Market Analysis & Healthcare Research
AUG-SEPT 2022
BIO-GENAGE GLOBAL FOUNDATION
HEALTH EVOLUTION WITH MISSION & GOAL

- **Aging Research with AI Technologies**
- **AI & Machine Learning, Blockchain to assist healthcare organization in the near future (SDG 3 for 2030)**
- **CRISPR Technologies with HEALTHCARE INNOVATION**
- **Bio-Genage Healthcare Proposal & Summary for SDGs**
- **Mission: Improve the healthcare ecosystem with AI & SDGs**
- **Goals: Improve healthcare with technologies such as Anti-ageing, Longevity, Cancer & HIV, other diseases with Human DNA Repair.**

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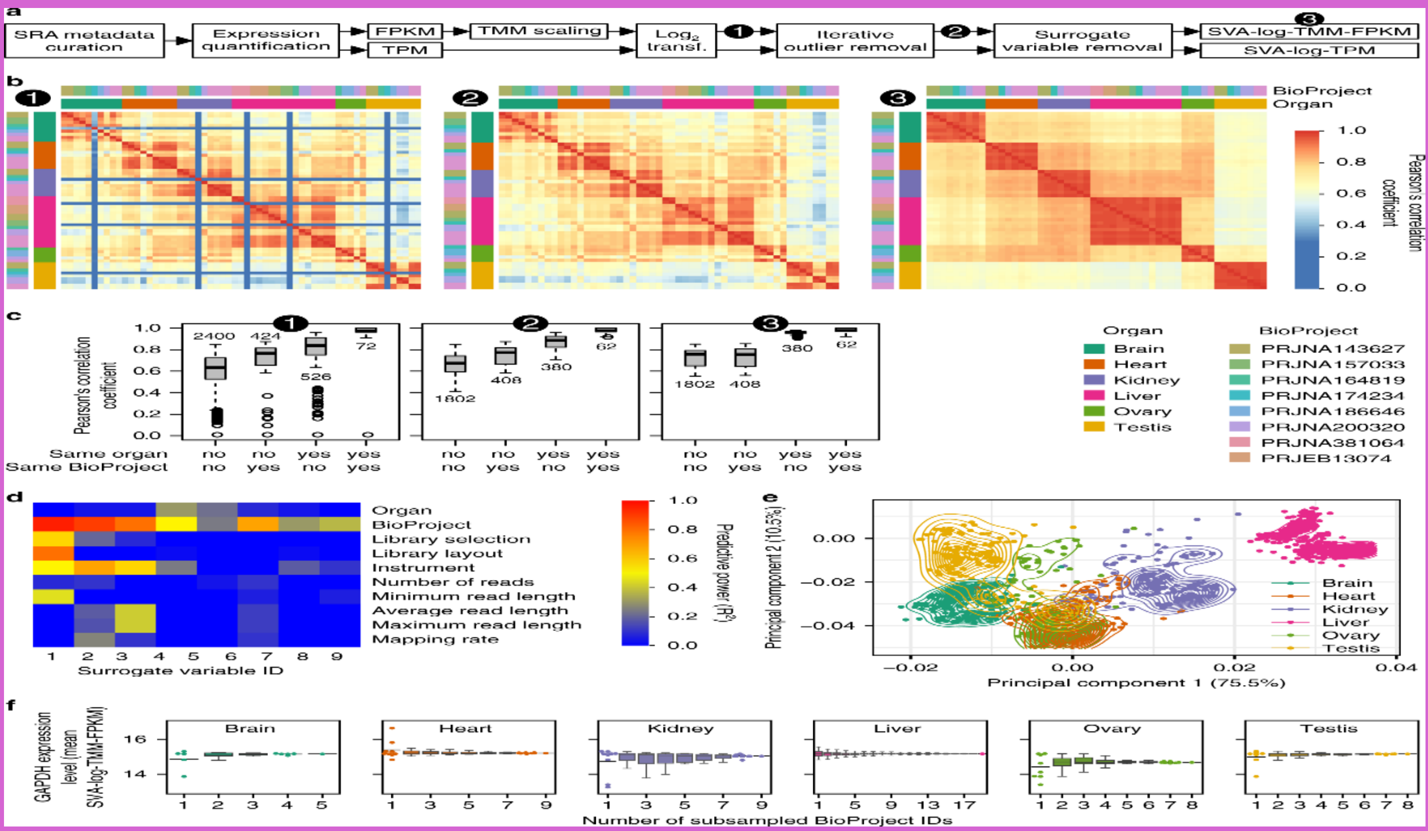
What the genomes of ancient humans can tech us about modern health. From aging research with Machine Learning, AI Analysis of Longevity-Associated Gene Expression; Crispy Technology for Future healthcare innovation, SDG 2030 Mission & Goals, what are Bio-Genage & Bio-Genage Global Foundation Brand Stand for Health innovation & sustainable?

