, but was ultimately rejected this Monday (March 1). The editors determined that it contained unsubstantiated claims and violated the journal's editorial policies.

By the end of last week, the abstract had been viewed more than 85,000 times, according to snapshots available on the internet archive.

The paper's removal has drawn anger from members of the FLCCC and its followers. In comments on Twitter and in an interview with The Scientist, the organization's president, Pierre Kory, describes the move as "censorship." He adds in the interview that the paper had already successfully passed through multiple rounds of review. In reversing the paper's acceptance, the journal is "allowing some sort of external peer reviewer to comment on our paper," he says. "I find that very abnormal."

After being contacted by The Scientist, the journal posted a statement from Frontiers's chief executive editor, Frederick Fenter, saying that "Frontiers takes no position on the efficacy of ivermectin as a treatment of patients with COVID-19, however, we do take a very firm stance against unbalanced or unsupported scientific conclusions."

## Indian Medical Association furious after Union Health Minister Harsh Vardhan 'promoting' Patanjali's Coronil

FEBRUARY 24, 2021

Patanjali Ayurved Ltd founder Ramdev, "again" at a press conference on February 19, had claimed that Coronil had received certification from the Ayush Ministry as a medicine supporting COVID-19 treat-

ment as per the WHO's certification scheme. Harsh Vardhan was also present at the ceremony.

Later, WHO's regional office for South-East Asia had clarified on Twitter that it has not "reviewed or certified the effectiveness of any traditional medicine" for the treatment of Covid-19 – a pointed reference to Coronil. The Indian Medical Association (IMA) hit out at the "blatant lie of WHO certification" made by Panjali Ayurved for its Coronil tablet, which the company claims is an evidence-based medicine to fight Covid-19, and demanded an explanation from Union Health Minister Harsh Vardhan, in whose presence the medicine was launched.

The IMA also demanded that the Health Minister address their queries on how appropriate and rationale it was to release such false projections in front of the whole country. "Being a Health Minister of the country, how justified is it to release such falsely fabricated unscientific product to people of the whole country and how ethical was it to promote the product in unethical, wrong and false ways," the statement said.

The association also pointed out that as per the code of act of the Medical Council of India, no doctor can promote any drug, "whether for compensation or otherwise, any approval, recommendation, endorsement, certificate, report or statement" and said that it was "surprising that the Minister himself is promoting the drug (Coronil)".

The IMA has also sought clarifications on the timeline for the clinical trial of Coronil and whether patients were involved in the double blind and/or single blind clinical trials. A series of questions have been asked, which include whether the patients were subjected to an informed consent for any such trials and others.

It is noteworthy to state here that many journalist and common people were arrested on the charges of terrorism who reported or made statement on COVID-19. Now the Union Minister and Baba Ramdev have promoted drug which has not gone under trial and certainly the acts are unethical and illegal in any way, one source said.

Earlier also Baba Ramdev and his allies promoted Coronil but later retract their statement on public outrage (http://www.biotechexpressmag.com/coronil-magical-medicine-from-self-proclaimed-ayurveda-doctor/).

# Drug researchers retract two papers, because "human stem cells were actually mouse stem cells"

March 10, 2021

A group of drug researchers has lost a pair of 2020 papers for a lack of reproducibility and other problems,

including the unfortunate mislabeling of murine stem cells as having come from humans. (In case you're wondering, mouse and human stem cells are at once quite similar and highly divergent.)

One article, "Divergent synthesis of 5-substituted pyrimidine 2-deoxynucleosides and their incorporation into oligodeoxynucleotides for the survey of uracil DNA glycosylases," appeared in Chemical Science. The second, "Convenient synthesis of pyrimidine 2-deoxyribonucleoside monophosphates with important epigenetic marks at the 5-position," was published in Organic & Biomolecular Chemistry. Both journals belong to the Royal Society of Chemistry.

The senior author on the papers was Yana Cen, a medicinal chemist now at Virginia Commonwealth University in Richmond. Cen has not responded to a request for comment.

The retraction notice states that efforts to confirm the findings foundered:

The Royal Society of Chemistry hereby wholly retracts this Chemical Science article due to concerns about the reproducibility of the data.

The Royal Society of Chemistry has been contacted by the authors of this article to alert us that recent experiments by their group have shown that some results are not reproducible, especially the yields of several key intermediates. Given the focus on the easy access to epigenetically important nucleosides and related ODNs, unreliable yields significantly impact the confidence in the results.

