

Nano Infection: Nature and NG Drugs Delivery Nature Transposon Transfection by Superparamagnetic Iron Oxide Nanoparticles (SPIONs) Vector CASE REPORT ARTICLE

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Abstract—

The uniqueness about the case: Infection could be in the form of macro (parasite), micro (bacteria) or nano (nucleic acid) meter size. RNA virus such as SAR-Co2 in this 3 years pandemic era of COVID-19, make everybody had known the different of PCR test and antigen rapid test. This cases, reported transfection of transposons DNA, RNA which not given inflammation reaction, but genomic or epigenomic changing which driven evolution, diversity, disparity or monoculture and proteomic/metabolomic changing in other species or genus. The Natural RNAi vector transfection in tropical rainforest area is occur in daily living, especially at night when the high relative humidity near 100%. Spinel ferrite extracted from salam, kelor, papaya and many others leaves are used for a novel non-vector-mediated gene delivery into mammalian cells, but this mechanism are neglected/reckless in the discussion on blue carbon vs. blue economy G20/B20 summit in November 2022 in Bali, Indonesia. SPIONs is associated with directly healthy and environment living, indirectly help recovery or worsen of food, energy, climate, and economic crisis.

Important clinical findings: High prevalence of Down Syndrome, Parkinson Diseases, Bipolar, Autism, LGBTQAI, hypospadias and Congenital Adrenal Hyperplasia (CAH), which is due to CGG repeat, associated parallel with source of sepsis high prevalence in wet-warm climate area: SPIONs.

Primary diagnosis: Self diagnostic or in social behavior like street fashion and zebra cross fashion in rainbow flag, and primary care health center. Local leaves rich of ferromagnetic stuff act as non-vector-mediated gene or epigenetic delivery.

The lessons from the case report are breaking the taboos of Martin Bell syndrome and Escalante syndrome (CGG repeat), and known the nanomolecular cause in wet condition, which become proteomic and metabolomic neuro-enzyme blocking health laden, tropical rainforest and Nordic area.

Keywords— Transfection; Metal Nanoparticles; SPIONs; Next Generation Drugs Delivery Systems; microRNAs; *Moringa oleifera*, *Syzygium*.

I. INTRODUCTION

Here are the Problem, Interference, Comparison, and Outcome (PICO):

Problem: Natural transfection in wet and warm climate is in high prevalence and give many health laden which the cause is neglected and not be handle in prevention and promotion stage. This iceberg health problem considered successful in the clinical stage and then, the rest New Generation (NG) drug delivery become a market share.

Interference: Knowing the cases and the SPIONs vector of the diseases.

Comparison: Genomic and Epigenomic vs. Proteomic and Metabolomic Aspect in Metallic Nanoparticles Drug Deliveries.

Outcome: The SPIONs vector in wet and warm climate, G20/B20 should be the frontiers of every negotiation and transaction of One-Earth recovery.

The epidemiology, sign and symptoms of transposon transfection in Wet and Warm Climate Area were still neglected and reckless handle. Why this transfection in natural large incubator (wet and warm climate area) at night is unique and may include medical literature references? Mantids,^{1,2} one of them, *Phyllium westwoodii* or *pulchrifolium* have the form of *salam* leaf (*Syzygium polyanthum*, bay leaf)² and like *jambu biji* leaf (*Psidium guajava*, guava leaf)¹ reported in tropical rainforest area, are exist by transfection.^{2,3} On the other hand, superparamagnetism^{3,4} is a form of magnetism which appears in small ferromagnetic nanoparticles, has opened the mystery. In sufficiently small nanoparticles, magnetization can randomly flip direction under the influence of temperature. In the superparamagnetic state, an external magnetic field able to magnetize the nanoparticles, similarly to a paramagnet. Ferromagnetic material undergoes a transition to a paramagnetic state above its Curie temperature. Superparamagnetism, is different from this standard transition since it occurs below the Curie temperature of the material. Curie temperature of Co ferrite 789 K (516 °C). Cobalt ferrite transfection agents is for drug delivery and diagnostic imaging.⁴ Ferromagnetic is a stuff that could be pull strongly by magnet: Cobalt (Co), iron, steel, nickel alnico, alcomax. Superparamagnetic is a form of magnetism which appears in small ferromagnetic or ferromagnetic nanoparticles (the influence of size). The typical time between two flips is called the Neel relaxation time. Superparamagnetic Iron Oxide Nanoparticles (SPIONs) are now the most extensively used functional nanoparticles as antibacterial agents, and for other biomedical applications due to their unique physical, chemical, magnetic and biocompatibility properties, such as MRI diagnostic and cancer/ viral therapy. Unlike ferromagnetic materials, superparamagnetic stuff does not retain any net magnetization once the external field has been removed. Means, they have no magnetic memory.