1.Aging Genetic Research is how differences in transcriptomics are associated with the longevity of various species. Unfortunately, at the level of individual genes, the links between expression in different organs and maximum lifespan (MLS) are yet to be fully understood. Analyses are complicated further by the fact that MLS is highly associated with other confounding factors (metabolic rate, gestation period, body mass, etc.) and that linear models may be limiting. Using gene expression from 41 mammalian species, across five organs, we constructed gene centric regression models associating gene expression with MLS and other species traits. Additionally, Scientist use Shapley additive explanations and Bayesian networks to investigate the non-liner nature of the interrelations between the genes predicted to be determinates of Our results revealed that expression patterns correlate with MLS, some across organs, and others in an organ specific manner. The combination of methods employed revealed gene signatures formed by only a few genes that are highly predictive towards MLS, which could be used to identify novel longevity regulator candidates in mammals.

What is cross-species research? Why we use AI algorithm? How does it work out with AI data analysis?

Cross-species studies combine animal and human research in the same study. They inform mechanisms at multiple scales of genetics, circuits and behavior. They bridge animal models and human neuropsychiatric research. They contribute to the development of targeted and personalized interventions. (Algorithm analysis)

Artificial intelligence enables comprehensive genome interpretation and nomination of candidate diagnoses for rare genetic disease. The example of using of artificial intelligence (AI) has made significant inroad in healthcare and a new class of genome interpretation methods are being developed with the promise of removing the interpretation bottleneck for rare genetic disease diagnose through electronic clinical decision support systems (eCDSS) a new AI based, clinical decision support tool for expediting genome interpretation.



A simplified flow chart of the transcriptome amalgamation. The full chart is available in Supplementary Fig. 1. b–d Transcriptome curation within species. Data from Monodelphs domestica with SVA-log-TMM-FPKM metrics are shown as an example. The heatmaps show Pearson's correlation coefficients among RNA-seq samples (b). Each row and column correspond to one RNA-seq sample. The expression levels of all genes were used to calculate the correlation coefficients. Note that anomalous samples contaminated in the curated metadata (low correlation samples in 1) are successfully removed, and that project-specific correlations visible in the uncorrected data (marked 2) are absent in the corrected data (marked 3). The boxplots show distinct distributions of the correlation coefficients depending on whether a pair of samples are the same organ or whether they are from the same research project (c). The numbers of comparisons are provided in the plot. The correlation coefficients are largely improved in within-organ comparisons when surrogate variables are removed, while within-project biases are attenuated. In this species, nine surrogate variables were detected against 52 RNA-seq data from eight projects (d). Analysis of those variables by linear regression highlights the Bio Project feature as the strongest source of removed biases. For full description of predictors, see Supplementary Fig. 4. e A principal component analysis using expression levels of 1377 single-copy orthologs from 21 species. Points correspond to RNA-seq samples. Curves show the estimated kernel density. Explained variations in percentages are indicated in each axis. f Estimated organ-wise expression levels of a housekeeping gene. Since data from relatively many Bio Projects are available, glyceraldehyde-3-phosphate dehydrogenase gene (GAPDH, Ensemble gene ID: ENSGALG00000014442) in Gallus is shown as an example. Points correspond to the average expression level calculated by random subsampling. All data points and the median value (bar), rather than a boxplot, are shown if the number of subsampled Bio Project combinations is <10.

Boxplot elements are defined as follows: center line, median; box limits, upper and lower quartiles; whiskers, 1.5 × interquartile range; points, outliers.

How are algorithms used?

An algorithm is set of rules or instructions used to solve complex problems. In may STEM fields, algorithms are used by computer programs to streamline processes.