In addition, it was discovered that one of the biological samples provided to the authors was mislabelled. The human stem cells were actually mouse stem cells, hence some discussion and conclusions in the article may no longer apply. Ahead of a thorough re-examination of the entire study, in order to preserve the rigor of the scientific record, the signing authors have chosen to retract the article and they would like to apologise for any inconvenience this may have caused for readers.

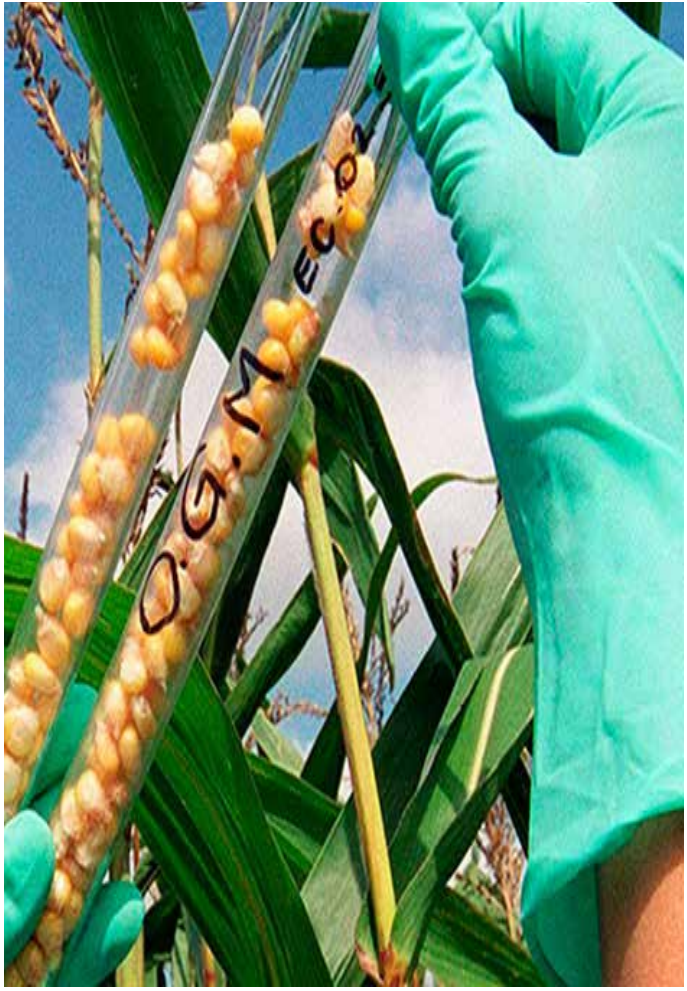
# Supplement-selling doctor reached up to 20 retractions

March 12, 2021

Dove Press, which late last year retracted more than a dozen articles by a U.S. physician who appears to have used the articles and other publications as marketing material for dietary supplements he sold, has pulled six more of his papers. The new retractions make 20 removals by Dove — a unit of Taylor & Francis — for Marty Hinz.

As reported, Hinz has a long history of running afoul of regulatory bodies, from the FDA to the Minnesota Board of Medical Practice, which in March 2020 reprimanded and fined him more than $7,000 following allegations including that he claimed on his website to have "reinvented the medical science foundation of Parkinson's disease" and to "treat and do things for our Parkinson's disease patients that most doctors of the world believe are impossible." Nearly three years ago, Stephen Barrett — a U.S. physician and founder of Quackwatch — alerted Dove to his concerns about Hinz's failure to disclose conflicts of interest on the 20 papers. Barrett says Hinz has used those papers to support claims that supplements made by Hinz's former company, now owned by his daughter but from which he has received royalties, are effective in treating various conditions.

# Bio Policy




## China's Five-Year Plan Prioritizes Modern Breeding Techniques for Agriculture

March 10, 2021

China revealed its initial policy statement regarding the new Five-Year Plan which focused on rural revitalization and agriculture modernization.

The previous Five-Year Plan, which ended in 2020, was focused on eradicating extreme poverty in the country. With the new Plan, the priority has shifted from rural work to modernization of the rural economy, particularly in building infrastructure for information technology, promoting agricultural technologies, and building modern breeding systems. Their focus on food security has been strengthened as well.