II. PATIENT INFORMATION

2.1 Alignment justifies

Indigenous studies, Herbal, Modern diagnosis Contrast Agents MRI, Cancer therapy, Antibiotic resistance therapy is associated with the New Generation (NG) drugs delivery and imaging with nanoparticles known as SPIONs.^{5,6,7,8,9} The SPIONs is also used for Antibiotic resistance therapy.^{10,11} Specific 'naturally' stuff in tropical rainforest area in mantids as transposon transfection.² Down syndrome, LGBTQ, Parkinson disease, autism, hypospadias, Congenital Adrenal Hyperplasia, are associated with the RNAi to silence/hypermethylation associated with CGG repeat, are in high prevalence in wet and warm countries.^{12,13,14,}

2.2 De-identified patient specific information^{15,16}

Decitabine using with too much demethylation associated to bipolar,¹⁵ Hypospadias and CAH as proteomic and metabolomic cases,^{13,16} has been reported for a long time ago and rare associated to RNAi. Transfection using SPIONs,¹⁷ and SPIONs using for DNA vaccine,¹⁸ has reported as a nurture inorganic vectors of DNA/RNA.

2.3 Primary concerns and symptoms of the patient

Mental and LGBT flags incl. mental and LGBTQAI, whereas the QAI are queer, asexual, intersex^{19,20} flags, and taboo/stigma and discrimination with social isolation, exclusion and rejection, are in high prevalence and the cases are received as a fate. These CGG repeat cases with broadly specific diagnosis is in one pedigree.²¹ The taboo, social stigma is not only for the family, but also for the whole village or countries, like Martin-Bell-Renpenning, Escalante Syndrome as CGG repeat cases,¹⁰ which

hypospadias alone is thought by Indonesia Science Academic/*Akademi Ilmu Pengetahuan Indonesia* (AIPI) as an ice-berg health laden.¹³

2.3.1 Medical

Down syndrome, Fragile X silencing of FMR1 gene, Parkinsonism, LGBTQ, hypospadias etc. were easily known by Primary care doctors.^{11,12,14}

2.3.2 Family

Parkinson diseases and FXTAS in one pedigree,²¹ or in one environment,²⁰ are like TBC cases, even though as an ancestral gift, not mycobacterium tuberculosis as a cause. Also leprosy, obesity, bipolarism,¹⁵ and others, such as hypospadias and CAH,^{13,16} while the environment of hypermethylation is frequently high.¹⁴

2.4 Psychosocial history incl. relevant genetic information

The CGG repeat, CpG islands, and epigenetic taboo, social justification and early psychological help effort is needed by the adolescence. Fashion street festival has been the escape for many villages. Epigenetics study hasn't been done in more than 3 genders, where there are now classes too 18 different gender identity in Thailand, South East Asia with wet and warm climate.

2.5 Relevant past interventions and their outcomes

Successful sport, fashion, humoral and reconstruction repair surgery, support by early psycho-social training has been done by many governments, private and village foundation, but they still neglected the cause and epidemiological high prevalence and also negligent as being exist in specific wet and warm area, tropical rain forest.¹²

III. CLINICAL FINDINGS

Proteomic and metabolomic disorders vs. early psychosocial help and vs. urogenital reconstruction surgery, being the clinical findings.

3.1 Alignment justifies

Genetic or epigenetic CYP 21 or cytochrome P450 blocking or polymorphism by CGG repeat,¹³ and the findings of CAH in sport gender verification,¹⁶ which nowadays has been diagnosed by failure of metabolomics and proteomics of CYP 21 and cytochrome P450 associated to steroid enzyme in androsterone production.¹³ On the other hand, failure of fusion on hypospadias was recorded due to pesticide – not genetic silencer in GMO.¹³ The same argumentation on Martin-Bell in Brazil and Escalante syndrome in South America, which has the clinical figures as this neurosteroid destruction, and anatomical face and ear.¹³

