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Gravitational-wave Background (GWB): A Breakthrough in Direct Detection



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COVID Testing in Less than 5 Minutes Using Novel RTF-EXPAR Method

Controlling the rate of COVID-19 spread requires an accurate and a faster virus testing strategy. RT-PCR (reverse transcriptase polymerase chain reaction), the most accurate testing method being currently employed is a two-step test that takes around 60 minutes per sample.

he researchers from the University of Birmingham have reported a novel method for detection of SARS-CoV-2. This could enable much faster testing and is sufficiently sensitive.

The viral RNA detection by RT-PCR (reverse transcriptase polymerase chain reaction) involves conversion of viral RNA to complementary DNA (cDNA) followed by amplification of cDNA by a quantitative PCR (gPCR). The cDNA is then detected using a fluorescent dye. This takes up to an hour.

The assay time is considerably reduced from about an hour to few minutes by the newly reported RTF-EXPAR method which uses reverse transcriptase-free (RTF) approach for conversion of RNA into DNA followed by EXPAR (Exponential Amplification Reaction) for amplification at single temperature. The amplification taking place at a single temperature is the key to speed, because it avoids lengthy heating and cooling steps of RT-PCR. Further, the section of DNA being amplified is smaller compared RT-PCR. Hence, EXPAR generates up to 108 strands of DNA product in few minutes. The duplex formation is monitored, as in RT-PCR method using fluorescent dye, SYBR Green.



Interestingly, the new method can be modified to detect several other infectious diseases caused by RNA viruses, for example Ebola, RSV, etc.

Source(s):

Carter et al (2020). Sub-5-minute Detection of SARS-CoV-2 RNA using a Reverse Transcriptase-Free Exponential Amplification Reaction, RTF-EXPAR. Preprint. Published at medRxiv Posted January 04, 2021. DOI: https://doi.org/10.1101/2020.12.31.20248236

Tocilizumab and Sarilumab Found Effective in Treating Critical COVID-19 Patients

The preliminary report of findings from the clinical trial NCT02735707 reported in preprint suggests that Tocilizumab and Sarilumab, the interleukin-6 receptor antagonists are effective in treating critically ill COVID-19 patients and improve survival.

everely ill COVID-19 patients receiving intensive care support responded well to the treatment with the IL-6 receptor antagonists, tocilizumab and sarilumab. The hospital mortality was 28.0 % for tocilizumab, 22.2% for sarilumab and 35.8% for control meaning survival rate improved supporting better efficacy of these repurposed drugs. (1)

The drugs tocilizumab (a humanized monoclonal antibody against the IL-6 receptor) and sarilumab (a human monoclonal antibody against the IL-6

receptor) are normally used as immunosuppressants in the treatment of rheumatoid arthritis.

In the current climate of COVID-19 pandemic when mortality and infection rates are high, it is very interesting to note that these two repurposed drugs significantly reduced COVID-19 patients' stay in intensive care wards of the hospital and reduced the mortality rate by about a quarter. This basically means fewer deaths and shorter stay in critical care, thus preserving hospitals capacity to deal with the pandemic.

This clinical trial was funded by EU which is supporting REMAP-CAP through the Platform for European Preparedness Against (Re-)emerging Epidemics (PREPARE) project. Additional support comes from the related Rapid European SARS-CoV-2 Emergency Research response (RE-COVER) project (2).

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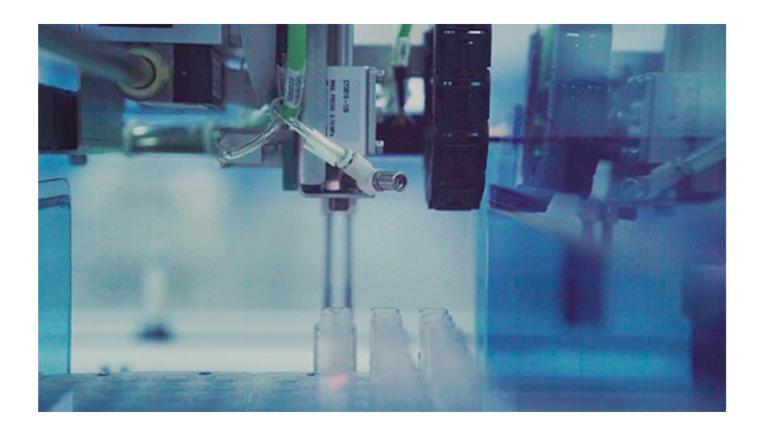
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Fibrosis: ILB®, Low Molecular Weight Dextran Sulfate (LMW-DS) Shows Anti-Fibrotic Effects in **Pre-Clinical Trial**

