Vision Paper

Global Trends to Improve Human Health (2022-2052): Plant Molecular Farming and Edible Plant-Based Vaccines

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Symbol of mRNA**

Introduction

Beginning of 2022, worldwide there are 298,915,721 confirmed cases of COVID-19 and **5,469,303 deaths** so far from the coronavirus COVID-19 outbreak since January 2020. Up to now, globally a total of 9,126,987,353 vaccine doses have been administered (WHO, 1/2022). A virus named COVID-19 has brought and continue to bring the world on its knees. The immune system of millions of people was/is not strong enough to tackle this virus. National restrictions, lockdowns and safety instructions were implemented in order to slow mote the pandemic. Functioning and registered pharmaceuticals or vaccines to tackle the problem were not on the market beginning 2021. But then, BioNTech & Pfizer have brought an Anti-COVID-19 vaccine to the market within 11 months only! These mRNA-based vaccines have safeguarded the life of millions of people

worldwide today and will do it in future as well. Nevertheless, it is crystal clear, that further COVID-19 mutations will happen in future. But nobody knows that this will happen with which infection rate or pathogenicity rate, or death rate. Consequently, the world is forced to foster solutions to overcome the actual pandemic and to be better prepared for coming ones.

Food to Boost DNA Repair/Nutrigenomics

"Should I eat for my DNA?"

Some headlines of papers and food recommendations to feed or repair your DNA are listed here:

- "Broccoli repairs DNA" (broccoli)
- "3 DNA Repair Foods" (berries, cruciferous vegetables, tea)
- "5 Superfoods are good for DNA repair" (turmeric, pomegranate, virgin coconut oil, mushrooms, green tea)
- "6 Foods to Boost DNA Repair" (lemons, persimmons, strawberries, broccoli, celery, apples)
- "7 Foods that will reverse DNA Damage – Eat this, not that" (watercress, blueberries, soy milk, spinach + tomato, broccoli, fruit juice, green tea)
- "7 Foods that will plug the holes in your DNA" (broccoli, wild caught salmon, berries of all varieties, avocados, chlorella, chocolate, green tea)
- "9 Foods will plug the holes in your DNA"
- "11 Genius, Science-Backed Ways to Save Your DNA"
- "30 Foods that help you beat bad genes, Your DNA isn't your destiny"
- "30 Vegetarian Capsules – DNA Protection Formula".

However, most of the recommendations are not proven by certified clinical trials.

Greger (2019) opined "It is estimated that, on average, there are 800 incidents of DNA damage (in our bodies) per hour," which is about 19,000 hits to our DNA every day. What's more, "that DNA damage can cause mutations and give rise to cancer, if not repaired." Humans have estimated 20,000-25,000 human protein-coding genes and five individually differentiated DNA repair systems encoded by >150 genes and protein products. DNA damages are happening frequently, with about 2×10^5 damaging events per cell per 24 hours. Meanwhile it is well known, that cancer is associated with DNA instability due to increased damage to DNA. DNA repair capacity is regarded as an indicator of individual cancer susceptibility and growing evidence suggests that DNA repair capacities are an important factor in tolerance to chemotherapeutics or herbs. Food, functional food, pharma foods, supplements, herbs and specific diets, can protect against DNA damages by upregulating the immune system and modulating the repair capacity (Tyson and

Mathers, 2007; Kiwerska and Szyfter, 2019; Blog, British Journal of Sports Medicine, 1/2022).

Consequently, nutrigenetics, nutrigenomics and nutraceuticals, metabolomics, transcriptomics, proteomics and metagenomics are more and more relevant in nutritional sciences. They are cornerstones for precision and personalized nutrition and trigger the shift in disease prevention from pharmaceuticals to neutraceuticals. According to Precedence Research (2021) the global nutraceutical market size was valued at $US 160.3 billion in 2020 and forecasted to reach $US 314.2 billion by 2030.

Food is becoming more and more health relevant, more diversified, more specified, more differentiated, more complex, and less transparent, not simple to manage, not simple to select, not easy to decide, and a lot of people become confused concerning healthy nutrition (Kern, 2019).