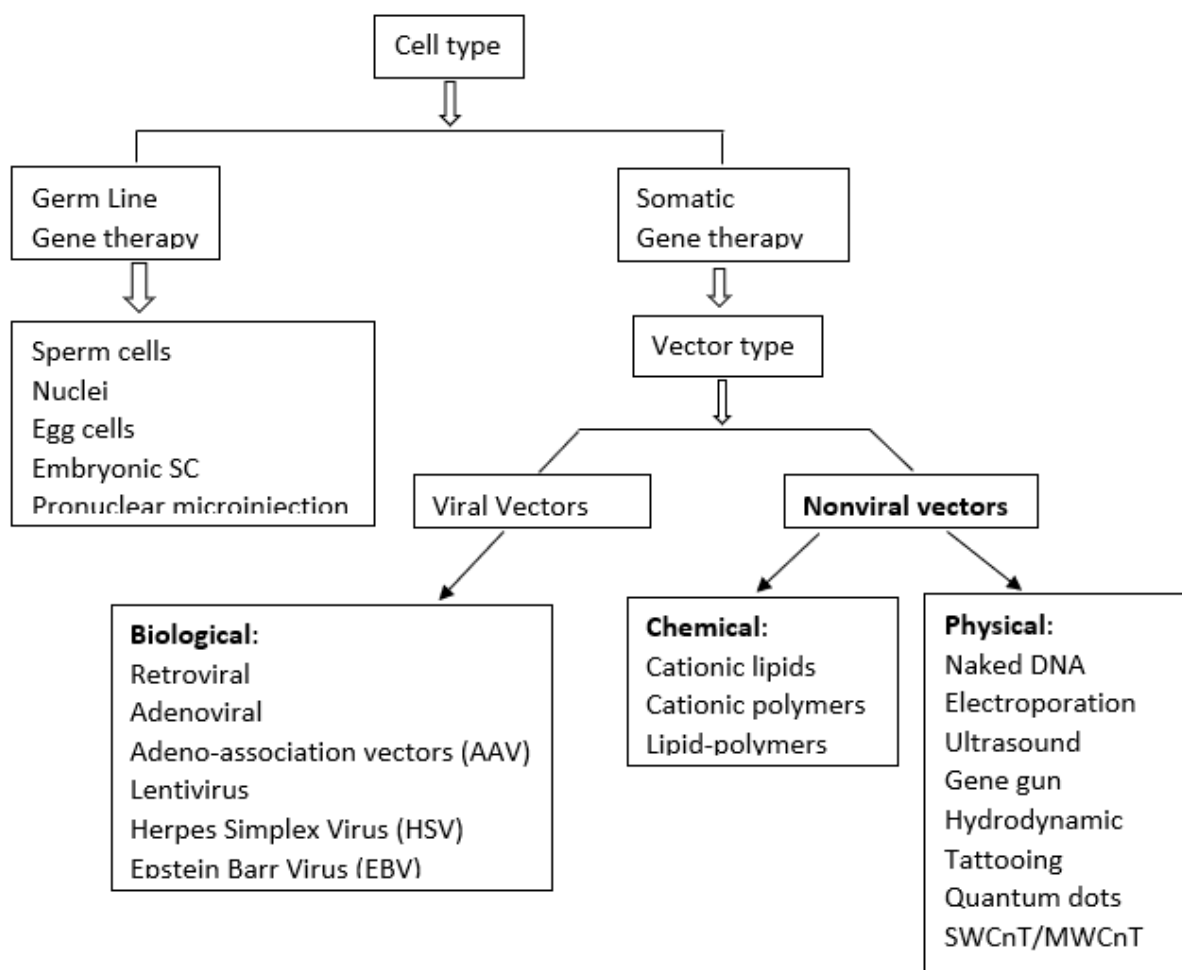
3.2 Describe significant physical examination and clinical findings

Psychosocial more than taboo physical report of hypospadias, CAH, bipolar etc. Somatotype and Waist Hip Ratio could also help.

IV. TIMELINE

4.1 Alignment justifies

Nickel ferrite are frequently utilized as magnetic-based drug delivery and contrast agents in MRI. There are many types doping on this nanoparticle with different size, morphology, and physical features of magnetic nanoparticles. All samples displayed superparamagnetic (SPM) behavior at room temperature, with no or negligible coercivity and retentivity. Historical and current information from this episode of care organized as a timeline (figure 1).



FIGURES 1: Schematic illustration on different vectors-mediated transfection especially by SPIONs's NG cell therapy vs. natural SPIONs in wet and warm climate area for gene therapy manufacturing and vaccine manufacturing (Modified from Bolhassani 2014)

Next Generation (NG) of nanoparticle and Nickel ferrite (NiFe_2O_4) are potential superparamagnetic nanoparticles act as semiconductor has electromagnetic power. Besides for gene delivery into mammalian cells, cobalt nano ferrite also used in silencing, increasing expression of genes, and editing CRISPR/Cas9 of virus infection therapy.²² This NG of non-viral vector-mediated gene delivery into mammalian cells.²³

V. DIAGNOSTIC ASSESSMENT

5.1 Alignment justifies

Orchid mantids and *Salam* mantids, have been reported as a translational RNAi indigenous as an insect fact in tropical rainforest country area such as Indonesia, Thailand, and many others SEA countries for a long-long times.²