Fibrotic diseases are known to affect several vital organs in the body and are a major cause of mortality and morbidity. There has been a little success in treatment of these diseases so far. ILB®, the Low Molecular Weight Dextran Sulfate (LMW-DS) has shown promising results in a pre-clinical trial. It has been found to resolve inflammation and activate matrix remodelling in rodent and human disease models. Apparently, ILB® seems to have the potential to treat fibrotic diseases. Of particular interest is the possibility of anti-fibrotic treatment for glaucoma. But before getting approved, it needs to undergo further large scale clinical trials.



When inflammation is triggered due to factors like infections, autoimmunity, toxins, radiation, mechanical injury etc. lasts for longer period (chronic inflammation), the tissue remodelling and repair processes occur simultaneously. The repair process has two phases – regeneration (new cells of the same type replace injured cells) and fibrosis (connective tissues replaces normal cells). When uncontrolled, the repair process results in deposition of extracellular matrix (ECM) leading ultimately to replacement of normal tissue with permanent scar tissue.

Abnormal fibrosis as result of chronic and unresolved inflammation is common and is key pathology behind large number of diseases affecting vital organs like lung, liver, heart, pancreas, eye, brain, intestine, skin etc. These diseases are a major cause of mortality and morbidity worldwide. According to an estimate about 45% of all deaths are attributed to fibrosis. Treatment of fibrotic diseases is not usually successful for want of a suitable therapeu

tic agent that could resolve inflammation, arrest abnormal fibrosis, and activate regeneration of normal tissues thus restoring normal tissue homoeostasis without adverse effects. Any such therapeutic agent would be of great societal and economic significance.

In earlier study, ILB® has already been demonstrated to be safe in humans. In this study, researchers investigated low molecular weight dextran sulfates (LMW-DS) in rodent and human disease models. It was found that ILB®, the Low Molecular Weight Dextran Sulfate (LMW-DS) –

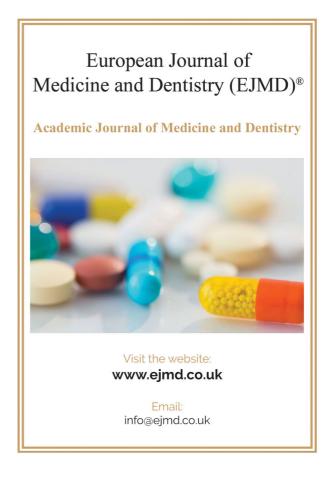
- 1) modulates inflammatory and wound healing responses in cultured human cells,
- 2) modulates expression of inflammatory and fibrogenic genes in cultured human cells, and
- 3) reduces fibronectin levels in cultured human tra

becular meshwork cells and resolves inflammatory scarring in a rodent model of glaucoma.

Thus, the results of this pre-clinical trial suggests that LMW-DS may resolve inflammatory scarring and promote functional tissue regeneration. This proof of concept makes ILB® a potential candidate for treatment of several fibrotic diseases including glaucoma.

Source(s):

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MHRA Approves Moderna's mRNA COVID-19 Vaccine

edicines and Healthcare products Regulatory Agency (MHRA), the regulator of all medicines and medical devices in the UK has approved Moderna's COVID-19 vaccine after meeting the required safety, quality and effectiveness standards for use in the UK (1).

This is the third COVID-19 vaccine to be approved in the UK after Pfizer/BioNTech's mRNA vaccine BNT162b2 and Oxford/AstraZeneca's ChAdOx1 nCoV-2019.

Like Pfizer/BioNTech's BNT162b2, this vaccine as well is a mRNA vaccine and works on the same principle of injecting viral mRNA in to the cells (2).

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Space Biomining: Inching Towards Human Settlements Beyond Earth

HILIP: Laser-Powered Rover to Explore Super-Cold Lunar Craters for WaterHuman settlements beyond Earth on Moon or on planets like Mars in space have long been the theme of science fiction. However, serious thoughts and research activities towards this have been in progress in the last two decades. One of the key questions before the scientific community has been on how to acquire the materials (such as oxygen, water, building materials including metals and minerals etc.) needed to establish a self-sustaining presence in space (1).

