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Research Article

NON-CARCINOGENIC GENOTOXIC DRUGS (NCGDS) COULD BE USED TO MAKE A NON-ANTIGEN-BASED CURE-ALL VACCINE FOR PREVENTING INFECTIONS OF ALL FIVE TYPES OF HUMAN PLASMODIUM SPECIES

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Abstract

Traditional vaccine is antigen-based vaccine, but mutated antigen can fail the previous vaccination. Therefore, production of non-antigen-based or altered- gene-expression-based cure-all vaccine could be a major breakthrough in vaccine development. Plasmodium sporozoites invade hepatocytes via infected female *Anopheles* mosquito bite and the sporozoites mature and multiply into thousands of merozoites inside cells, which is quite like viral infection and as such, the antiviral theory I proposed in 2020 could be used to explain the reason why the sporozoites can specifically invade hepatocytes and consequently, changing gene expression patterns randomly in hepatocytes by non-carcinogenic genotoxic drugs (NCGDs) could prevent all malaria infections. If one dose of NCGD treatment can cause long duration of action, the treatment could be a NCGD-induced cure-all vaccine for prevent all malaria infections. Recently, N- acetylgalactosamine (GalNAc)-conjugated small interfering RNA (siRNA) can prevent rodent and *Plasmodium falciparum* infections and its pharmacodynamics are long duration of action for silencing the target gene with quarterly or bi-annual dosing regimens in human, which indicates that GalNAc-conjugated siRNA treatment is a special vaccine for malaria prevention. Since GalNAc-conjugated siRNA might belong to NCGDs, it is possible that GalNAc-conjugated siRNA could alter gene expression patterns in hepatocytes. Therefore, the special vaccine produced by GalNAc-conjugated siRNA might be a NCGD-induced non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing infections of all five types of human plasmodium species and hepatitis viruses without causing drug resistance in the pathogens. Furthermore, this approach could be used to make non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing all viral infections, indicating that the antiviral theory I proposed in 2020 could also be a theory for making non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing all plasmodium and viral infections. The successful achievement for cure-all vaccine production could mark a historic advance in vaccine development.

Keywords: Non-Carcinogenic Genotoxic Drugs (NCGDs), Malaria, Plasmodium, Malaria Prevention, Antiviral Theory, siRNA, Malaria Vaccine, Non-Antigen-Based Cure- All Vaccine, Altered-Gene-Expression-Based Cure-All Vaccine.

INTRODUCTION

Malaria remains a global health burden with an estimated 282 million cases and 610 000 deaths in 2024 [1]. About 90% of cases occur in 38 countries of Africa, while the remaining are distributed across Southeast Asia and the Eastern Mediterranean Region [2]. There are five types of plasmodium (P) species that infect human, they are named as *P. falciparum, P. vivax, P. malariae, P. ovale* and *P. knowlesi* [3]. Prevention of malaria infection is a complicated approaches including vector control, chemoprophylaxis, and vaccination. Vector control is difficult in some endemic countries. Chemoprophylaxis is still playing a major role in prevention of malaria infection. The vaccine used in human such as RTS,S/AS01 and R21/Matrix-M vaccine for preventing *P. falciparum* infection has recently been found after vaccine study of about 60 years [2]. Based on mainstream theory, it is unable to produce a vaccine for preventing infections of all five human plasmodium species. Recently, I proposed that low dose of X-ray irradiation of related body surface location might prevent all viral infections [4], and irradiation of whole liver might prevent infections of all five human plasmodium species [5] because according to our antiviral theory [6][7], this 'irradiation vaccine' is non-antigen-based or altered- gene-expression-based cure-all vaccine. Unfortunately, mainstream researchers seem not interested in conducting clinic trial to validate this cure-all vaccine that might contribute a lot to malaria eradication and might be possible to replace routine vaccines.

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In this paper, I present an assumption that liver-targeted siRNA for preventing rodent malaria and *P. falciparum* infections [8] is not a simple siRNA treatment but might be a NCGD-induced cure-all vaccine that could be used to protect people from infections of all five types of human plasmodium species and hepatitis viruses.

N-ACETYLGALACTOSAMINE (GALNAC)-CONJUGATED SMALL INTERFERING RNA (SIRNA) MIGHT BELONG TO NCGDS

All drugs used in medical practice belong to NCGDs [9], some are powerful NCGDs (pNCGDs), other are second-class or weak NCGDs (wNCGDs). pNCGDs have a powerful regulation of gene expression and obvious cure-all feature, while wNCGDs have a weak regulation of gene expression and unclear cure-all feature except multiple effects. Both pNCGDs and wNCGDs are harmful to human when overdose is used. The reason why all drugs must be NCGDs is because all internal diseases have abnormal gene expression patterns in related cells, which needs NCGDs' correction. As for nucleic acid drugs such as sRNA, siRNA and antisense oligo [10], the NCGDs' classification above might be unsuitable because siRNA and antisense oligo have no clear genotoxicity, but their alteration of gene expression is powerful due to base pair annealing chaos. Therefore, all nucleic acid drugs might belong to pNCGDs no matter they have or not genotoxicity. Theoretically, GalNAc-conjugated siRNA is a drug for preventing internal disease, indicating that GalNAc-conjugated siRNA might belong to pNCGDs. Practically, GalNAc-conjugated siRNA might have no genotoxicity [11] but could powerfully alter gene expression patterns [12][13][14].