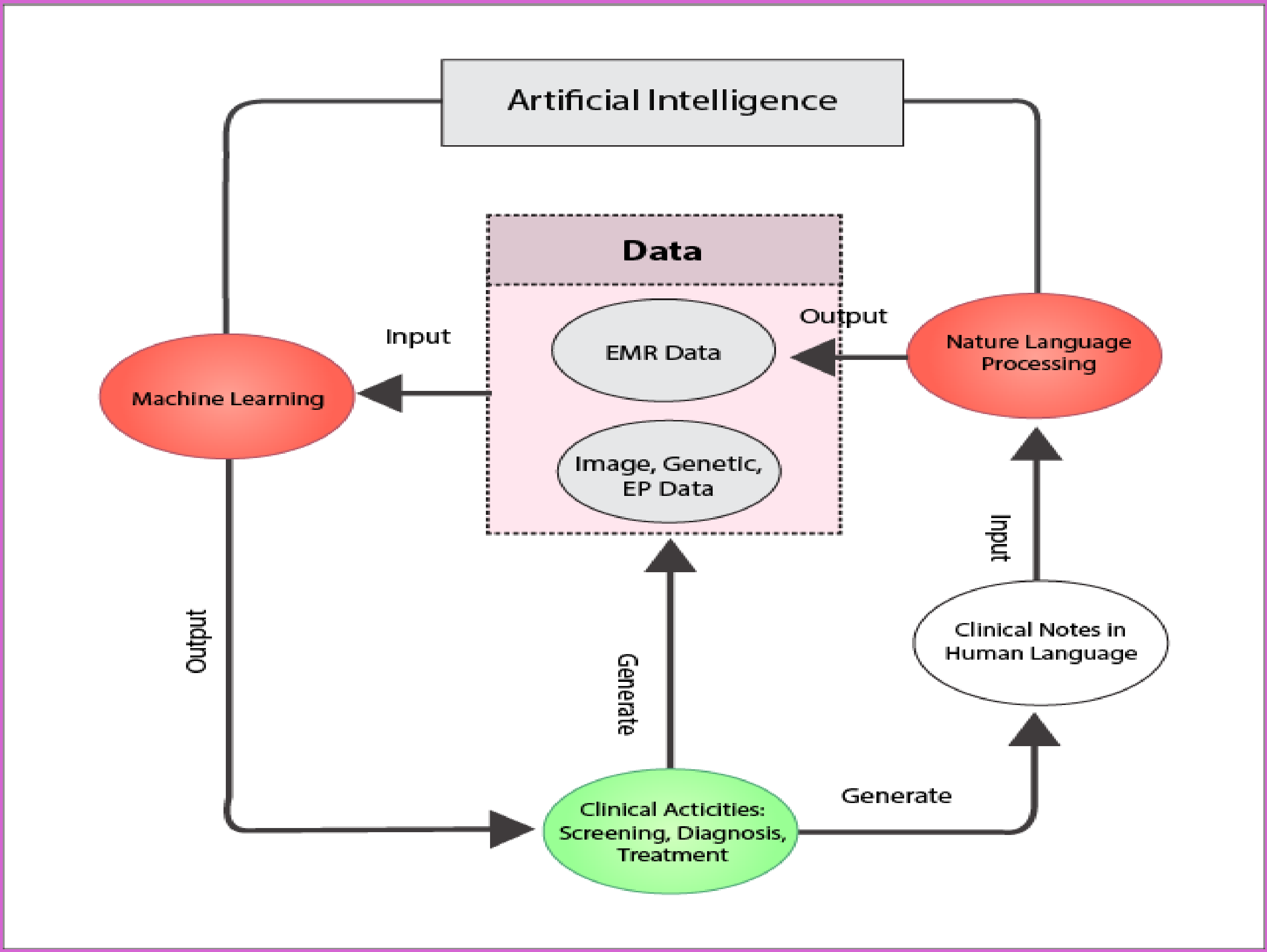
How to build an algorithm in six steps

1. Determine the goal of the algorithm.
2. Access historic and current data
3. Choose the right models.
4. Fine Turning
5. Visualize your results
6. Running your algorithm continuously

Conclusion:

Based from MIT and Harvard researches about their health administration issues. Algorithm is one of the first languages to enables computers to run multiple programs simultaneously. Today it powers the entire veteran health administration's clinical records management system and Epic, America's largest electronic health record software company**. The second benefits and best friends which helps for clinician-scientists are probabilistic data matching. For examples, the high-throughput sequencing which called analyzing gene and protein sequences has ushered in a new age of genetic discovery, making it possible to cheaply and quickly find mutations among the 3 billion base pairs of the human genome**. If identifying mutations is just the first step, though. If it falls to biologists, aided by computer algorithms, to make sense of the growing body of data, to work out which genes and proteins confer disease and how. Those algorithms are the search tool of Blast (Basic Local Alignment Search Tool). Another study explaining the "neighbor-joining" algorithm, which, when paired with genetic sequencing, allows biologists to better understanding the evolutionary relationships among species or populations. Also, the other common use one is google search by page ranking. Whatever the platform, it's a complex algorithm known as "page rank" that does the work by scouring the Internet for pages containing the key words It's certainly democratized it and put more information within easy reach of patients.