Plant-based Diet and COVID-19

"A vegan or plant-based diet cannot prevent a person from developing COVID-19, but it may help support a healthy immune system. This could aid in SARS-CoV-2 infection prevention and lower the risk of severe symptoms. People should note, that there is no direct evidence to support a link between a plant-based or vegan diet and protection from COVID-19 or other severe diseases" as stated by Richards (3/2021) in a summary note.

Due to the fact, that vaccine access is still uneven in a lot of countries, especially in Asia, many people are looking for herbal treatment, because they trust more in traditional medicine, rather than Western, ones (Fawthrop, 2021). Herbal and natural do not always mean that they are safe. For example, in India, '*Giloy*', from heart-leaved moonseeds (*Tinospora cordifolia*) was marketed as an herbal supplement to booster immunity against COVID-19. Actually, the consumption of '*Giloy*' without prescription and monitoring can cause damage to organs. It causes acute hepatitis with autoimmune features. The causality assessment revealed probable liver injury in 76 % of analysed people, who have consumed unprescripted doses of '*Giloy*' for an average of 46 days (Chauhan, 2022).

Nevertheless, traditional and complementary medical services as well as Western supplements are booming during the running COVID-19 pandemic as well as post COVID-19 period. COVID-19 pandemic especially surged the demand for immunity dietary supplement products.

The global herbal medicine market has generated a value of $US 83.0 billion in 2019 (insightSLICE, 2/2021), and it is expected to increase to $US 136.02 billion by 2023 (Market Research Future, 2021), and to $US 550.00 billion by 2030 respectively (insightSLICE, 2/2021).

The global dietary supplements market size was $US 61.20 billion in 2020. The market is projected to grow from $US 71.81 billion in 2021 to $US 128.64 billion in 2028 (Fortune Business Insides, 1/2022).

Nevertheless, all recommendations and products must be evidence-based by clinical trials, safe, with assured quality, and authorized in order to contribute to a holistic personal approach and to achieve health and wellbeing.

A disclaimer written *e.g.*, on the first pages in the book of Wilkens and Meyer (2022) titled: "*Corona natürlich behandeln*" is very important for clarifying the context and point of view, is very helpful, fair, and appeals on the personal responsibility of each individual.

> "*We are not responsible for any damage caused by the use of the treatment agents through the omission of other possibilities which could arise.*"

Personalized Nutrition

"The 'Personalized Nutrition' concept of the past (Dr. T. Addis, early 1920s) was significantly advanced by Dr L. Pauling in 1968 when he coined a new term: "*orthomolecular*" nutrition. This concept focuses on meeting the genetically determined nutrient needs of the individual in optimal concentrations to support the proper structure and function of the body" (Bland, 2019).

'Personalized nutrition' is becoming big business combining artificial intelligence, digital nutrition with health. Nutrigenomic, metabolomics, biometrics, and informatics are being harnessed to create an evidence-based approach to medical nutrition therapy to prevent and manage chronic degenerative diseases. Bland (2019) is realizing this concept by having founded the 'Personalized Lifestyle Medicine' Institute in Seattle, Washington, USA. Worldwide more and more nutrition research institutes established Professorships for 'Personalized Nutrition' to develop science-based diet recommendations specific to an individual, to optimize the wellness and future health of people around the world.

PD Dr. Ölzem Türeci from BioNTech has taken over a Professorship for '*Personalized Immune Therapy*' against cancer at the Johannes Gutenberg University in Mainz and the Helmholtz-Institute for '*Translational Oncology (HI-TRON)*' in December 2021 (Deutsches Krebsforschungszentrum in der Helmholtz-Gemeinschaft, 12/2021). She will translate mRNA knowledge and technology to combat cancer individually.

Prof. Ugur Sahin, CEO of BioNTech was ushering a new area of cancer medicine. Sahin did outline the following:

"When we started BioNTech in 2008 we asked ourselves a fundamental question – if every patient's tumor is unique, why do we treat all patients the same? We saw immense potential in leveraging a tumor's unique profile to enable

the patient's immune system to locate and target the specific cancer cells and engage to attack the tumor. We founded BioNTech to advance and develop key technologies and bring together the right people to realize our vision for the future of cancer medicine" (Sahin, 12/2021).