Biomining i.e., extracting metals from ores through bio-catalysis using microorganisms like bacteria and archaea is in practice for long on planet Earth. Currently, this method is used to leach copper sulfides and pretreat gold ores and also to extract metals from oxidised ores and to recover metals from wastes (2). Can the technique of biomining be effectively used under microgravity conditions in outer space to extract materials needed for human settlements? Can microorganisms help extract metal and materials using asteroid materials or rocks available on Moon or Mars? Knowledge of microbe—mineral interactions in space is also considered important because of its potential in soil formation, formation of biocrusts in enclosed pressurised spaces, use of regolith (layer of solid material over bedrocks) and production of construction materials. Space biomining experiments were designed exactly for these reasons to understand effects of altered gravity.

To this end, European Space Agency carried out the BioRock experiment on the International Space Station (ISS) in 2019. Experiments were designed to study bioleaching of rare-earth elements from basaltic rock in three gravity conditions viz. microgravity, simulated Mars gravity and simulated Earth

gravity. Three bacterial species, Sphingomonas desiccabilis, Bacillus subtilis, and Cupriavidus metallidurans were used in the study. The hypothesis tested was if "different gravity regimens can influence the final cell concentrations achieved after a multi-week period in space". The results suggested no significant effect of different gravity conditions on final bacterial cell counts implying that efficacy of the bleaching process remains same under different gravity conditions. These findings of the BioRock experiment indicate that bacterial supported mining can be carried out in the space. Space biomining is a significant discovery that seems to have a great potential going forward (3,4).

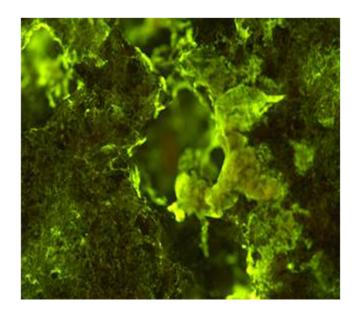
Following the success of BioRock study, the Bio-Asteroid experiment is currently underway now. In this study, bacteria and fungi are being grown on asteroidal material in an incubator under microgravity condition of the space station in order to study biofilm formation, bioleaching and other chemical and biological changes including the genetic transcriptional changes(5).

With these stepping stones, the humanity is surely inching forward towards human settlements beyond planet Earth.

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The Science of Brown Fat: What more is Yet to be Known?

Brown fat is said to be "good". It is known that it plays an important role in thermogenesis and maintains body temperature when exposed to cold conditions. An increase in amount of BAT and/or its activation has been shown to be positively correlated with improvement of cardiometabolic health. Animal studies have shown that the brown fat can be increased/activated by exposure to cold conditions, reduced exposure to light and/or upregulation of specific genes. Further research and extensive human trials are needed to establish the importance of increased activation of BAT in improving cardiometabolic health

rown fat is also called brown adipose tissue or BAT in short. It is a special type of body fat that is turned on (activated) when we experience cold. The heat produced by brown fat helps maintain our body temperature in cold conditions. The function of BAT is to transfer energy from food into heat; physiologically, both the heat produced and the resulting decrease in metabolic efficiency is of great significance for the body. Heat production from brown adipose tissue is activated whenever the organism is in need of extra heat, e.g., among

new-borns soon after birth and during fever when body temperature increases. Brown fat cells possess multilocular lipid droplets and large numbers of mitochondria that contain a unique protein called uncoupling protein 1 (UCP1) (1). The development of brown adipose tissue along with its uncoupling protein-1 (UCP1), is probably responsible for the evolutionary success of mammals as homeothermic creatures, as its thermogenesis enhances neonatal survival and allows for active life under cold conditions (2).



The presence of BAT has been positively associated with cardiometabolic health. Individuals with BAT have reduced obesity and have less prevalence of type 2 diabetes (increased insulin sensitivity), dyslipidaemia, coronary artery disease, cerebrovascular disease, congestive heart failure and hypertension. These findings were supported by improved blood glucose (low values), and increased high-density lipoprotein values. Moreover, the beneficial effects of BAT were more pronounced in obese individuals, indicating that BAT might also play a role in mitigating the harmful effects of obesity (3). The presence and function of BAT may have implications for the recent pandemic caused by COVID-19. It is becoming increasingly clear that obese individuals with more white adipose tissue (WAT) may be more prone to having and contracting severe COVID-19 (4) and it may be postulated that presence of BAT may have a beneficial effect with regards to contracting COVID-19 disease.