Whether GalNAc-conjugated siRNA is pNCGDs must be decided by standardized comparative transcriptome analysis of GalNAc-conjugated [9]. Overall, I believe that the GalNAc-conjugated siRNA might belong to pNCGDs.

GALNAC-CONJUGATED SIRNA COULD BE A NON-ANTIGEN-BASED OR ALTERED GENE EXPRESSION-BASED CURE-ALL VACCINE FOR PREVENTING ALL MALARIA AND HEPATITIS INFECTIONS

Plasmodium life cycle is complex involving developments in female *Anopheles* mosquito and vertebrate host. Briefly, infected female mosquito bites human and injects plasmodium sporozoites into the skin. The sporozoites specifically invade hepatocytes in the liver and mature and multiply into thousands of merozoites which are then released into bloodstream. The merozoites from liver specifically invade red blood cells, starting erythrocytic stage cycle that causes malaria symptom. In a word, to prevent malaria infection, blocking sporozoites from entering hepatocytes in the liver is the key to prevention of malaria infection. Based on the antiviral theory I proposed in 2020, the reason why sporozoites of malarial parasites can invade hepatocytes, and then mature and multiply into thousands of merozoites inside cells is because the gene expressions patterns in hepatocytes are suitable for sporozoite invasion, which is quite like viral infection. Therefore, alteration of gene expression patterns randomly in hepatocytes by NCGDs will reduce the susceptibility to sporozoite invasion, for example, metformin, curcumin and berberine belong to NCGDs and many research results have shown that they all have malarial prevention effects [15][16][17]. If a dose of NCGD treatment can prevent malaria infection for a long time, it would be a NCGD-induced cure-all vaccine. Recently, the report that liver-targeted siRNA could be used to prevent rodent malaria and *P. falciparum* infections by blocking the gene expression of hepatic receptor (CD81) for malaria sporozoite invasion has reminded me to assume that this GalNAc-conjugated siRNA treatment might be a NCGD-induced vaccine for preventing malaria infection [8]. The biological half-life of using GalNAc-conjugated siRNA in human cells is 1.5–14 weeks in human [18], and GalNAc-conjugated siRNA pharmacodynamics are long duration of action for silencing the target gene with quarterly or bi-annual dosing regimens in human [8], which supports my vaccine assumption. Therefore, the vaccine produced by GalNAc-conjugated siRNA could be a non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing infections of all five types of human plasmodium species and hepatitis viruses because GalNAc-conjugated siRNA that might belong to NCGDs could alter gene expression patterns in hepatocytes. Furthermore, the similar approach could be used to produce non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing all viral infections.

I think that GalNAc-conjugated siRNA for silencing the gene expression of CD81 in the liver could cause global changes in transcription, which further indicates that prevention of malaria by GalNAc-conjugated siRNA might be through alteration of gene expression patterns in hepatocytes that could be determined by standardized comparative transcriptome analysis [9]. To obtain a good cure- all vaccine, biological half-life of siRNA must be longer and siRNA design should focus on causing global gene expression chaos and not on silencing a gene expression specifically. Additionally, gene expression patterns in cells could be taken as a complex tree with thousands of branches that have interacted each other through signaling pathways. Small number of branches are genes, and majority of branches are uncoded DNA. Even an epigenetic change in DNA or receptor being targeted by a drug might cause the whole tree trembling, causing changes in global gene expression patterns. This is reason why GalNAc-conjugated siRNA induced vaccine is named as NCGD-induced non-antigen- based or altered-gene-expression-based cure-all vaccine for preventing all malaria and hepatitis infections, which could be a historic advance in vaccine development. Besides, this cure-all vaccine might never cause drug resistance in viruses and malaria parasites because the vaccine will not target the pathogens [19]. To sum up, the novel antiviral theory I proposed in 2020 could become a theory for producing non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing all plasmodium and viral infections.

CONCLUSION

Development of vaccine plays an important role in prevention of malaria infections in global endemic countries. But complicated life cycle of malaria parasites can make the vaccine success difficult. Also, when mutated antigen occurs, the previous vaccination will be failed. Therefore, antigen-based vaccine research is a big problem in vaccine development. mRNA vaccine is new-tech product, but long-term harmfulness to human body could be debated. I propose using low dose of X-ray irradiation of whole liver could be a cure-all vaccine for preventing infections of five types of plasmodium species, but no researchers have interest in this approach. In this paper, a recent report that liver-targeted GalNAc-siRNA could prevent rodent malaria and *P. falciparum* infections has reminded me to assume that this GalNAc-siRNA treatment could be a NCGD- induced non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing infections of all five types of human plasmodium species and hepatitis viruses because GalNAc-siRNA treatment might alter gene expression patterns in liver cells. GalNAc-siRNA pharmacodynamics are long duration of action for silencing the target gene with quarterly or bi-annual dosing regimens in human, which further supports this NCGD-induced vaccine assumption. Furthermore, this approach could be used to produce non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing all viral infections. To summarize, the antiviral theory I proposed in 2020 could also be a theory of making non-antigen-based or altered-gene-expression-based cure-all vaccine for preventing all plasmodium and viral infections without causing drug resistance in the pathogens, which could be a historic advance in vaccine development.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