The question will be: "How long takes the time to see a joint Professorship of both disciplines – the first Professorship for 'Personalized Nutrition & Personalized Immune Therapy'?

In July 2021, the World Economic Forum in Davos, Switzerland attracted a lot of attention with the following questions: "What if? You are what you eat: January 2035 - What if everyone's nutrition was personalized?

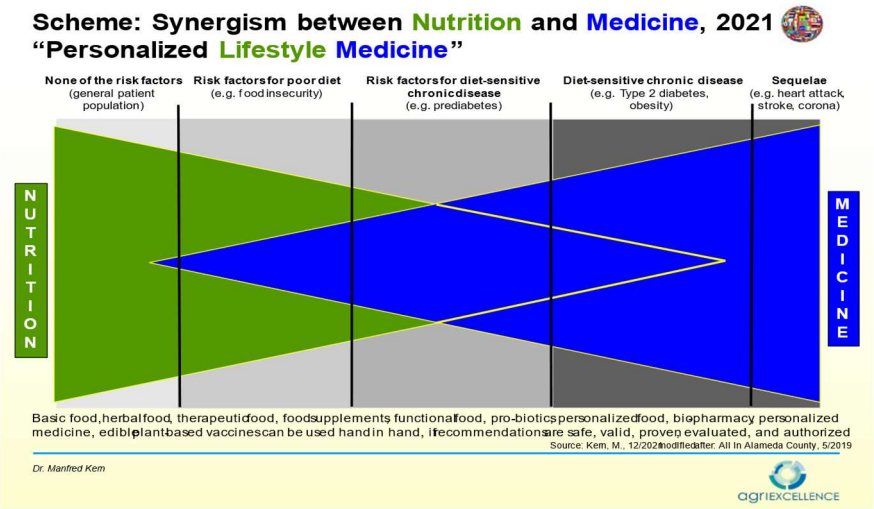

FIG. 1: Scheme: Synergism between Nutrition and Medicine - "Personalized Lifestyle Medicine", 2021

A similar question can be raised beginning 2022: "What if? You are what you are: February 2052 -What if everyone can avoid or can be cured by personalized cancer medicine?" (Kern, 2021)

COVID-19 pandemic has clearly shown, that vaccination and chemical drugs are key solutions to safeguard human life worldwide. Demonstrating the joint potential to provide people with medicines to safeguard health and life, to reduce hospital stays and long-term care costs.

Global bio-pharmaceutical market is around $US 1.3 trillion (IFPMA, 4/2021), whereby the global vaccine market was valued at $US 187 billion, with COVID-19 vaccines contributing $US 137 billion (Research and Markets, 2021) or $US 150 billion (World Economic Forum, 2021).

Already in January 2018, Pardi *et al*., published a visionary paper, titled: "mRNA vaccines – a new *era* in vaccinology". They concluded the following: "*The future of mRNA vaccines is therefore extremely bright, and the clinical data and resources provided by these companies and other institutions are likely to substantially build on invigorate basic research into mRNA-based therapeutics.*" Nowadays, mRNA technologies are being used in a wide variety of fields.

mRNA Technology and Nanoengineering - Vaccine Production in Plants

Referring to the introduction of this paper addressing mRNA technology being used producing anti-COVID-19 vaccines in an extremely short time, mRNA technology and nanoengineering in plants are offering new horizons to produce anti-virus vaccines or other valuable products.