Diagnostic methods SPIONs (Superparamagnetic Iron Oxide Nanoparticle) for contrast MRI, and waste water treatments aqueous supercapacitors electrodes low-cost sustainable energy storage are recorded. Cu Zn nanoparticles can be used as a contrast agent for MRI thermometry (temperature-sensitive contrast agent. SPIONs coated with a polymer layer are widely used for biomedical applications. Embedding these particles into an agarose gel resulted in significant modification of water proton relaxation times T_1 , T_2 and T_2^* determine by NMR measurements. Copper-Zn ferrite nanoparticles (NPs) coated with a poly (ethylene glycol) (PEG) layer are synthesized using one-step thermal decomposition method in a polymer matrix.³

5.2 Laboratory testing

Epigenetic report of CGG repeat in LGBTQ, Parkinson disease, Autism, Hypospadias, CAH etc.: CpG island, Hormonal, CYP21,¹³ cyt P450 mutation,¹³ and quantitative CGGr.^{12,13,14,15,16}

ARMGs for sepsis or Sensitivity and Resistance test,² ever Kanamycin has been used in treatment of tuberculosis and certain sexually transmitted diseases.²⁴ Multi Drug Resistance (MDR) TB is in high prevalence in India, Thailand, and Indonesia.

Mantids with DNA sequencing and miRNA chain/associated with the leaves.²

Concentration of cobalt ferrite^{29-34,40-43} or nickel ferrite^{26,27,30,44} in *jambu batu* (*Psidium guajava*) and *kelor* (*Moringa oleifera*)³⁴ and *salam* (*Syzygium polyanthum*), *binahong* (*Anredera cordifolia*), *papaya* (*Carica papaya*) leaves as the source of spinel ferrite in translational medicine. Ferrite synthesis using variable part of plants.²⁵ Concentration of spinel ferrite in each type of leaves and other part of plants are kept secret from each other manufactures.

5.3 Imaging

Nickel ferrites (NiFe_2O_4) also known as spinel ferrites (SF),²⁶ and Structure, Morphological and Electrical/Magnetic Properties of Ni-Mg nano-ferrites from new perspective has been reported.²⁶

Greener methods for the synthesis of various nanostructures with well-organized characteristics and biomedical applicability have demonstrated several advantages, including simplicity, low toxicity, cost-effectiveness, and eco-friendliness. Spinel nickel ferrite (NiFe_2O_4)²⁷ also known as Nickel ferrite nanoparticles or Ni ferrite NP. Biosynthesis of spinel nickel ferrite nanowhiskers and their biomedical applications has been reported.²⁷

Nano-spinel ferrites means spinel ferrite with nanometer size, which is become superparamagnetic. Biosynthesis effect of *Moringa oleifera* leaf extract on structural and magnetic properties of Zn doped Ca-Mg nano-spinel ferrites are recorded.²⁸ This green synthesis nanoparticle has been determine by NMR measurement.³

5.4 Survey

Green synthesis Nd substitute Co-Ni change the size, morphology, and physical features of magnetic nanoparticles. Besides the *Moringa oleifera* leaf extract on structural and magnetic properties of Zn doped Ca-Mg nano-spinel ferrites,²⁸ also have done from others leaves. Biosynthesis of spinel NiF extracted nanowhiskers and their biomedical applications,²⁷ also in other part of plants, with other methods, size, structure, and function. There is CoF dope and nano-powder strontium-substituted CoF.²⁹ Cobalt doping on nickel ferrite nanocrystals enhances the micro-structural and magnetic properties: Shows a correlation between them.³⁰ Synthesis and magnetic properties of Cobalt ferrite nanoparticles prepared by Wet chemical route,³¹ sonochemical synthesis,³² and characterization of zinc and vanadium cobalt substituted cobalt ferrite nanoparticles synthesized by using the sol-gel combustion.³³

Cobalt ferrite using *binahong*, *salam*,² *papaya*, *kelor*³⁴ for drug delivery, vaccine and therapy, where *Moringa oleifera* leaf extracted by ethanol 96% to make silver nanoparticles as antioxidant.³⁴ Nanoparticles Potent Vectors for Vaccine Delivery targeting Cancer and Infectious Diseases, published in Human Vaccines & Immunotherapeutics.³⁵ SPIONs as nanocarriers with various dope and biological properties have been extensively applied for in vitro/in vivo drug and gene delivery.³⁵ Green synthesis of biocompatible superparamagnetic iron oxide-gold composite nanoparticles for MRI, hyperthermia, and photothermal therapeutic applications report in Materials Chemistry and Physics.³⁶

Aluminum-Doped cobalt ferrite as an efficient photocatalyst for abatement if methylene blue degradation. The synthesis of spinel ferrites nanoparticles was performed by a facile sol-gel method, and characterized by FTIR, XRD, SEM, EDS, Nitrogen adsorption/desorption and UV-Visible spectroscopy.³⁷

Khoriah et al³⁸ report the influence of doping ion aluminum to absorption curve using FTIR and nanoparticle crystal structure of cobalt ferrite result from Coprecipitation. Many types doping this nanoparticle with different size, morphology, and physical features of magnetic nanoparticles as semiconductor could be seen in Table 1.

