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Research Article

STUDY OF NON-CARCINOGENIC GENOTOXIC DRUGS (NCGDS) MIGHT REVEAL THREE MEDICAL PRINCIPLES

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Abstract

Aetiology is the study of the causes or origins of diseases. A thorough understanding of aetiology is vital for all diseases' prevention, diagnosis, and treatment. Further study of non-carcinogenic genotoxic drugs (NCGDs) might reveal three medical principles, the first one is abnormal gene expression patterns that exist in all internal diseases and might be considered as a unified cellular aetiology for all diseases; the second one is changing abnormal gene expression patterns in the cells associated with all diseases that is named as unified drug action for all drug treatments; the third one is a unified mechanism of action of all drugs that could be used to explain the mechanism of action of every drug. Both internal and external disease-causing factors could cause abnormal 3D genome structure in related cells that causes abnormal gene expression patterns in related cells, which leads to clinical manifestations including subjective symptoms and physical signs. Changing abnormal gene expression patterns by NCGDs or second-class NCGDs is the essence of all drugs' action. NCGDs have powerful effects on alteration of gene expression patterns, and second-class NCGDs might have weak effects but are necessary for treating some diseases. If the three medical principles are proven true, focussing on these three medical principles are vital important in developing drugs and improving consequences of all diseases.

Keywords: Non-Carcinogenic Genotoxic Drugs (NCGDs), Unified Cellular Aetiology, Unified Drug Action. Unified Mechanism of Action of All Drugs, Comparative Transcriptome Analysis, Differentially Expressed Gene, Gene Expression Patterns.

INTRODUCTION

I am the person who first proposed non-carcinogenic genotoxic drugs (NCGDs) for preventing and treating COVID-19 in 2020 [1], hoping they will care for human health. The original criterion for identifying NCGDs was to find if the old drug had genotoxicity, based on this unique criterion, many NCGDs have been found in medicines [2]. Since some old drugs don't have clear genotoxicity, modulating expression of many genes has been proposed as second unique criterion for identifying NCGDs, according to these two criteria, antioxidants have been found to be NCGDs [3]. Recently, NCGDs have cure-all effects and the cure-all feature have been added as third unique criterion, based on these three criteria, hormones and neurotransmitters have been found to be NCGDs [4]. So many drugs including antioxidants and hormones and neurotransmitters have belonged to NCGDs, which indicates that many diseases have abnormal gene expression patterns in related cells that need to be changed by NCGDs when the diseases are treated. An imagination appears in my mind: All diseases (mainly internal diseases) have a unified cellular aetiology that is abnormal gene expression patterns in cells associated with all diseases, and all drugs have a unified drug action in treating all diseases, which is changing abnormal gene expression pattens in related cells by NCGDs. The unified mechanism of action of all drugs is also possible. In this paper, I present an assumption that there are three principles in medicine, that is unified cellular aetiology for all diseases, unified drug action for all drug treatments and unified mechanism of action of all drugs.

ALL USEFUL DRUGS MIGHT INCLUDE NCGDs AND SECOND-CLASS NCGDs

NCGDs refer to old drug's alteration of gene expression patterns through interfering with 3D genome structure directly or indirectly.

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Except NCGDs, the rest drugs might be classified as second-class NCGDs because these drugs also involved in alteration of gene expression but not obviously as NCGDs. If all useful drugs might include NCGDs and second-class NCGDs, they indicate that all drugs used in medical practice have ability of altering abnormal gene expression patterns in human cells associated with all diseases. The reason why all used drugs must have this ability is because all internal diseases have abnormal gene expression patterns in related cells that are caused by abnormal dynamic 3D genome structure that is a response to internal and external disease-causing factors[5] [6]. Theoretically, if a substance has none of this ability, it will not be a useful drug. Practically, many medicines including antioxidants, hormones and neurotransmitters belong to NCGDs, which supports the assumption that all useful drugs might include NCGDs and second-class NCGDs. NCGDs could be identified by three criteria for identifying NCGDS [4]. But second-class NCGDs have no clear feature as NCGDs do, their ability of induction of gene expression patterns in related cells could be weak but could be detected by comparative transcriptome analysis [7][8]. A drug-induced expression of many genes suggests that the drug has interfered with dynamic 3D genome structure in a direct or indirect ways. Unfortunately, current transcriptome analysis is not standardized. Therefore, I propose that comparative transcriptome analysis must be standardized by using standard cells, drug dose and course, and number of differentially expressed genes being reported.

Some people think that the drug they discovered is receptor-binding drug and has nothing to do with gene expression patterns, but the drug is NCGDs that could enter cells as well [9]. Even a drug just binds the receptor without entry into the cells, it could induce gene expression patterns in related cells because of signaling pathway complexity. Gene targeting is a therapeutic avenue for treating diseases [10], but the treatment results are not determined by the targeted genes but by the gene expression patterns caused by the targeted genes. In a word, all diseases have abnormal gene expression patterns in

related human cells, and all drugs' induced gene expression patterns in the same cells. NCGDs and second-class NCGDs have a more or less effects on alteration of gene expression patterns, which is required by treating all diseases in medical practice.