- "Grow and eat your own vaccines?" was the title of a paper published by Bernstein (UC Riverside, University of California) 9/2021. Plant-based mRNA vaccines, which can be eaten are under development. mRNA vaccines can be successfully delivered into the part of plant cells. By using nanoengineering, leaves of. *e.g*., spinach or lettuce were covered with nano-formulated droplets of mRNA vaccines, so the chloroplasts are triggered to produce the vaccine within the leaves of the plants. The vision is to turn edible plants into mRNA vaccine factories.
- Medicago, a biopharmaceutical company and pioneer in '*plant-based therapeutics'* in Quebec City, Canada (12/2021) presented positive Phase 3 data about their plant-based vaccine using the tobacco plant, *Nicotiana benthamiana*. The vaccine candidate has not yet been approved by any health authorities. If authorized, this COVID-19 vaccine would be the world's first ever plant-based vaccine approved for human use. The vaccine is made with virus-like particles, which have the same structure as the coronavirus but do not contain any of its genetic information. It uses exclusive technology for creating Virus-Like Particles (VLP) for protein vaccinations. VLPs are engineered to look like viruses in their natural state, allowing the immune system to recognize them more easily. VLPs are non-infectious and unable to multiply because they lack core genetic material (Kuluru, 1/2022). After approval, the company has capacities to produce millions of doses.
- Mid December 2021, Walter Reed Army Institute of Research (WRAIR), USA, published a Spike Ferritin Nanoparticle (SpFN) COVID-19 vaccine, which may provide a broad protection against SARS-CoV-2 variants as well as other coronaviruses; clinical trials are running.

Plant Molecular Farming (PMF) and Human Health

PMF in High-Income Countries (HICs)

In UK, Moolec Science Limited, an Ag-Food company in the field of alternative proteins and food ingredients is using plants as bioreactors. For example, they put the genome of animal protein's gene DNA codes inside the genome of main plants used for food ('plant-produced proteins' 'PPPs') (Moolec Science Limited, 2021) to produce protein-based meat. Their mission is to produce real animal protein in plants and to develop affordable animal-free ingredients. In 2021, Moolec Science Ltd. Formed a joint venture with Grupo Insud, a globally acting conglomerate producing biosimilars and other ingredients for the pharmaceutical industry (Veganomist, 8/2021).

They are pushing forward 'plant molecular farming' to produce animal-free and healthy products. They are convinced to speed up the protein transition worldwide. Depending on international and national regulations 'plant molecular farming' will contribute to food security and health (Southey, 2020).

Convinced from the necessity of plant molecular farming Kern (2007) has written: "Plant-made pharmaceuticals (PMPs) provide several advantages over traditional production of bio-pharma: they can be produced at significantly lower costs and in higher volumes; they avoid risks associated with animal-based products (e.g., mammalian infection); they can be stored by drying rather than expensive and energy intensive refrigeration; and they can be delivered in alternative modes (e.g., oral vaccine rather than by needle) that are often cheaper, safer and more convenient." Furthermore, it was addressed, that: "Pharma/BioPharma will not believe in PMP technology until a therapeutic protein based on this technology comes to the market."

Big Pharma is still staying on traditional fermentation-systems, only small companies or start-ups are going for the development of PMF. Implementing a low-cost production, the prices for medication will go down and will contribute to reduce the health care costs of societies, especially in low- to middle-income countries.

Big Pharma as well as investors are reserved concerning the implementation of PMF, because there is uncertainty in intellectual property rights, biosafety, and regulatory framework. They prefer and relay on their established production platforms.

Meanwhile, the first plant-based therapeutic was launched by Protalix in 2012 and many proof-of-concept and plant-based therapeutics and vaccines for humans and animal are available. For example, the production of antibodies in tobacco plants against *Ebola* by the Start-up ZMAPP Biopharmaceutical in 2014 (Qiu *et al*., 2014).

To go into more detail concerning PMPs, have a look to the comprehensive review written by Chung *et al*. (12/2021) titled: "*Integrating plant molecular farming and materials research for next-generation vaccines.*"

Beginning 2022, plant molecular farming is a niche market, but will gain in market share triggered by the application of cutting-edge technologies. Especially, transient transformation, which induces only a temporary expression of a gene, is very promising and used meanwhile in many laboratories worldwide, but transgene plants would significantly increase the production of plant-based bio-fortified products or medicines including vaccines.