For Medical Algorithms which create decision aids for better, safer care. A medical algorithm can be as low-tech as a look-up table or decision tree (if symptoms A, B and C are evident, then use treatment X). Or it can be as complex as the programming behind mechanical ventilators. Medical Algorithms remove some of the uncertainty from medical decision-making and improve the efficiency and accuracy of provider teams. They developed by providers for providers, and they're evidence-based and data driven. The last example for using AI Algorithms are their scoring systems, like Apgar for evaluating a newborn's condition at birth or APACHE for determining the severity of patients in intensive care, help physicians monitor and predict a patient's prognosis based on multitude of factors, from heart rate, oxygen levels to neurological reflexes. It's a system for seeing a patient holistically, a prognosis or wellness meter. So far, the most benefits of AI healthcare can learn features from a large volume of healthcare data, can obtain information in treatment design or risk assessment, can help develop precision medicine and new drugs based on the faster processing of mutations and links to disease; Also, AI can provide digital consultation and health monitoring services even extent of being "digital nurses" or "Health bots"

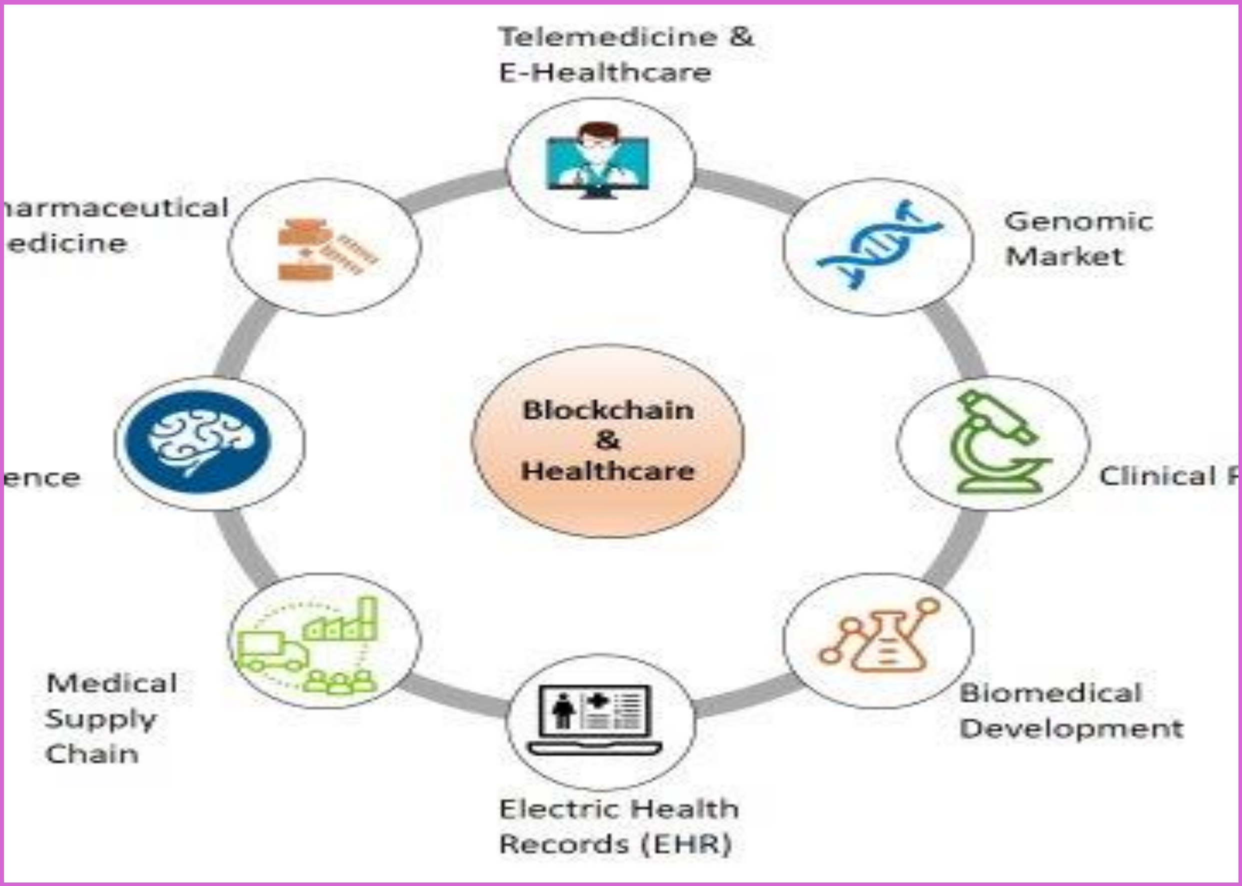


1. AI & Machine Learning to assist healthcare organization in the near future (SDG 3 for 2030)

A panoramic view and swot analysis of artificial intelligence for achieving the sustainable development goals by 2030: progress and prospects. The development and implementation of new technologies usually raises certain fear and aversion amongst people against them. This sense of antagonism is typically motivated by collective lack of knowledge or familiarity towards the features and potential benefits of these technologies. AI in particular currently originates some degree of hostility in certain communities, owing to the feeling that its extensive use may trigger unknown changes in human daily lives. Nonetheless, the use of AI is enabling the automation, traceability and optimization of several human activities, many of which would facilitate the attaining of the SDG. Check below reference regarding the SWOT of AI healthcare for SDG 3 as well.
https://sci2s.ugr.es/sites/default/files/ficherosPublicaciones/2906_Palomares2021_Article_APanoramicViewAndSwotAnalysisO.pdf

2. How is blockchain technology used in healthcare?

- Healthcare blockchain technology
- Blockchains in healthcare can be envisaged in five primary areas:
- Managing electronic medical record (EMR) data.