Recent research evidence suggests that using therapeutic interventions such as use of mirabegron, a beta 3 adrenergic receptor agonist, can improve obesity-related metabolic disease by increasing brown adipose tissue (BAT) thermogenesis. In fact, results of chronic mirabegron therapy showed increased BAT metabolic activity, without significant changes in body weight or composition. In addition, plasma levels of beneficial lipoprotein biomarkers HDL and ApoA1 (apolipoprotein A1) were found to be higher. Adiponectin, a WAT-derived hormone that has antidiabetic and anti-inflammatory capabilities, also showed a 35% increase upon completion of the study. These were coupled with higher insulin sensitivity and insulin secretion(5).

What are the implications of the presence or beneficial effects of BAT for the common man? Can we activate BAT by reduced exposure to light or by upregulating genes expressed in BAT or by exposure to cold conditions? At least, the research on mice shed some light on these (6,7) and may pave a way for further initiation of studies on humans.

Does that mean that exposure to colder temperatures activates BAT and/or increases BAT volume? A randomised trial of cold exposure in humans for 1hr per day for 6 weeks resulted in increased volume of BAT (8).

Further research and extensive human trials are required to bring out the beneficial effects of BAT on humans.

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The Fireworks Galaxy, NGC 6946: What Make this Galaxy so Special?

ASA recently released the spectacular bright image of the firework galaxy NGC 6946 taken earlier by Hubble space telescope (1)

A galaxy is a system of stars, remnants of stars, interstellar gas, dust, and dark matter that are bound together by gravitational force. According to an estimate, there are about 200 billion galaxies in the observable universe (2). The solar system along with the sun is part of the galaxy called Milky Way which is our home galaxy.

NGC 6946 (NGC stands for New General Catalogue which is a common way of labelling astronomical objects) is one of the galaxies situated at a distance of 7.72 Mpc {1 Mpc or Megaparsecs equal to a million parsecs; in astronomy, the preferred unit of distance is parsec (pc). 1 parsec is the distance at which 1 Astronomical Unit subtends an angle of 1 second of arc viz.1/3600 of a degree; 1 pc equals 3.26 light years} or 25.2 million light-years in the constellation Cepheus.

The galaxy, NGC 6946 has an exceptionally high rate of star-formation hence classified as a starburst galaxy. This type of galaxies are characterised by high star-formation rates in the order of 10 - 100 M \square /year which are far higher than in normal galaxies, for example in our home galaxy Milky Way, the star-formation rate is about $1 - 5 \text{ M}\square$ /year (3) (M \square is the solar mass, the standard unit of mass in astronomy, $1 \text{ M}\square$ is equal to approximately $2 \times 1030 \text{ kg.}$).

On our time scale, stars appear to be unchanging but on the time scale of billions of years, stars undergo a life course, they are born, age and finally die. The life of a star begins in a nebula (cloud of dust, hydrogen, helium and other ionized gases) when the gravitational collapse of a giant cloud give rise to a protostar. This continues to grow further with accretion of gas and dust until it reaches its final mass. The final mass of the star determines its life time (lesser the mass, higher the life span) as well as what happens to the star during its life.

All stars derive their energy from nuclear fusion. The nuclear fuel burning in the core creates strong outward pressure due to the high core temperature. This balances out the inward gravitational force. The balance is disturbed when the fuel in the core runs out. Temperature drops, outward pressure diminishes. As a result, the gravitational force of the inward squeeze becomes dominant forcing the core to contract and collapse. What a star finally ends up as after collapse depends on the mass of the star.

In the case of supermassive stars, When the core collapses in a short span of time, it creates enormous shock waves. The powerful and luminous explosion is called supernova. This transient astronomical event occurs during the last evolutionary stage of a supermassive star. The galaxy NGC 6946 is called the Fireworks Galaxy because it has experienced 10 observed supernova in the last century alone. In comparison, the Milky Way averages just one to two supernovae per century. Therefore, a good number of supernova remnants are expected in NGC 6946 galaxy. The total number of supernova remnant candidates identified in NGC 6946 is about 225 (4,5). For stars more than 10 times the mass of the sun, the remnants would be black holes, the densest objects in the universe.