PMF needs no high sophisticated infrastructure, can be done very quickly and locally in each region of the world. However, impact of weather can put the production at risk, and needs specific protection measurements.

Furthermore, the level of the recombinant protein or peptide in plants has to be increased significantly, because the expressive level affects the cost of growing, processing, extraction, purification and waste disposal. The whole downstream processes such as extraction, purification and formulation have to be optimized analog GMP (good manufacturing practice) to enable, that products will reach the industry or clinics.

In the review of Buyel (2019) the multiple-purpose use of such plant bioreactors is well described. For example, the use of secondary protein products, the recovery of bulk protein, the isolation of secondary metabolites and chemical building blocks as well as the use as bioenergy or biofuel.

Other drawbacks are the unclear regulatory/biosafety framework for biopharmaceutical manufacturing, which hampers investments in plant-based expression systems and last, but not least the socio-political and ethical acceptance.

Very relevant is the fact, that links to operative partners down the value chain are often not established (Schillberg and Finnern, 2021). To come from bench to market implicates, that it is necessary to run preclinical and clinical trials, which are complex, expensive, risky and time consuming. This requires significant industry resources or collaboration with powerful partners and must be considered from the early beginning – a positive example of a synergistic cooperation is realized by BioNTech and Pfizer.

Science based clinical trials are prerequisites for all products or recommendations in the field of healthcare, not for PMF only.

Nevertheless, in Italy, Lico *et al*. (12/2020) have made an assessment concerning the potential of plant molecular farming using transient expression of COVID-19 vaccines. They concluded that two large-scale automated vertical farming facilities as described by Holtz *et al*. (2015) and Buyel *et al*. (2017) would be sufficient to produce enough biomass in one week to meet Italy's entire demand for VLP (virus-like-particle)-based vaccine and diagnostic reagents. All

this could be done with 10 percent of the capital costs for fermenter-based production. PMF, in form of vertical farming would be very suitable to improve the preparedness for future epidemic or pandemic diseases.

Capell *et al*. (7/2020) have outlined, that the advantages of PMF were not persuasive to displace the major production platforms used in pharma industry during the past. But now, "*the PMF community is extremely active in establishing plant-based processes for the production of diagnostic and therapeutic proteins to fight against COVID-19*." The pandemic will be an unprecedented test for PMF.

Labato Gomez *et al*. (2021), a paper written by 53 scientists from 10 countries, concluded that up to now, PMF was not ready for a large-scale response to tackle endemic diseases (SARS, MERS, Ebola, Zika fever, HIV/AIDS, Human papillomavirus, Hepatitis). Scientific advances done by scientists are not sufficient to guarantee a solution. They address, that PMF has to overcome the barriers of industry inertia, to consider the requirements of GMP, and needs a globally accepted regulatory framework.

Beginning 2022, realistically, an appropriate solution to fight COVID-19 by PMF was not realized in time. PMF is not a silver bullet solution and needs interdisciplinary cooperation from the early beginning. PMF has to be significantly improved in order to provide an alternative effective tool to combat epidemics, pandemics, or other dangerous diseases.

PMF in Low- and Middle-Income Countries (LIMICs)

"The uneven diffusion of technology – both old and new – is well documented in the UNDP report 2001. If developing countries have no or only limited access to biotechnology as such, they will increasingly fall behind industrialized nations. They run the risk of missing out on potential opportunities in the field of biotechnology. Ismail Serageldin, former chairman of CGRIAR (Consultative Group on International Agricultural Research) has described this as "Scientific apartheid" (Kern, 2002). Unfortunately, this is the bitter reality 20 years later in 2022 and it is necessary to repeat the following: "There is an ethical imperative not only to keep technology portfolio open to biotechnology and genetic engineering, but also not to lose time. Everyday lost, every decision delayed, will kill people, increase poverty and will damage the environment, and put out future at risk."

The potential of PMF in LIMICs is often addressed because there are so many positive perspectives, but practical use is not the reality.