- Protection of healthcare data.
- Personal health record data management.
- Point-of-care genomics management.
- Electronics health records data management.



3. How is CRISPR innovative?

CRISPR's search-and-snip functionality is especially useful in the presence of natural repair enzymes that lurk near DNA, looking for and patching up breaks. By delivering beneficial DNA fragments to the vicinity of sequences that are targeted and cut, scientists can leverage those repair enzymes to rewrite the genome.

4. What advancements have been made with CRISPR?

CRISPR technology is the newest and most advanced gene-editing tool that allows researchers to modify and alter gene functions for transcriptional regulation, gene targeting, epigenetic modification, gene therapy, and drug delivery in the animal genome.

5. **CRISPR is a family of DNA sequences found in the genomes of prokaryotic organisms such as bacteria and archaea. These sequences are derived from DNA fragments of bacteriophages that had previously infected the prokaryote.** The CRISPR tool together with Cas endonuclease is a powerful programmable nuclease system (Barrangou et al., 2007). Studies conducted by Jinek et al. (2012) unveiled a double RNA, known as a guide RNA (gRNA) which consisted of a 20-bp CRISPR RNA (crRNA) and universal trans-activating crRNA (tracrRNA). This RNA coupled with Streptococcus pyogenes type II Cas9 protein can induce cleavage of specific target DNA sequences in virtually any organism. The Cas9 nuclease activity is initiated by protospacer adjacent motif (PAM) sequence NGG, which is usually located next to the target site (Anders et al., 2014). It is possible to engineer DNA Cas9-mediated DSBs at a specific genomic locus. Non-homologous end-joining (NHEJ) can induce DSB repair that disrupts the target gene, generating insertions and deletions. Another way of repairing Cas9-mediated DSBs is by homologous directed repair (HDR), which allows specific gene editing by integrating genetic modifications into the target template (Thomas and Capecchi, 1987; Salsman and Dellaire, 2017).

Applications of CRISPR/Cas9 in Biomedical Research-Genome Editing

Genome editing is a major development in biomedical research, with the current trend of innovative approaches providing directions for the treatment of various genetic and non-genetic diseases in the future. The availability of the CRISPR/Cas9-mediated gene and genome editing system has enabled the advent and use of more efficient strategies in gene targeting and the creation of gene edited avian species. This has guided recent and on-going advancements in biomedical research in the animal biotechnology field.

