

EDITORIAL

TOWARDS SYNTHETIC GENOMICS: WHAT NEXT TO COME AFTER GENOME EDITING?

1. The recent times had seen a technological outburst in all domains of life. Healthcare, biotechnology and bioinformatics is no exception to the rule, where we now in real-time anticipate the evolution from conventional medicine to molecular medicine. It has been established that molecular medicine and related diagnostic pathology is already changing the landscape of personalized medicine with now curative therapeutics seem well in sight than ever before. Current day genome engineering technologies like Cluster Regularly Interspaced Short Palindromic Repeats (CRISPR) and its various novel innovations is now providing "hope" and a "way forward" for complete eradication of various communicable and non-communicable ailments¹. Advances can already been made to address some of the major health related metabolic killers like diabetes, hypertension, stroke, heart disease and genetic diseases of multiple categories².

2. Though traditional "genome editing techniques" is still under improvements and being modified for better with several novel ideas by every single day, and has shown some genuine promise to provide a microscopic insights with upgraded nanotechnology tools to cause gene alteration at the codon level, final protein products still suffer much due to exactness of payload delivery into cellular region including nucleus, off-target mutagenesis (OTMs) and with compromised net processing efficiency³. Provided ongoing technological refinements allowing wave fronts to touch the desirable areas of shores with optimal capability providing mega promises of curative therapeutics, a newer dimension has dawned on the horizon of gene therapy and molecular technologies. "Synthetic genomics" is one more addition to the arsenal under the umbrella of genomic biotechnologies⁴.

3. "Synthetic genomics" is defined as making gene or gene product from the beginning, implying in simplistic way to create something

from scratch⁵. Conceptually, the life's true essence remains in the four basic life codons once mixed in an appropriate way, with needful stimuli and congenial environment to the (possible) creation of a life structure like a cell or a multicellular structure⁶. Lou *et al* have reviewed the idea of genome synthesis and discussed the "Human Genome Project-Write (HGP-Write)" along with the various prospects and obstacles⁴. The complete grasp of this technology in the right hands will have enormous potential like obviating the need of organ donors, organoid developments, blood donation, and possibly the in vivo management of embryo health issues⁷. Slightly different but another linking technologies as researched by Beads *et al* and Marti-Figueroa *et al* provide single cell genomics to generate specific gastrointestinal cells like paneth cells and 3-D kidney organoids by manipulating genomic engineering^{8,9}. So the shared evidence, albeit not involving completely "synthetic genomics" still can point towards the tide of research in molecular methodologies and thus raises promises within healthcare industry to incorporate human /animal donation free transplant strategies, cure for currently considered permanent disease stamps and a lot more to improve in vivo and in vitro genome handling to provide treatments for infertility¹⁰. Apart from this the concept of "Biocatalyst" in Marine science and engineering can provide novel solutions to the field of pharmaceutical industry by incorporating bio-synthetic drugs¹¹. So the technology as anticipated today can bring a paradigm shift in medical practice and may possibly lead us in towards longevity and a prosperous future.

4. The appeal to "synthetic genomics" is therefore not only attractive, overtime cost-effective, emergence of preemptive medicine and leading disease to optimal cure with much needed availability in the organ transplant markets. While the aforementioned promises linked with synthesizing life structures from

scratch stays, we need to understand the limitless expansion of this biotechnology which may not coincide with the current definition of human and animal life as we see today. Such biotechnological resource given in the wrong or inexperienced hands can cause previously considered mistakes and errors. The fiction movies once considered a thing of fun, could now be created to have the gigantic creatures from past, designer babies, super humans, and probably much more than that¹². Heidari *et al* discussed the birth of synthetic genomic engineering following the evolution of CRISPR technologies highlighted the loads of bioethical issues, human's current day concept of life and death and deontological aspects of genome synthesis and engineering¹³. Bioethics aside the technology is still in its infancy stage with a lot of hit and trial ongoing, animal experiments and attempts to refine the biotechnology from small-scale to large industrial usage. Furthermore, the market place for such technology can only emerge once the techniques and methods could be able to demonstrate optimal efficiency, minimal off-target mutagenic effects and desirable translation of end-products. The worst fear generating shackles for mankind is the biotechnology of synthesis of genome getting out of human kinds, a possible nightmare shared by researchers like Lawrence *et al*¹⁴. Fraser *et al* in this regard has also shared their concerns for its possible use as a biological weapon, which over the last two decades is now getting closer to a real possibility¹⁵. Similarly, others have also shown the misuse of genomic data alteration through scientific novelty in research for probable use as in bioterrorism¹⁶.

5. As we clearly anticipate the incoming biotechnology to evade healthcare market we need to be aware of its lefts and rights, well-oriented about the use of such methodology and know-ledgeable enough to manage such technology. We also need to be aware of its appropriate use, rather be more concerned about misuse and abuse in the world currently dealing with newer faces of terrorism. In order to step further towards the appropriate usage of this

biotechnology we need to define methodologically error-free path for its implementation. Following are the recommendations and suggestion to translate the shared vision into actionable and plausible steps:

- a. Requisite human resource be trained in the field molecular pathology, molecular technology, genetics, bioethics, legal experts and bioinformatics to create a framework of specialties dealing with technical issues regarding genome altering techniques and synthetic genomics.
- b. "Bioethics Oversight Committee" under public sector ownership at national level be formulated to help plan ethically sound molecular methods and use of synthetic genomics for medicinal purpose.
- c. Biotechnology in the field of genome editing and synthetic genomics must be procured/managed within our country on priority basis to help boost healthcare markets, avoiding dependency on other countries and reducing the massive demands of organ donation within our resource scare country.
- d. Timely arrangements of "Molecular Pathology Think Tanks" be managed at Higher Education Commission (HEC) or National Institute of Health (NIH) to discuss incorporation of such technology into health care industry, providing regulatory guidelines, framework for deployments in hospital and pharmaceutical set ups, decisions on bioethics, legal issues, opinion of religious scholars, and finally use in hospital set ups.
- e. Concerned authorities must overview the overall process of genome editing and synthetic genomics for possible use in bioterrorism and misuse of any biotechnology in any other ways.

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Dr Sikandar Hayat Khan

Department of Pathology

Pakistan Naval Ship (PNS), Hafeez

Islamabad Pakistan

Email: sik_cpssp@yahoo.com