Zeghibe (5/2021) from Wellesley College, Massachusetts, USA has published an extensive investigation, titled: "Growing into Their Own? Plant Molecular Farming and the Pursuit of Biotechnological Sovereignty for Lower- and Middle-Income Countries." Some key results are summarized in the following:

- In most of LIMICs, there is no secure supply of affordable pharmaceuticals nor cannot produce their own medication (see COVID-19 pandemic)
- PMF has a potential, that LIMICs can improve the sovereignty to produce healthy ingredients or pharmaceuticals in their own country
- Local production in LIMICs could create a first line of defense against diseases spreading across the globe
- Optimization of downstream processing of plant-based proteins is essential (80% of production costs)
- Barriers for PMF in LIMICs are specifically in the sociopolitical area (lack of political willingness, no clear regulation of plant-based proteins, no clear regulation of pre-existing patents, insufficient funding from public and private investors)
- Public perception concerning '*transient expression*' as a non-GMO must be made transparent by trust building campaigns
- PMF can be used for non-pharmaceutical products
- Own PMF can be attractive for scientific talents
- PMF should be an integral part of education at the university level.

Furthermore, Zeghibe (5/2021) has found, that in her google-based recherche about PMF covering 305 articles, more than 50 percent were from U.S., 30 percent from Europe, the rest from Australia, India, Canada, Middle East, and South Africa. Target audience was discussing the topic by two-third in professional and by one-third public oriented. Most of the articles were focusing to business. This shows, that PMF has not reached LIMICs by end of 2021.

Well, there is a little ray of hope for Africa shown by Tsekoa *et al*. (2/2020) in their paper titled: "*Molecular farming for therapies and vaccines in Africa*". The authors report, that there is an increasing number of scientists attracted by plant molecular farming, and plant-based pharmaceuticals are in different stages of development. Furthermore, that there is a significant growth in the translation of these technologies to commercial operations and that Africa will realize significant benefits from molecular farming within the next five years. They try to reduce trade deficit and poor access to essential medicines by the underprivileged. Consequently, academia has to adopt a business-oriented approach to service industry and people's needs.

Currently, February 2022, WHO has started together with public and private partners to develop and build a WHO global mRNA vaccine technology transfer hub in South Africa to overcome vaccine inequity in LIMICs. The central aim is to establish a training facility center where mRNA technology is developed to the scale required for mass production of vaccines in LIMICs. This mRNA hub will significantly strengthen the biomanufacturing capacity and putting Africa on the

path to self-reliance. In this center PMF can be evaluated, developed, and used to support the health care of LIMICs.

Edible vaccines and plant-based therapeutics

Since beginnings of civilization, plants or essential ingredients from plants have been used for health reasons, very often combined with religious aspects. For example, 'Monastery Medicine' and 'Herb Gardens' were the centers for plant-based therapeutics. A monastery was characterized by running a vegetable garden, an orchard garden, which was used as a cemetery, and the 'Herbularius' – a herb garden for medical care. Hundreds of medicinal plants ("There is a Plant for Every Illness") were grouped according to areas of application such as cancer, respiratory tract, prostate, immune system, pain, gastrointestinal, etc. The intension was not to relay on expensive spices from the orient, but to use common herbs from domestic meadows and hills, so everyone can afford it, and not for the one, who lives in abundance.

"During the last hundred years, plant-based ingredients have been extracted, purified, and finally chemically synthesized to improve human health and to safe life. Natural products were often the blueprint for the successful chemical synthesis of highly active pharmaceuticals. Aspirin, for example, is a synthetic version of salicin, from the bark and leaves of willow trees." (Kern, 1/2007).

But now, at the beginning of the Third Millennium, new cutting-edge technologies based on DNA and mRNA technologies or nanobiotechnology are available for improving human health and pleasure in future. The door for 'Personalized Nutrition' and 'Personalized Medicine' is opened.

'Personalized Nutrition' and 'Personalized Medicine' by edible plants is a vision which is still very attractive and very challenging – from "*Seeds-to-Fork*".

Relevant and comprehensive reviews were made in Chile by Concha *et al*. (2017) and in Kerala, India by Kurup and Thomas (11/2019).