6. **CRISPR/Cas9 technology has ushered in an innovative era in genome editing technology for the manipulation of invaluable avian models such as chickens. By** applying CRISPR/Cas9 gene editing technology, researchers will be able to create an efficient bioreactor system for producing valuable proteins in poultry species. In chickens, the bioreactor system will enable efficient production and easy purification of egg white protein in large amounts (Lillico et al., 2005). The development of chickens as bioreactors for the production of target proteins has mostly utilized ovalbumin promoters (Park et al., 2015). The development of transgenic hens for protein production in eggs is highly necessary for the expression of therapeutic proteins which has resulted in significant advances in the generation of transgenic chicken models in this advancing era of genome editing. Oishi and colleagues have shown recently that the human interferon beta (hIFN-β) can be integrated into the chicken ovalbumin locus used in the production of hIFN-β in egg white (Oishi et al., 2018). Oishi et al. (2016) used CRISPR/Cas9 technology to demonstrate that disruptions of ovalbumin and ovomucoid genes had the potential to produce low allergenicity in eggs, which allowed a reduced immune response in egg white sensitive individuals. Therefore CRISPR/Cas9-mediated genome editing is expected to be key in the mitigation of allergic reactions caused by chicken eggs in some individuals by ensuring that chicken meat and eggs are allergen-free. This can be achieved by knocking out allergen-related genes such as ovalbumin and ovomucoid. This type of progress is important in the production of safe food products as well as the production of vaccines in the pharmaceutical industry.

The production of therapeutic antibodies against antigens is now possible through humanized chicken for therapeutic applications. The loxP site was inserted into the variable region of the immunoglobulin heavy chain using the CRISPR/Cas9-mediated approach (Dimitrov et al., 2016). Production of these genome-edited chickens will provide numerous opportunities for the discovery of therapeutic antibodies: a game-changer in biomedical research.

CRISPR allows the benefit of accessing genetic characteristics that cannot otherwise be used for poultry production. Therefore CRISPR/Cas9 becomes a very powerful and robust tool for editing genes that allow for the introduction or regulation of genetic information in poultry genomes. However, the CRISPR/Cas9 technology has several limitations that need to be addressed to enhance its use in the poultry industry. This review evaluates and provides a summary of recent advances in applying CRISPR/Cas9 gene editing technology in poultry research and explores its potential use in advancing poultry breeding and production with a major focus on chicken and quail. This could aid future advancements in the use of CRISPR technology to improve poultry production.

7. Important Applications of CRISPR Technology

- Cell and gene therapies. CRISPR is poised to revolutionize medicine, with the potential to cure a range of genetic diseases, including neurodegenerative disease, blood disorders, cancer, and ocular disorders
- Diagnostics. ...
- Agriculture. (Improve our crops)
- Bioenergy. (Reduce the biofuel, clean energy, good for climate change purpose)

8. What is an example of an application of CRISPR technology for human health?

For example, CRISPR-based strategies could reduce infectious disease morbidity by gene editing **mosquitoes to prevent transmission of malaria** as bill gate mentioned in his foundation news. https://www.gatesfoundation.org/ideas/media-center/press-releases/2005/10/gates-foundation-commits-2583-million-for-malaria-research10. Immunogenicity

In vivo delivery of CRISPR systems can induce immune reactions toward the foreign materials through inducing significant innate immunity and/or adaptive immunity (humoral immunity and cellular immunity) in humans.139 Innate immune responses might be triggered by guide RNAs. To overcome this issue, phosphatase treatment of in vitro–transcribed guide RNAs is designed, which showed subdued innate immune responses without impairing the role of guide RNAs.140 Unfortunately, a major concern is that humans may have pre-exposure to the same antigens of Cas nuclease effectors (e.g. Cas9) and/or delivery vectors (e.g. adenoviral vectors) that are needed to carry the effectors for the target treatment.141,142 The exposure to these materials may trigger the body's humoral immunity mediated by antibodies or cellular immunity directed by cytotoxic T cells, which may result in severe adverse reactions, death of Cas-expressing cells and treatment failure.143,144 Engineering the Cas protein to create a low-immunogenicity Cas effector and developing new delivery vectors with lower chances of prior exposure in humans may be possible strategies to minimize the immune responses, improve safety, and maximize therapeutic effects of the CRISPR-Cas system. Importantly, prior to every clinical trial, one may have to detect related immune reaction components, such as antibodies against Cas proteins and T cells reacting with Cas proteins or vectors, and continue to monitor immune responses during treatment.