TABLE 1
MANY TYPES DOPING MAGNETIC NANOPARTICLES WITH DIFFERENT SIZE, MORPHOLOGY, AND PHYSICAL FEATURES OF SPIONS AS SEMICONDUCTOR

Metal - Ferrite	Particle size (ps)/ λ Size	Reference	Synthesis ²³	Function
Cobalt ferrite	15-48 nm ps NIR-light ^{L22} (<980nm) 690 nm	Maaz, 2007 ³¹	Wet chemical route	Gene delivery into mammalian cells, silencing, increasing expression of genes, editing CRISPR/Cas9 of virus infection therapy ²²
Nickel ferrite	<100 nm ps	Alijani, 2021 ²⁷	Doping	Biomedical applications
Zinc ferrite mod	7.3-8.2 nm ps 15-18 nm ps 4.5 nm ps etc.	Zhu 2022 ⁴⁸	Doping etc.	Nanofibers photocatalytic Degradation of Organic Pollutants
Al ferrite	57.75 \rightarrow 46.2 nm ps ³⁸	Abbas, 2020 ³⁷	Doping	Photocatalyst of Methylene Blue Abatement
Ag ferrite	82.9 nm ps	Abdul Karim, 2012 ³⁴	Extract etanol 96%	Antioxidant
	<200 nm ps	Bolhassani, 2014 ³⁵	Polymeric nanoparticles	Human vaccine targeting Cancer and Infectious diseases
Au ferrite	20 nm ps ⁵⁰	Karey, 2022 ³⁷	Cobalt ferrite doped by aqueous plant extract	MRI contrast agent, hyperthermia
Ni-Mg ferrite	84-136.5 nm ps	Mostafa, 2022 ²⁶	Auto Combustion	Electrical/Magnetic properties New perspective
Zn & Vanadium ferrite	~ 45-24 nm ps	Immanipour, 2022 ³³	Sol-Gel Auto-Combustion Method	Characterization
Co-Zn ferrite	10-30 nm ps 600 nm wave	Omelyanchick, 2020 ⁴¹	Green Synthesis	Antimicrobial Properties
Co-Zn ferrite	+	Lachowicz, 2022 ³	One-Step Preparation in Water Suitable	Contrast agent for MRI Thermometry
Zirconium ferrite	16-26 nm ps	Kavitha 2019 ³⁹	Doping	microstructure, magnetic, dielectric properties
Lithium ferrite	100 increase to 110-120 nm ps Improved light absorbance	Cai, 2022 ⁴⁶	Doping	enhanced photoelectrochemical water oxidation
Ag-Au ferrite	AgF 20 nm ps, AuF 20 nm ps	Broska 2019 ⁵⁰	Purchased	Alter miRNA Expression but Do Not Affect DNA Methylation

Besides, several dope has been studied: ZnF and CoF in bacterial culture,⁴⁰ CoF as cancer therapy,⁴² CoF plant extract,⁴³ NiF,⁴⁴ ZnF for degradation organic pollutant,⁴⁸ AgNPs induce a global methylation.⁵¹ AgNPs and SiNPs in epigenetics. Inorganic Vector,⁵³ and AuNPs.⁵⁸

In using inorganic NPs for 'epi-drugs': first, the role that epigenetics play in mediating nanotoxicity, and the second is the possibility to overcome the limitations.⁵² The Green synthesis SPIONS for industry 4.0 directly do stronger and faster recovery, or worsen the one-earth by the climate, economy, environment, food and energy crisis, due the GMO and hypermethylation side effort.

The currently available nonviral vectors e.g. SPIONS and epigenetic RNAi, that has been used for practical applications, such as circulation lifetime, low environmental responsiveness, and complex preparation procedures.⁵³ This transducing the nucleic acid into cancer cells, the SPIONS must overcome the trafficking barriers: escape immunity, effectively taken up by cancer cells, and protect and release the therapeutic RNAi.⁵³

Five years ago, 2018, mechanisms by which miRNAs are secreted and taken up by cells are not well understood and require further investigation, without SPIONs.⁵⁴ In 2020, DNMT3A/AGO4-mediated cytosine methylation of miRNA negatively associated with poor prognosis in glioblastoma multiforme (GBM).⁵⁵

Then, optical vibration of Nano- and Micro-Metallic Materials for the development of NG virus detection technology has been reported.⁵⁸

Vector and Non-Vector Infection up to Nano-Vector in Association with RNAi Transfection,⁶⁰ and Bioelectric Transfection and transposon bullet-High Relative Humidity: Poor conductor and efficiency of the electrostatic field, pledge the nowadays NG therapy and diagnosis based on nucleic acid.^{60, 61}