Although, in India, the vision and knowledge concerning plant-based vaccines and edible vaccines is running since more than 20 years (Tripurani *et al*., 2003; Appaiahgari *et al*., 2017) the translation or transformation to produces on the market is very limited.

Kurup and Thomas (11/2019) outlined the relevance of edible vaccines in the pre-COVID-19 period very well. Edible vaccines offer better choices especially for developing countries, they are:

- easy to grow,
- allowing quick responses to epidemic or pandemic threats,
- growing very quick,
- cost-effective,
- affordable,
- available in remote area,

- independent from a cold chain
- easily accessible,
- producible at home,
- suitable for vegans,
- without the necessity for a needle,
- not depending on sterile environments,
- easily administrable,
- without storage issues,
- environment friendly,
- producible at large scale, thousands of hectares
- …

Actually, a broad spectrum of transformed edible plant species producing vaccines is under development such as: tomatoes, papaya, carrot, bananas, peanuts, quinoa, lettuce, 'tobacco', potatoes, rice, soybeans, corn, alfalfa, peas, apples. These sixteen foods are already producing antigens to counter human and animal diseases (Concha *et al*., 2017; Kurup and Thomas, 2019).

Edible plants expressing drugs against dangerous diseases such as dengue fever, yellow fever, rabies, malaria, tuberculosis, cholera, measles, or polio are addressed by He *et al*. (2021). For example, successful clinical trials based on orally delivered leaves of *Artemesia annua* against malarial parasite strains were done. Let's see, what's going on in future.

However, key obstacles for edible drugs in plants are:

- the unclear regulation and its acceptance by the society,
- often an academic proof of concept only and no bench to market approach,
- missing links to partners in big pharma and food companies,
- underfunding,
- large-scale outdoor production of edible vaccines and the potential risk of gene transfer by hybridization or dispersal of pollen to other plants,
- variability of immune response after oral administration,
- the regulation of recommended ingestion dosage to avoid possible intoxications in the population,
- lack of data about possible deleterious effects in the long run
- the possible contamination of other food,
- the accidental consumption by people, especially children,
- the unreflective consumption by people,
- ethical and religious concerns,
- anti-VAXX movement,
- difficulty to exclude misuse and to counter bioterrorism (Kern, 2018a,b; 2020c,d)
- …

As mentioned before: "Grow and eat your own vaccines?" (Bernstein, 9/2021) is a breakthrough, that Plant-based mRNA vaccines can be produced in leaves of spinach or lettuce.

Edible vaccines and plant-based therapeutics can be grown in the field, in the back yard garden, indoor farming (Diego-Martin *et al*., 2020), in underground farms, in containers, in vertical farms, in urban farms, in green houses, climate chambers or at your 'personal farm at home'. For example, in 2021, Agrilution Ltd., in Germany is offering "*plantcubes*", so that people can grow their own fresh herbs at home. They have fresh herbs always available at home, whereby everyone is independent from delivering chains and does not need plastics at all.

Via a Green App it is possible to order 40 different herb varieties, put them to the plant cube, grow them 1-5 weeks and harvest and enjoy the fresh home-grown herbs. Furthermore, the Green App is functioning as a 'gardener' informing about the running production system.

Such a system would nicely work to produce biofortified food, functional food, plant-based therapeutics, or plant-based vaccines. This would be an interesting business model, if herbs boosted by using modern biotechnologies would be available. This would push forward "*Personalized Nutrition*' and '*Personalized Medicine*', very comfortable and very cost-effective at home.

Leaving the earthly horizon, genetically boosted crops or plants enabling biofortified food are cornerstone for an appropriate space agriculture in future. If humankind is ever to go for long-term space missions and colonization a functioning space farming system has to be developed (Liu *et al*., 2021).

Role of Food and Health in Transition (2007-2022-2052)

"Health and health care are in the midst of a transformation. Medicine is becoming more proactive, with its increasing knowledge of intrinsic genetic factors affecting disease risk and socio-economic, environmental, and behavioral determinants of health. Lifestyle-related chronic diseases and the increasing costs of health care are other driving forces behind the search for creative, innovative, and cost-effective ways to improve human health and prevent diseases. An over-arching trend in health care is 'do it yourself'." (Kern, 12/2006/1/2007).