Want the latest in-depth analysis of how the CRISPR market is developing? Download PatSnap's exclusive new report. Posted March 1, 2022

YOUR LOGOTYPE

What is BIO-GENAGE stands for?

- **BIO-GENAGE stands for Global Biotechnology which specific researches for Anti-Aging & Longevity to regenerate cells, DNA Repair for inner cells or stem cells. Even research for CRISPR Technology regarding the Caspr9 System, Gene-Editing, DNA Repair.**

What are the 3 main types of biotechnology from BIO-GENAGE?

Types of Biotechnology Innovation for Powerful House of Our Future Health:

- Medical Biotechnology. Medical biotechnology is the use of living cells and other cell materials to better the health of humans- Anti-Aging, DNA Repair for genes, Immune System, HIV, Cancer,
- Agricultural Biotechnology- research for Biofuel reduce warm temperatures
- Industrial Biotechnology- DNA Repair Products or Tools, Natural Nutritious foods and vitamins.
- Environmental Biotechnology-Reduce Air & Sea Pollutions, Green Energies, Agricultures Improvements.

What are the benefits from Bio-Genage Global Bio-Health?

Like earlier technologies, biotechnology promises to provide many advantages, especially in three broad categories: environmental protection, higher yields, and improvements in human health. Our company researches with AI healthcare which could build strong powerhouse to our future human health with honest figures and evidences.

Bio-Genage Powerful House of Health including the following parts:

- Bio-Science Nutrition Products
- Skin Care Products. (Rejuvenation)
- Bio-Environment Clean Products -Biofuels
- Genetically Modified (GM) Crops. - Bio-Food

Why are Bio-Genage Global Foundation having great potential to achieve in BIOTECH part for the sustainable development goals?

- We improve people's lives and the planet's sustainability
- End hunger, achieve food security and improved nutrition and promote sustainable agriculture.
- Ensure good healthy lives and promote well-being for all at all ages. SDG 3
- PERSONALISED precision Medicine and Diagnosis
- Advance therapies- Bio health solution (Gene, Cell and Tissue Therapies)
- Development innovation of global organic nutrition foods & vitamins with solutions
- Gender Equity- health developments with Science for Girls and Women to improve their lives in better conditions and understanding.
- Influencers for Biotechnology offers up alternatives to produce
- Clean energy and ensure more efficient power use, as well as reusing urban and forestry waste and by-products from certain industries, reducing them

- impact on the environment. Alternative sources of biomass, from forestry and agriculture, are used. More and more to produce clean, renewable energy.
- Biotechnology solutions:
- Biofuels and biomass from waste or by-products.
- Climate Actions, Impact others to promote use AI products to reduce air temperatures for indoor or even our door.
- **Life Below Water** Biotechnology helps preserve marine ecosystems by using techniques to monitor marine habitats and cleaning contaminated water through microorganisms, microalgae and cyanobacteria.
- Biotechnology solutions:
- Bioremediation uses living organisms to clean up and **break down pollutants like plastics in the oceans.** Biotechnology applied to fish farming improves fish health system.

What is Bio-Genage Mission & Goals within these 5 years?

- Improve human's health life with great ecosystem
- Overcome climate change caused more health diseases from food pollutions
- Less metallic and chemical for nutrition and foods
- Health Education and Training regarding protecting our health with natural foods and water.
- Professional knowledges and researches about the whole figures in the global markets should alert in what parts to avoid more health diseases, especially after Covid-19.
- Discover and explore more about DNA repairs from foods and nutrition sides to improve our future health
- Less meat eaters to reduce more carbon dioxide especially those beef-lovers.
- Food waste and Zero Hunger are very important, Biotech can help discover we can help
- end hunger by making crops more efficient and nutritional using techniques like genetic engineering. Plus, by adding probiotics and prebiotics to foods, biotechnology helps make them even healthier. Furthermore, biotechnology techniques can be used to detect toxins and contaminants in food, helping ensure food safety. End human hunger, can achieve food security and improved nutrition and promote sustainable agriculture.

Biotechnology Future Solutions from Bio-Genage:

- Gene editing tools like CRISPR for sustainable human health & agriculture
- Personalized nutrition for better diets that guarantee optimal health and Zero Waste.
- Probiotics and prebiotics in foods to improve their nutritional properties avoid diseases
- Biosensors and biotechnology techniques to guarantee food safety Feeds and probiotics and treatments as and disease detection for healthier livestock production
- Proper nutritional supplements and products could slow aging and longevity for normal ages.