Effect of zirconium doping in the microstructure, magnetic, dielectric properties of cobalt ferrite nanoparticles has been reported.³⁹ Biogenic Zn doped particles are promising for combined diagnostics and cancer therapy.⁴⁰ Gold SPIONs for MRI, hyperthermia, and photothermal therapeutic applications.³⁶

Many studies of variable metal doping ferrite such as Ni, Zr, Zn, Au, Ag, Li etc. with the role of green synthesis are recorded

Green synthesis of Co-Zn Spinel ferrite nanoparticles: Magnetic and Intrinsic Antimicrobial Properties,⁴¹ Exploiting Unique Alignment of cobalt ferrite Nanoparticles, Mild Hyperthermia, and Controlled Intrinsic Cobalt Toxicity for Cancer Therapy.⁴²

Control Toxicity for Rx/ Ca.⁴² Photocatalytic and Antibacterial Activity of CoFe₂O₄ Nanoparticles from Hibiscus rosa-sinensis Plant Extract.⁴³ Lime peel extract induced NiFe₂O₄ NPs: Synthesis to applications and oxidative stress mechanism for anticancer, antibiotic activity.⁴⁴ A physiologically based pharmacokinetic model to predict the superparamagnetic iron oxide nanoparticles (SPIONs) accumulation in vivo.⁴⁵ Elemental doping which introduces a second or even a third element has been shown by the role of lithium doping on a-Fe₂O₃ photoanode for enhanced photoelectrochemical water oxidation.⁴⁶

5.5 Diagnostic challenges

All patients with Down Syndrome, LGBTQ, Parkinson disease, Autism, Hypospadias, CAH, Bipolar, Alzheimer, and hypermethylation/ repeat CGG. CpG, and psychosocial flag community are challenges.^{12,13,14,15}

5.5.1 Diagnosis (incl. other diagnosis considered) without caused

All failure of proteomic and metabolomic such as Hypospadias and CAH incl. LGBTQAI and more than 2 gender verification should be a challenges diagnostic.

5.5.2 Prognostic characteristics when applicable

Clear Environment without methylation threat with decitabine. Clear Environment without ARMGs in GMO and decrease threat by NG antibiotics (market share).

VI. THERAPEUTIC INTERVENTION

6.1 Alignment justifies

Psychology and Reconstructive urogenital Operation as therapeutic intervention was successful for the patients, but has failed to decrease the prevalence of this epigenetic cases. There is also high in subjects due infectious and autoimmune diseases.

6.2 Types of therapeutic intervention (pharmacologic, surgical, preventive)

Besides early psychological approach, hormonal, pharmacological, surgical, new antibiotic and biomedical application in the market share of these cases and become a prestige for NG drug delivery. Prevention of viral vaccine, and cases associated with pesticide not methylation agent. It is also associated with new pesticide using due to pesticide resistance.

6.3 Administration of therapeutic intervention (dosage, strength, duration)

Dosage symptomatic and control for clinical cases are known widely, but not dose of leaves consist of spinel ferrite as translational medicine.⁴¹ The aspect of Cobalt ferrite as cancer therapy and toxicity.⁴²

6.4 Changes in therapeutic interventions with explanation.

No change in therapeutic and prevention of hypermethylation CpG island and CGG repeat health laden, and Cobalt ferrite (CF) dope and nano-powder strontium-substituted CF modeling for heavy metals toxicity for waste water treatment synergistic NG for diagnostic agent and therapeutic which only a market share to the need of energy crises recovery, while hypermethylation cases has been said a fate to indigenous people. Neglected cases plus a share market to the other vaccine and cancer therapy. ZnFe₂O₄ nanoparticles have been synthesized using grinding, combustion, ceramic, hydrothermal, solvothermal, co-precipitation, sol-gel, and biosynthesis methods. These nanoparticles comprise of metals and their oxides can be produced using alternative biological compounds such as the extracts from plant roots and leaves, fruit peels, seeds, biomass waste, sugar and bacteria.⁴³ Due to the biodiversity of plants, the preparation of nanoparticles via biosynthesis has a promising future.⁴⁵ Since the band gap of ZnFe₂O₄ was only 1.9 eV, the photogenerated electron-hole pairs quickly recombined, thus decreasing its photocatalytic activity. To improved its photochemical performance, three ways of catalyst modification have been proposed, one of them is elemental doping which introduces a second or even a third element⁴⁶ This technique can have a positive effect on its photochemical, electrical, and magnetic properties. The diameter of Al-doped ZnFe₂O₄ nanofibers decreased significantly.⁴⁷ Another doped ZnFe₂O₄ prepared with carbon-nitrogen, make the energy band position slightly negatively shifted, which expanded the absorption range of visible light, produce a stronger scattering of incident light.⁴⁸