"Medicines are unique, but patients are very different. Nearly 30 percent of patients do not benefit from medicines. Significant numbers of patients suffer from negative side effects. Consequently, the health care system and health care business will be shaped significantly using pharmacogenomics. Ultimately it will be possible to go not only for an individualized health therapy but also for a predictive/preventive care. Individual genetic differences in response to specific dietary components for pharmaceuticals have been known for years, but genetic information will be used in future to understand the reasons for individual

differences in response to specific nutrient, dietary patterns, or to pharmaceuticals." (Kern, 1/2007).

The future of farming, the future of food production/manufacturing, and the future of health care is revolutionized at an unprecedented speed driven by science and technology.

Agriculture, food production/manufacturing and health care have to go hand in hand in a synergistic way. Crossbreds from these essential sectors using cutting-edge genome editing technologies will enable to address successfully the following individual and global all over all targets by 2052:

- elimination of hunger and malnutrition
- avoidance of social unrests, conflicts, migration, and war
- improvement of health and life
- protection of the environment.

"The seed sprout", or in other words: "Planting the right ideas, so that they can also be harvested in future." (Kern, 2015).

Last, but not least: "Science and technology will win, to enable a better life and a better future!"

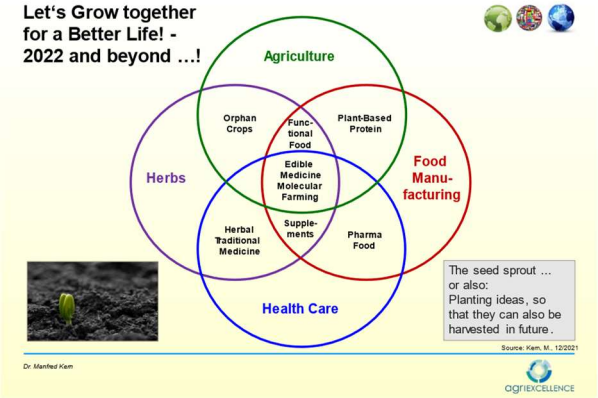

Fig. 2: Let's Grow together for a Better Life! – 2022 and beyond ...!

Concluding Remarks

Food for thought concerning: "Change" ...

- "A change will come one way or another."
- "Change before you have to." (Jack Welsh)
- "For a change, you have to leave your comfort zone"
- "If you do not change, you will be changed."
- "Change is inevitable. Growth is optional." (John Maxwell)

- “Be the change that you wish to see in the world.” (Mahatma Gandhi)
- “Change is the law of life. And those who look only to the past or present are certain to miss the future.” (J.F. Kennedy)
- “Change is the prerequisite of life.”
- “Without a permanent change of the genetic material no evolution is possible.” (Lecturio, 12/2021)
- “No change, no life.”
- “It is not the strongest of the species that survives, nor the most intelligent that survives. It is the one that is most adaptable to change.” (Charles Darwin)

Nevertheless, “All power is within you. You can do anything and everything. Believe in that.” *(Swami Vivekananda, 1863-1902)* as well as the statement made by *Mahatma Gandhi* (*1869-1948*): “*If I have the belief that I can do it, I shall surely acquire the capacity to do it even if I may not have it at the beginning*” are food for thought.

In doing this, you have to leave your comfort zone and enjoy the challenging zone and you have to be ready to exceed limits. Some relevant questions for consideration are the following ones:

- Do you have an innovative mind?
- Do you have a vision?
- Do you have the relevant skills?
- Do you do the right things?
- Do you have the heart to lead?

As a take home message let me reiterate: “As for the future, your task is not to foresee, but to enable it” *(The Wisdom of the Sands,* Saint-Exupéry*, 1948)*, and: Do more with less, do it better, do it with less waste, do it with less emissions, do it for people, do it for the planet and do it in time!

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11. Personal Remarks

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* In the year 2052, the author would be 100 years old.

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