The 2021-2025 plan, which is stated in the "No. 1 central document", highlights the following tasks and targets to modernize agriculture:

ensure the supply of grain and major agricultural products, including maintaining the planting area of grains, enhancing yield per unit area, speeding up the development of the modern breeding system, fostering sustainable aquaculture, and maximizing agricultural products trade;
fortify the protection, development, and utilization of agricultural germplasm resource and speed up the application of S&T projects involving biological breeding for agriculture;
maintain at least 120 million hectares of arable land with high-standard farmlands producing high and stable yields regardless of drought and flood; and
reinforce the support for modern agriculture by science, technology, and equipment, create agricultural modernization demonstration zones with a target of 500 by 2025, and advance the green development of agriculture.

# Notice

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**Advertisement No.1-1/2021**

| IMPORTANT DATES |
|---|
| Last Date for Submission of Online Application is 23:59 HRS on 22/03/2021<br>Last Date for Printing of Online Application is 23:59 HRS on 23/03/2020<br>Last Date of receiving print out of online application at CSIR-IGIB is 07/04/2021 by 5:00 PM<br>**Please send your queries to recruit@igib.res.in** |

The details of the positions and the respective emoluments as well as age limit are given below:

| Designation | No of Vacancy & Reservation | Pay Level (PL) & Pay Matrix | *Total Emoluments (approx) | Age Limit** |
|---|---|---|---|---|
| Scientist | 4<br>UR – 2<br>OBC – 1<br>EWS – 1 | **PL - 11**<br>Rs 67700-208700 | Rs 83948/- | 32 Years |
| Senior Scientist | 1<br>UR | **PL - 12**<br>Rs 78800-209200 | Rs 97712/- | 37 Years |
| Principal Scientist | 2<br>UR | **PL - 13**<br>Rs 123100-215900 | Rs 152644/- | 45 Years |

* Total Emoluments means approximate total emoluments on a minimum of scale including House Rent Allowance (HRA).

# TePP OUTREACH CUM CLUSTER INNOVOTATION CENTRE – PRISM

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**PRISM Phase - 2**

**Category-II:** Up to Rs.50.00 lakhs or 50% of the approved cost whichever is lower to successful PRISM-Phase I innovators.

**PRISN-R&D Proposals:** Limited to the financial support of Rs. 50 lakhs or 50% of the approved cost whichever is lower.

## Eligibility

- The support for micro budget innovations to initiate a promising development.
- Prove functionality by a lab model / computer model / mathematical model, apply for patenting etc.
- Proposals to convert an original idea/ invention/ know-how into working prototype/ process and proposals to demonstrate novel delivery models to take S&T innovations leading to inclusive growth.
- Proposals from successful PRISM innovators. Those who have developed products/ process of concept proving stage under PRISM phase-I, for innovations having significant market potential.
- Proposals from autonomous institutions/ R&D labs/ IITs/ NITs/ other statutes etc., who have developed products/ process at concept proving stage and has potential for development in MSME clusters.

**For more details visit: www.dsir.gov.in**


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# International Conference on Biotechnology for Sustainable Agriculture, Environment and Health

# XVII Convention of BRSI

# (BSAEH-2021)

ISSN: 2454-6968
RNI No. UPENG/2013/54102

## April 4-8, 2021 Jaipur

**Details: http://brsi2020jaipur.in/**

**Conference will be held in Hybrid mode (Physical and Virtual)**

**The event will be jointly organized by the MNIT, Jaipur; CDC India, Jaipur, BISR, Jaipur and NIT-Uttarakhand in association with the International Solid Waste Association (ISWA), The Institute of Chartered Waste Managers (ICWM) and B Lal Institute of Biotechnology, Jaipur. This will be supported by the International Bioprocessing Association, France; Centre for Energy and Environmental Sustainability (CEES)-India and Amity University, Jaipur. The event will be held at BISR, Jaipur. Prof TP Singh, Prof AB Gupta and Dr Vivek Agarwal are conference chairs. Dr V Vivekanand is the convener of BAEH-2020 and Dr P Binod, COE, BRSI; Dr Krishna Mohan, BISR, Jaipur and Dr B Lal, BIB, Jaipur, Dr Rakesh Kumar Mishra, NIT-Uttarakhand are its co-conveners. Details can be found at http://brsi2020jaipur.in/**