VII. FOLLOW-UP AND OUTCOMES

7.1 Alignment justifies

Down Syndrome, Parkinson disease, Autism, LGBTQAI, Neuro Degenerative Diseases, Hypospadias, CAH, Justify by CGG repeat, caused by neuro-enzyme blocking, mutation, silencing, failure, polymorphism is familial.^{12,13,15,49} This is also for Martin-Bell-Renpenning Syndrome and Escalante Syndrome, which is like Parkinsonism FMR1 permutation carriers.^{13,49}

7.2 Clinician-and patient-assessed outcomes if available

Decitabine patient prevalence increase, taboo, hypospadias and CAH, mental illness seldom surgery, successful urogenital repairment should be decrease in prevalence.

7.3 Important follow-up diagnostic and other test results

Primary care diagnostic of patients and seldom pedigree and environment, often pesticide cause, not miRNA and its natural and synthetic vectors. In the other hand Silver Gold and Iron Oxide alter miRNA but do not affect DNA methylation in Hep G2 Cells.⁵⁰ Silver NPs exposure effect on miRNA and global DNA methylation Endothelial cells.⁵¹ The epigenetics affect in SPIONs has been report,⁵² support by the reversion of DNA methylation to miRNA silence via SPIONs.⁵³ Whereas MiRNA biogenesis, Mechanism of Actions, and Circulation⁵⁴ then the methylation which inhibits their functions associated with poor prognosis.⁵⁵

7.4 Intervention adherence and tolerability (how was this assessed?)

Cultural and fashion street activity has been melting the atmosphere of hypermethylation and demethylation.

7.5 Adverse and unanticipated events

SPIONs for water treatment, MRI contrast, biomedical application, and a new quantitative optical biosensor for protein of nanophotonic biosensors for signal output Fourier transform has been lure everyone and again neglected the cause of miRNA nature and nurture of health laden that we have to prevent by separating green and blue activity based on wet n warm vs. dry n warm climate condition, where bioelectric situation successful miRNA bullet.

VIII. DISCUSSION

8.1 Alignment justifies

Spinel ferrite from *kelor* (*Moringa oleifera*), *salam* (*Syzygium polyanthum*), *jambu biji* (*Psidium guajava*), *binahong* (*Anredera cordifolia*) leaves is a ferromagnetic/diamagnetic/SPIONs in RNAi transfection is a sign by their mantids or cobalt ferrite.³⁴

The mystery of semiconductor principle in *Moringa oleifera* leaves is not a mystic, has opened the physiology how laden sociology and health problem in tropical rainforest and other wet-warm areas, our huge natural incubator laboratory function as non-viral vector. Careful principle is in our hand to guard one-Earth for recover together and not to be a market share of

another topic of NG drug delivery using Cooper-Zn ferrite NPs coated with a poly(ethylene glycol) PEG/EG³ which give a new side effect such as Acute Kidney Injuries were broadly promote by the ministry of health in Indonesia.

8.2 Strength and limitations in your approach to this case

This is the first study report the association of SPIONs – miRNA methylation epigenetic, not genetic laden problem. The application is not to used recklessly nano biomedical industry as new market without prevention on the proteomic and metabolomic blocking that already happens by the methylation that used for silencing the gene, should be recovered. The limitation in my approach in this case is sensitive to market sharing and should be done by all to fight against power barrier in G20/B20 recover together, recover stronger and faster of food crisis, energy crisis, climate crisis, economy crisis but not epigenetic crisis. High relative humidity in tropical rainforest climate area associated bioelectric transfection to monoculture and nano-vector in association with RNAi transfection should be though as a one-earth problem. It is safe to do the crisis effort in dry-hot and dry-cold area with low relative humidity. Greener methods for the synthesis of various nanostructures with well-organized characteristics and biomedical applicability, have demonstrated several advantages, including simplicity, low toxicity, cost-effectiveness, and eco friendliness. Nickel ferrites nanoparticles with *Moringa oleifera* were synthesized using a simple and green method.

8.3 Discussion of the relevant medical literature

8.3.1 Optical biosensor for organ-on-chips

Organ-on-chips become a NG drug development.⁵⁶

8.3.2 A new quantitative optical biosensor for protein

The demand for quantitative analytical techniques increases with the growth in proteomics. The new optical biosensor is described based on a dual waveguide interferometric technique. The tech has been verified using standard protein systems and by comparing the data with published work using X-ray Crystallography and neutron reflection techniques. Typical film thicknesses for streptavidin layers were in the range 5.5-6.5 nm compare with the short axis crystal structure 4.8-5.6 nm. The precision of the measurements taken was of the order of 40 pm with respect to absorbed adlayer thickness.⁵⁷