REFERENCES

1. World Health Organization. (2025) World Malaria Report 2025. World Health Organization, Geneva, Switzerland.
2. Kaithamanakallam, R.P., Patel, T., Balachandran, B., Fernandez, N., Jillwin, J., Kashyap, D., et al.(2025) Malaria Vaccines and Global Equity: A Scoping Review of Current Progress and Future Directions. *Biomedicines*,13(6):1270.

3. Fikadu, M., Ashenafi, E. (2023) Malaria: An Overview. *Infect Drug Resist*. 16:3339-3347.
4. Li, G.D. (2024) Could X-Ray Irradiation Be Used as an "Irradiation Vaccine"?, *Open Access Library Journal*, 11: e11337.
5. Li, G.D. (2025) Non-Carcinogenic Genotoxic Drugs (NCGDS): A New Concept of old Drugs with Genotoxic Side effects. *International Journal of Science Academic Research* Vol. 06, Issue 08, pp.10460-10462.
6. Li, G. D. (2020) Non-Carcinogenic Genotoxic Drugs Could Be Used to Prevent and Treat COVID-19. Open Access Library Journal, 7: e6536.
7. Li, G. D. (2022) Taking Paracetamol and Vitamin C or Ibuprofen and Vitamin C Every Day Could Be a Simple Way to Prevent COVID-19 Infection. *Open Access Library Journal*, 9: e9544.
8. Steel, R.W.J., Schepis, A., Nguyen, T., Milstein, S., Yucius, K., Tu, H.C. *et al*. (2025) Protection from Malaria Infection Using Liver-Targeted siRNA. *Mol Ther Methods Clin Dev*, 33(3):101516.
9. Li, G. D. (2026) Study of Non-Carcinogenic Genotoxic Drugs (NCGDs) might reveal Three Medical Principles. *International Journal of Science Academic Research*, 07, Issue 05, pp.808-810.
10. Naeem, S., Zhang, J., Zhang, Y., Wang, Y. (2024) Nucleic Acid Therapeutics: Past, Present, and Future. *Mol Ther Nucleic Acids*, 36(1):102440.
11. Janas, M.M., Jiang, Y., Duncan, R.G., Hayes, A.N., Liu, J., Kasperkovitz, P.V., *et al*. (2016) Exposure to siRNA-GalNAc Conjugates in Systems of the Standard Test Battery for Genotoxicity. *Nucleic Acid Ther*, 26(6):363-371.
12. Semizarov, D., Kroeger, P., Fesik, S. (2024) siRNA-Mediated Gene Silencing: a Global Genome View. *Nucleic Acids Res*, 32(13):3836-45.
13. Ahmed, W., Xia, Y., Li, R., Zhang, H., Siddique, K.H.M., Guo, P. (2021) Identification and Analysis of Small Interfering RNAs Associated with Heat Stress in Flowering Chinese Cabbage Using High-Throughput Sequencing. *Front. Genet*. 12:746816.
14. Zhang, J., Chen, B., Gan, C., Sun, H., Zhang, J., Feng, L. (2023) A Comprehensive Review of Small Interfering RNAs (siRNAs): Mechanism, Therapeutic Targets, and Delivery Strategies for Cancer Therapy. *Int J Nanomedicine*, 18:7605-7635.
15. Vera, I.M., Grilo Ruivo, M.T., Lemos Rocha, L.F., Marques, S., Bhatia, S.N., Mota, M.M. *,et al*. (2019) Targeting liver stage malaria with metformin. *JCI Insight*, 4(24):e127441.
16. Jamil, S.N.H., Ali, A.H., Feroz ,S.R., Lam, S.D., Agustar, H.K., Mohd Abd Razak,M.R., et al.(2023) Curcumin and Its Derivatives as Potential Antimalarial and Anti-Inflammatory Agents: A Review on Structure-Activity Relationship and Mechanism of Action. *Pharmaceuticals* (Basel), 16(4):609.
17. Silikas, N., Mccall, D.L.C., Sharples, D., Watkins, W.M., Waigh, R.D. and Barber, J. (1996), The Antimalarial Activity of Berberine and Some Synthetic Analogues. *Pharmacy and Pharmacology Communications*, 2: 55-58.
18. Boianelli A, Aoki Y, Ivanov M, Dahlén A, Gennemark P.(2022) Cross-Species Translation of Biophase Half-Life and Potency of GalNAc-Conjugated siRNAs. *Nucleic Acid Ther*, 32(6):507-512.
19. Li, G. D. (2023) Antiviral Theory Might Help to Develop Drug-Resistance-Free Antimalarial Drugs. *Open Access Library Journal*, 10: e10505.

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