

Precision editing the cells and engineering or re-engineering life, the era of geno-pharmacology/therapeutics has begun!!



Advancement in life science is happening at a rapid scale, with occasional reports of blockbuster discoveries. One such discovery, which is currently trending, is the report on CRISPR-Cas9 technology, which is a powerful and precise gene-editing tool. While the medical benefits of such a technology are obvious, the risks and, most importantly, the ethical concerns collaterally associated with such risks need in-depth analysis, so as to place appropriate preventive measures to avoid abuse of such technology. Although only a few studies are published on CRISPR technology so far, the products of such gene editing approach are already appearing commercially. One such example is the micro-pig created by BGI, Shenzhen, China, which is evolving the era of designer pets amid ethical concerns. While the legality and ethical perception on such products developed may vary across the geographical domains; nevertheless, there is a need for universal consensus on socially responsible use of such a powerful technology, specifically considering equipotential risks and benefits of such technology. Nevertheless, progression in this technology will add considerably to the next domain of therapeutics, which over the years has evolved from crude extracts, receptor targeting, and specific small molecule therapeutics to the ultimate holy grail of precision engineering (repair/replacement) of biomolecules. This advancement brings considerable refinement to the field of pharmacology by incorporating the biomolecular-engineering which can be broadly be classified as genopharmacology/therapeutics (a therapeutic approach involving precise editing/engineering of genes/biomolecules). Such a paradigm shift in the field will necessarily involve successful replication of studies reported using this technology by multiple

independent research groups globally. Such replications are necessary in addressing a very important issue on reliability of scientific reports, which has been intensively discussed recently as currently a significant amount of data reported in scientific literature cannot be replicated. The reasons for lack of study replications may be multi-factorial, including poor study designs, inappropriate use of experimental models, and in some instances gross neglect or oversights. Hence, as highlighted in our previous editorials, it is necessary to have transparency and avoid biasness in all aspects of scientific research to improve its validity. Unless these two important parameters can be fully achieved, the reliability of any scientific research will continue to be questioned. Surprisingly, such lack in replicability of scientific results has also led some sceptics to question the utility of experimental animals as reliable models to understand human diseases, which has disappointingly led to unnecessary restrictions in the use of animals in scientific research. This is despite the enormous wealth of information available in the public domain supporting the benefits animal models has contributed in development of almost all the available medicines used for therapeutics currently. Such scepticism can only delay but not deny scientific advancement and probably, this will hold good for CRISPR-Cas9 technology as well.

Again, we have included broad spectrum of scientific articles in this issue. Among them are, review articles on utility of vedolizumab in the treatment of inflammatory bowel disease and current challenges and advances in optimizing liver allografts. Both these reviews are very timely considering several recent studies associating the

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health of gastrointestinal (GI) track with systemic well-being and the relative rise in the incidence of GI disorders in developing nations. In addition with the improvement in quality of hospital care, increasingly organ transplant procedures are becoming more successful nevertheless with challenges, which needs to be addressed. These challenges are critically discussed in the review article. One of the major limitations in organ transplant has been the availability of suitable organs from donors, and I think CRISPR-Cas9 gene-editing technology will be valuable in creating bio-engineered organs suitable for transplants.