8.3.3 Localized SPR for bacterial and virus detection

By automating the PCR system to detect the extracted viral RNA, in nanoscale virus sensing systems. Optical vibration NG virus detection advances and application at nanophotonic resonance with the using of a nano solid material such as a metal with a free charge, the surface charge is called surface plasmon resonance (SPR).⁵⁸

8.3.4 SPRi advances and applications at nanophotonic biosensor⁵⁹

Nanophotonic devices, which control light in subwavelength volumes and enhance light-matter interactions, have opened up exciting prospects for biosensing. Using SPR in metals and added functionalities by leveraging nanostructures and on-chip and optoelectronic integration increase the impact in term of improving health and safety, food safety, environmental monitoring, security, pharmaceuticals and forensics. Harnessing Artificial Intelligent in the SPR imaging are essential.

8.4 The rationale for your conclusions

Semiconductor CoFe₂O₄ extracted from many leaves from tropical rainforest act as a nano-carrier transposon bullet in transfection process in wet-warm tropical rainforest countries. From fruit peels also act as nano-carrier transposon bullet. Green synthesis Method of cobalt ferrite doped to Silver NPs exposure on miRNA and global DNA methylation in Endothelial cells.⁵¹ Ultrasonic irradiation of nano-spinel ferrite with and without *Moringa oleifera*, all samples displayed superparamagnetic (SPM) behavior at room temperature, with no or negligible coercivity and retentivity.²⁸

8.5 The primary “taken-away” lessons from this case report (without references) in a one paragraph conclusion

Natural RNAi vector transfection in tropical rainforest area with wet-warm climate area, is occur in daily living, especially at night when high relative humidity is high, near 100%. This nano-vector transfection is parallel with high prevalence of neuro-enzyme proteomic and metabolic polymorphism, blocking, failure.¹³ This nano-carrier of nanoparticles have electromagnetic power which act as semiconductor. The neuro-enzyme polymorphism/ mutations are like tuberculosis ever, it is cause by nature (faith), not nurture. Spinel ferrite extracted from leaves, are used as novel non-viral vector-mediated gene and epigenetic delivery into mammalian cells, but this mechanism is neglected/ reckless in the discussion on blue carbon vs. blue economy

G20/B20 summit November 2022 in one-earth recover together, recover stronger. SPIONs as nanocarriers with various dope and biological properties have been extensively applied for in vitro/in vivo drug and gene delivery.

IX. PATIENT PERSPECTIVE

9.1 Alignment justify

Sepsis as the cause of ARMGs,²⁴ Gentamycin resistance therapy¹¹ has been reported as the association of SPIONs-ARMGs¹⁰ should be prevented and promoted VS. market share of NG antibiotic in this more than 2 decades.

LGBTQAI has been reported in high prevalence and simple find by primary care doctors and community.

Cancer diagnostic and Therapy using NG drug delivery or promotion, and prevention has been heard by the patients from social media, which is also the hope of stem cell therapy.

9.2 The patient should share their perspective on the treatment(s) they received

1. Hormonal therapy for hypospadias and CAH
2. Mental psychology early help for LGBTQAI is cover by villager stigma
3. Urogenital successful reconstructive operation vs. the cause prevention and promotion of demethylation therapy
4. SPIONs for fighting Antibiotic Resistance/sepsis and new antibiotics market share vs. not using ARMGs in GMO seed production
5. SPIONs for non-viral vector / inorganic vectors of NG drug and vaccine delivery incl. immune and cancer therapy

9.3 The decision maker and environment doer should not omit

1. High Relative Humidity nature transposon-SPIONs in tropical rain forest incl. BRICS area
2. The using of ARMGs for GMO due to drop the cost of separation successful seed vs. the inferior one, but only in dry-cold and dry-hot climate area due to Low Relative Humidity

9.4 The Parliament Law maker should not reckless about:

1. Industry 4.0 without Society 5.0
2. SPIONs nature and nurture
3. Wet and warm vs. dry and cold/ dry and hot climate associated hypermethylation cases
4. PEG toxicity vs. water extracted green SPIONs synthesis
5. Be aware on crime of omittance, crime of allowance, crime of omission and crime of acceptance.
6. Crime, hate crime and LGBTQAI social harassment as the effect of nature and nurture SPIONs

Discretion is the better part of valor for the policy maker.

Semiconductor cobalt ferrite and nickel ferrite mostly extracted from many leaves,^{26, 27, 30, 44} from fruit peels, act as transposon bullet is a rational case.^{60,61}

X. COMPETING INTEREST

Nothing but One-Earth

XI. ACKNOWLEDGMENTS

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which has electromagnetic power function as non-viral vector transposon transfection. Thank to the pandemic COVID-19, who has opened the non-viral nano-carrier or nano-vector RNAi transfection mechanism for diagnostic, vaccine, and therapy.

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