UNIFIED CELLULAR AETIOLOGY FOR ALL DISEASES AND UNIFIED DRUG ACTION FOR ALL DRUG TREATMENTS

Further investigation of NCGDs have made me to propose an assumption that in medical practice, there might be three principles. The first one is unified cellular aetiology for all internal diseases, such as Infectious diseases, cardiovascular diseases, endocrine and metabolic diseases, respiratory system diseases, etc. which is that both internal and external disease-causing factors cause abnormal 3D genome structure that causes abnormal gene expression patterns, which leads to clinical manifestations including subjective symptoms and physical signs. The period of having abnormal gene expression patterns in related human cells could be short such as cold or longer such as chronic disease or permanent such as genetic disease. The second one is unified drug action for all drug treatments, indicating that changing abnormal gene expression patterns could be achieved by NCGDs or second-class NCGDs. The third one is a unified mechanism of action of all drugs that could be used to explain the mechanism of action of every drug, which will be described in detail later. The 3D genome structure regulates vital biological processes including cell cycle, DNA replication, cell differentiation, and transcription [11].But I assume that the dynamic 3D genome structure also functions as disease-causing machinery because abnormal 3D genome structure could be caused by both internal and external disease-causing factors. The dynamic 3D genome structure is also involved in disease treatment, making it become a therapy machinery.

NCGDs have powerful effects in alteration of gene expression patterns in related cells, and second-class NCGDs might have weak effects but are necessary for treating some diseases. For treating difficult or chronic diseases, combinations of multi-targeting drugs are important for good consequences of diseases because few different abilities of NCGDs in altering gene expression patterns could be well balanced for improving therapy results [12]. Collectedly, the three medical principles are assumed based on NCGDs' study and need clinical trial to prove. If the three medical principles are proven true, remembering and focusing on these three medical principles might be vital impotent for developing drugs and improving treatment results of all diseases.

UNIFIED MECHANISM OF ACTION OF ALL DRUGS

If all diseases have a unified cellular aetiology, that is abnormal gene expression patterns in the cells associated with all diseases and all drugs have unified drug action, that is alteration of abnormal gene expression patterns in all treatments. Now we know that all drugs might include NCGDS and second-class NCGDs. Do they have a unified mechanism of action of all drugs? My answer is yes. Alteration of abnormal gene expression patterns in the cells associated with all diseases is alteration of abnormal 3D genome structure in the same cells. But it is difficult to control abnormal 3D genome structure at present time. Forty years ago, I published a paper on an abnormal chromatin configuration and cancer formation, in which 3D genome structure could be reflected by gene expression patterns [13]. Therefore, we could use abnormal gene expression patterns to reflect abnormal 3D genome structure because drug-induced gene expression patterns could be detected by comparative transcriptome analysis [7][8]. We can set up normal gene expression patterns in healthy human cells as the standard. If gene expression patterns in related cells caused by a drug are approaching or reaching the standard, the disease might be improved or cured. If the drug treatment makes the gene expression patterns in related cells unchanged, the disease will remain unchanged. If the gene expression patterns in related cells caused by a drug are away from the standard, the disease will get worse. If the gene expression patterns in human cells caused by a drug are far away from the standard but within the safe range, the human cells could become resistant cells against single-cell pathogen infections though the original disease remains unchanged or becomes worse. If the gene expression patterns in related cells caused by a drug are very far away from the standard and have reached an extreme point or death point where the gene expression patterns can't promote cell survival, the related cells will die. If a drug kills a single-cell pathogen, it means that the gene expression patterns in the pathogen caused by the drug has reached the death point from the point of untreated pathogen's gene expression patterns because we can't set up standard in single-cell pathogens. Honestly, this is a novel mechanism of action of drugs, which could be considered as a unified mechanism of action of all drugs.

Using this unified mechanism of action of all drugs, we can explain the mechanism of action of every drug, for example, chloroquine (CQ) is a NCGD drug and has therapeutic activities against malaria, cancers and viral diseases. The current mechanisms for these activities are presented here [14], which is challenged by this unified mechanism of action of all drugs. The mechanism of killing malaria parasites by CQ is that CQ accumulates free hematin that is highly toxic to malaria parasites and thus causes death of the parasites. Using the unified mechanism of action of all drugs, the gene expression patterns in malaria parasites caused by CQ has reached the death point, that is the reason why the parasites are killed. CQ is regarded as an autophagy inhibitor and could be an adjuvant to anticancer chemotherapies. Also, CQ renders cancer cells more sensitive to many anticancer drugs and enhances their therapeutic activity. According to the unified mechanism of action of all drugs, the gene expression patterns in cancer cells caused by CQ are closer a bit to the standards, which makes CQ's anticancer effects occur. With lysosomotropic, immunomodulatory properties and as autophagy inhibitor, CQ has crucial roles in antiviral effects, based on the unified mechanism of action of all drugs, the gene expression patterns in human cells caused by CQ, are far away from the standard but within safe ranges, which makes human cells have reduced susceptibility to all viral infections [1].

To sum up, mainstream theory states that every drug has its unique mechanism, and thus thousands of drugs have thousand different mechanisms. I doubted about this theory and proposed a viewpoint of focusing on drug-altered gene expression patterns and giving up the mechanisms of action of drugs [15]. I believe that improvement or getting worse of a disease is determined by gene expression patterns and therefore, using gene expression patterns as the core in unified mechanism of action of all drugs is reasonable, which looks simple but reliable, flawless and suitable to explain mechanism of action of every drug.

CONCLUSION

Further investigation of NCGDs have made me to propose an assumption that in medical practice, there might be three principles, the first one is unified cellular aetiology for all internal diseases, which is that both internal and external disease-causing factors cause abnormal 3D genome structure in cells associated with all diseases that causes abnormal gene expression patterns, which leads to clinical manifestations including subjective symptoms and physical signs; the second one is unified drug action for all drug treatments, indicating that changing abnormal gene expression patterns in related cells could be achieved by NCGDs or second-class NCGDs; the third one is a unified mechanism of action of all drugs that could be used to explain the mechanism of action of every drug. NCGDs have powerful effects in alteration of gene expression patterns, and second-class NCGDs might have weak effects but are necessary for treating some diseases. If these three medical principles are proven true, focussing on them could be vital important in developing drugs and improving treatment results of diseases.

CONFLICTS OF INTEREST

The author declares no conflicts of interest.

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