We also continue to include articles on antibiotic resistance which remains one of the major healthcare concerns globally. With new antibiotic pipeline being fairly dry, the continuing emergence of resistance to currently used antibiotics is a significant issue for concern. Specifically, one of the articles in this issue reports multidrug-resistance in uropathogenic *Escherichia coli* strains; this is of concern as in recent times there are several epidemics outbreaks of *E. coli* leading to not only mortality and morbidity but also significant socioeconomic loss. We also have included another article reporting antimicrobial resistance of *Klebsiella pneumoniae* isolated from urine samples. Both *E. coli* and *K. pneumoniae* reported in these studies are routinely associated with GI and respiratory tract infections often with significant morbidity and mortality levels, and the emergence of resistance in these pathogens will further curtail the clinical management of diseases caused by the resistant strains of these pathogens. Hence, in addition to implementing measure to judicious use of antibiotics, it is also necessary to understand the molecular mechanisms of antibiotic resistance developed by these pathogens. One of the articles included in this issue reports the role of virulence factors as the major mechanism of carbapenemase-producing *Acinetobacter baumannii* pathogenesis. Understanding these antibiotic resistance mechanisms will help develop optimal and efficient anti-microbial therapeutic approaches. In addition, it is also necessary to look at natural resources for anti-microbial therapeutics. In this issue, we include an article which reports Ziziphus honey as a natural preservative and antibacterial agent even at 10% dilution against *Listeria monocytogenes*, *Salmonella typhimurium*, *E. coli*, and *S. aureus*. Such natural products may play a very vital role in combating microbial infections and must be looked into as potential preventive measures. Also included in this issue is an article on utility of *Morinda lucida* leaf in the traditional treatment of *Plasmodium* infection. Malarial infections are re-emerging albeit with resistance issue as observed with bacterial pathogens. Hence, measures such as use of plant-based products to combat *Plasmodium* infections are timely and necessary. It will also be interesting to foresee

if gene-editing approach such as CRISPR-Cas9 technology can be used to develop designer intermediate hosts to curtail *Plasmodium* infections, such an approach will be specifically useful in endemic regions.

The advancement in therapeutics must be collaterally supported by advancement in diagnostics. Although gene editing may not have much role in diagnostics, simple techniques tend to be reliable. Reporting in this issue is one such simple technique reliable in identifying potentially malignant diseases by assessment of micronuclei in exfoliated oral epithelial cells. Similarly, another study in this issue reports the utility of evaluating dermatoglyphic patterns in identifying patients prone to developing bronchial asthma. Although both studies need confirmation in large randomized multi-centric studies, nevertheless offers a simple and effective diagnostic/predictive potential. Also, reported in this issue is a study comparing the efficacy of general and local anesthesia in extracting a sufficient quality of sperm for men with azoospermia, who intend to undergo intra-cytoplasmic sperm injection. It was indeed interesting that this study did not see any difference in quality of sperms collected using either general or local anesthesia. Indeed, this study necessitates re-evaluation of clinical practice wherein from patient safety and pharmacoeconomics point, use of local anesthesia should be preferred over general anesthetics when feasible. Such re-evaluation of clinical practice can happen by increasing awareness among both patients and clinicians on advances in science and medicine. Awareness and attitude are key indexes in bringing any positive change not only in clinical practice but also for therapeutic compliance. Included in this issue are articles, which reports perceptions, knowledge, and attitude, related to vitiligo among adults and mobile-health (health utilities of mobile phones) in general population. We have also included an article on patterns of burn injuries in the pediatric population. Understanding such epidemiological patterns is vital to initiating optimal public health measures, and we very much look forward to such studies from all geographical regions. Another study reports the incidence of metabolic syndrome in patients with severe mental illness patients in Middle East while one study reports the problems encountered in controlling diabetes progression in patients. We have also included studies which report the incidence of hepatitis B virus and hepatitis C virus co-infection in hemodialysis patients and subclinical hypothyroidism in pregnancy (which is seen as an emerging problem). These are vital epidemiological information which will be valuable for devising simple public health strategies for optimal control of these diseases.

While the advancement in science and medicine continue, a major problem with the quality of medicines used

currently in emerging in the background including the issue of counterfeit medicines. It is estimated that counterfeit medicines drain our economy by 200-250 billion Euros every year. While there are also other quality concerns such as variations in the quantity and quality of information available on indications about drugs available in various sources. In this issue, we have included an article which assessed 50 commonly used drugs for information on indications mentioned in commonly used drug information sources such as Central Drugs and Standards Control Organization website, National Formulary of India, Monthly Index of Medical Specialties, and product information of medicines. Alarming, significant variations were observed both in quantity and quality of information available, warranting immediate measures to harmonize

drug information available in public domain and promote rational drug use.

We have also included a few case reports in the area of rhinosporidiosis of lacrimal sac, unilateral conjunctivitis, novel postendodontic restoration procedure, and bilateral thalamic stroke due to occlusion of the artery of Percheron. I believe you will enjoy and gain knowledge from the contents of this issue. A very happy new year wishes to you all from the JNSBM team.

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