The high star-formation rate (starburst), the high rate of supernova events (fireworks) features, spiral structure and it being positioned face-on with us sets this galaxy apart giving rise to its spectacular appearance in the images taken by the Hubble telescope.

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Gravitational-wave Background (GWB): A Breakthrough in Direct Detection

Gravitational wave was directly detected for the first time in 2015 after a century of its prediction by Einstein's General Theory of Relativity in 1916. But, the continuous, low frequency Gravitational-wave Background (GWB) that is thought to be present throughout the universe has not been detected directly so far. The researchers at North American Nanohertz Observatory for Gravitational Waves (NANOGrav) have recently reported detection of a low-frequency signal that could be 'Gravitational-wave Background (GWB)'.

eneral theory of relativity propounded by Einstein in 1916 predicts that major cosmic events such as supernova or merger of black holes should produce gravitational waves that propagate through the Universe. Earth should be awash with gravitational waves from all directions all the time but these are undetected because they become extremely weak by the time they reach earth. It took about a century to make a direct detection of gravitational ripples when in 2015 LIGO-Virgo team was successful in detecting gravitational waves produced due to merger of two black holes situated at a distance of 1.3 billion light-years from the

Earth (1). This also meant the detected ripples were bearer of information about the cosmic event that took place about 1.3 billion years ago.

Since the first detection in 2015, a good number of gravitation ripples have been recorded till date. Most of them were due to merger of two black holes, few were due to collision of two neutron stars (2). All detected gravitational waves so far were episodic, caused due to binary pair of black holes or neutron stars spiralling and merging or colliding with each other (3) and were of high frequency, short wavelength (in milliseconds range).



However, since there is possibility of large number of sources of gravitational waves in the universe hence many gravitational waves together from all over the universe may be continuously passing through the earth all the time forming a background or noise. This should be continuous, random and of low frequency small wave. It is estimated that some part of it may even have originated from the Big Bang. Called Gravitational-wave Background (GWB), this has not been detected so far (3).

But we may be on the verge of a breakthrough – the researchers at the North American Nanohertz Observatory for Gravitational Waves (NANOGrav) have reported detection of a low-frequency signal that could be 'Gravitational-wave Background (GWB) (4,5,6).

Unlike LIGO-virgo team who detected gravitational wave from individual pairs of black holes, NANO-Grav team have looked for persistent, noise like, 'combined' gravitational wave created over very long period of time by countless blackholes in the universe. The focus was on 'very long wavelength' gravitational wave at the other end of 'gravitational wave spectrum'.

Unlike light and other electromagnetic radiations, the gravitational waves cannot be observed directly with a telescope.

The NANOGrav team chose millisecond pulsars (MSPs) that rotate very rapidly with long term stability. There is steady pattern of light coming from these pulsers which should be altered by the gravitational wave. The idea was to observe and monitor

an ensemble of ultra-stable millisecond pulsars (MSP) for correlated changes in the timing of the arrival of the signals at the Earth thus creating a "Galaxy-sized" gravitational-wave detector within our own galaxy. The team created a pulsar timing array by studying 47 of such pulsars. The Arecibo Observatory and the Green Bank Telescope were the radio telescopes used for the measurements.

The data set obtained so far includes 47 MSPs and over 12.5 years of observations. Based on this, it is not possible to conclusively prove direct detection of GWB though the detected low frequency signals very much indicate that. Perhaps, the next step would be to include more pulsars in the array and study them for longer period of time to enhance sensitivity.

To study the universe, scientists were exclusively dependant on electromagnetic radiations like light, X-ray, radio wave etc. Being completely unrelated to electromagnetic radiation, detection of gravitational in 2015 opened a new window of opportunity to scientists to study celestial bodies and understanding the universe especially those celestial events which are invisible to electromagnetic astronomers. Further, unlike electromagnetic radiation, gravitational waves do not interact with matter hence travel virtually unimpeded carrying information about their origin and source free of any distortion.(3)

Detection of Gravitational-wave Background (GWB) would broaden the opportunity further. It may even become possible to detect the waves generated from Big Bang which may help us understand origin of universe in a better way.

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Earth's Magnetic Field: North Pole Receives More Energy

New research expands role of Earth's magnetic field. In addition to protecting Earth from harmful charged particles in incoming solar wind, it also controls how the energy generated (by charged particles in solar winds) is distributed between two the poles. There is northern preference meaning more energy is diverted to magnetic north pole than magnetic south pole.

Earth's magnetic field, formed due to flow of superheated liquid iron in the outer core of Earth below 3000 km from the surface plays very important role in our life. It deflects the stream of charged particles emanating from the Sun away from the Earth thus shielding life from the harmful effects of ionising solar winds.

When the electrically charged particles in the solar wind flows in the atmosphere, they generate energy. This terrestrial electromagnetic energy is hitherto understood to be symmetrically distributed between north and south poles. However,

new research using the data from the Swarm satellite in polar low-Earth orbit (LEO) at an altitude of around 450 km, has shown that this is not the case. The energy is preferentially distributed to the north pole. This asymmetry of northern preference means more of terrestrial electromagnetic energy heads towards magnetic north pole than towards magnetic south pole.

Earth's magnetic field thus, also plays role in distribution and channelising of the terrestrial electromagnetic energy (generated due to entry of electrically charged particles) in the atmosphere.



lonising radiations in the solar wind is known to have potential to cause damages to communication networks, satellite-based navigation systems and electrical grids. Better understanding of earth's magnetic field would be helpful in planning safety and protection against solar winds.

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20C-US: New Coronavirus Variant in the USA

Researchers at Southern Illinois University have reported a new variant of SARS COV-2 Virus in the USA.

According to reports published on preprint server which is yet to be peer-reviewed, researchers have identified a new variant using genomic virus surveillance approach.

Referred as 20C-US, this variant appeared in the USA early in the pandemic and has now become one of the most prevalent variants in the USA. Apparently, this has not spread to other countries widely.

The US variant adds to the growing list of SARS-CoV-2 variants including UK and South Africa variants.



Coronaviruses have very high rate of mutation because of lack of proofreading nuclease activity hence evolve constantly.

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DNA Vaccine Against SARS-COV-2: A Brief Update

A plasmid DNA vaccine against SARS-CoV-2 has been found to induce immunity in animal trials. Few other DNA based vaccine candidates are at early stages of clinical trials. Interestingly, plasmid DNA vaccines can be developed in a short period of time. Compared to attenuated and inactivated vaccines, it has several advantages. But, unlike mRNA vaccines, DNA vaccines may possibly replicate in the cell.

According to a research report published on a preprint server, the pVAX1-SARS-CoV2-co, a plasmid DNA vaccine candidate against SARS-CoV-2 has been found to induce potent immune response in animal model when delivered intradermally via pyro-drive jet injector (PJI) (1). This vaccine candidate may proceed into clinical trials soon.

Earlier, the preclinical development of DNA-based COVID-19 vaccine, INO-4800 using plasmid pGX9501 has been reported (2). This vaccine candidate is currently undergoing clinical trial (3). Few other DNA based COVID-19 vaccines are at early

stages of clinical trials. For example, recruitment is in progress for NCT04673149, NCT04334980 and NCT04447781 while the trials NCT04627675 and NCT04591184 are not yet recruiting (4).

The idea to use genetically engineered plasmid DNA in vaccine form to elicit immune response has been in vogue for more than two decades. Its biology is well understood now. The results from several preclinical studies have been encouraging. Also, four DNA vaccines have been licenced recently for veterinary use (5). Efforts have been made for regulatory convergence across the world and to promote guidelines for trials of DNA vaccines to assess its

safety and efficacy (6).

In view of extraordinary situation presented by the pandemic and because plasmid DNA vaccines can be developed in a short period of time, there have been spurt of activities in the area of DNA vaccine development.

DNA based vaccines offers several advantages. Unlike attenuated or inactivated vaccines, non-live vaccines based on plasmid DNA or mRNA do not have safety issues associated with live vaccines like reversion risks, unintentional spread or production errors. DNA vaccines induce antibody production (humoral immunity). It also induces killer cytotoxic T lymphocytes offering cellular immunity (5).

Compared to mRNA vaccines which are unstable and need storage at very low temperatures, DNA vaccines have an advantage as DNA is relatively stable and can be stored and distributed at 2-8 degree centigrade. But unlike mRNA vaccines which cannot replicate in the cells (7), DNA vaccines can theoretically replicate and incorporate with the genome. Long term implications of this possibility will not be easy to know in short span of clinical trials.



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