www.toxicologydigest.org.ng

Nnenna et al., Toxicology Digest Vol. 5 (1): 108-118 (2026)

Toxicology Digest

Critical Roles of Micronutrients against Genetic Toxicity: Connecting Molecular Defense to Clinical Chemistry Applications

Nnenna Linda Nwobi[1], Nwobi Joseph Chigbo Nwobi[2], Oladayo Thomas Odedoyin[3], Anuoluwapo V. Adeyemi[1], Gloria O. Anetor[4], John I. Anetor[5]

[1.] *Department of Chemical Pathology, Benjamin Carson (Snr) College of Health and Medical Sciences, Babcock University, Ilishan Remo, Nigeria.*

[2.] *Department of Biochemistry, Benjamin Carson (Snr) College of Health and Medical Sciences, Babcock University, Ilishan Remo, Nigeria.*

[3.] *Chemical Pathology Laboratory, University College Hospital, Ibadan, Nigeria.*

[4.] *Department of Public Health Science, Faculty of Health Sciences, National Open University of Nigeria, Abuja, Nigeria.*

[5.] *Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Nigeria*

DOI: https://doi.org/10.71637/toxicologydigest.vol5no1.57

Correspondence: 08135388049; nwobin@babcock.edu.ng; nwobinnenna2022@gmail.com.

Abstract

Background: Genotoxic exposures from environmental toxicants and endogenously produced excess free radicals damage the DNA and other cellular components involved in replication and repair. This damage if left unchecked, can lead to genome instability, mutations, cancer and other pathologies. However, micronutrients, though play a highly significant role in genome integrity, function and damage repair are often overlooked. **Objectives**: This review was aimed to highlight the evidence of the protective roles of micronutrients against genetic toxicity and potentials of assimilation into clinical laboratory medicine. **Methods**: Relevant literature that linked micronutrient functions (selenium, zinc, iron, manganese, vitamins B9 (folate), B12, C, and E) to DNA damage and repair were analysed. Literature survey involved the use of general search engines (Google and Bing), subject-specific search engines (GoPubMed) and scholarly literature databases (Google Scholar Embase). **Results**: Micronutrients were found to be important cofactors in three major defence mechanisms: antioxidant defence (direct radical scavenging - vitamins C and E; enzymatic antioxidant activity - selenium, zinc, manganese), DNA repair enzyme function (zinc, iron), and epigenetic maintenance via one-carbon metabolism (folate, B12, B6). Human studies using proven indicators of effect such as the comet assay, micronucleus test, and urinary 8-hydroxy-2'-deoxyguanosine, showed that low micronutrient status is associated with increased genetic damage. Targeted supplementation in populations with high exposure demonstrated the capacity to alleviate this damage and emphasised the significance of genetic polymorphisms and need for personalised nutrition. **Conclusion**: Micronutrients are significant biochemical foundation for genome stability. Linking molecular roles of micronutrients with their application in clinical chemistry appears to be an important arsenal against genotoxic damage thus of great public health significance.

Keywords: DNA repair, Genetic polymorphism, Genome, Genotoxicity, Micronutrients.

Date Received: 07/04/2026
Date Accepted: 12/07/2026
Date Published:06/07/2026

INTRODUCTION

Humans are constantly exposed to genotoxic insults from both endogenous and exogenous genotoxicants that damage DNA and other cellular components involved in genetic replication and repair (Xu et al., 2025). These include free radicals generated from normal cellular metabolism such as reactive oxygen species (ROS), environmental contaminants, industrial chemicals, pharmaceutical agents, dietary genotoxins and ultraviolet radiation. Unrepaired or misrepaired DNA lesions lead to genetic instability and mutations that may be foundational in diverse disease pathways such as cancer, inherited genetic disease, and other chronic disorders if unresolved (Gujar et al., 2025).

Micronutrients, composed of vitamins and minerals, are significant biochemical foundation that protect against genetic damage (Fenech, 2020; Gofrey et al., 2025). Bruce Ames in the 1990s, proposed that micronutrient deficiencies could compromise the intergrity of the genome by leading to various DNA breaks and chromosomonal abberations. These findings have continued to be corroborated by numerous scientific reports (Ames, 1999; Ames, 2010; Collins et al., 2012; Fenech, 2020; Wu et al., 2021; Wong et al., 2025; Dinu et al., 2026). Despite these numerous crucial reports, micronutrients are yet to be incorporated into risk assessment and genetic toxicity testing protocols.

Genetic toxicity could be curbed by three main routes of defense in the human body: antioxidant enzymes, DNA repair pathways and epigenetic maintenance systems, all of which require essential micronutrients such as zinc, selenium, manganese, magnesium, iron, vitamins B9 (Folate), B12, B6, C and E. These micronutrients act as essential cofactors for DNA enzymes, maintain structural integrity of important proteins such as p53, maintain genomic stability as well as controls gene expression (Godfrey et al., 2025). Despite this wealth of knowledge, there is still a significant gap between molecular toxicology and clinical practice. Although there is extensive laboratory evidence supporting micronutrient-mediated genome protection, clinical evaluation of this evidence has received insufficient (Fenech, 2014; Milne et al., 2015; Fenech 2020).

The purpose of this review was to link these two domains by:

1. Gathering molecular mechanisms on micronutrients prevention of genetic toxicity via antioxidant defence, DNA repair, and epigenetic maintenance.
2. Evaluating clinical application by determining both micronutrient status and genetic damage using direct biomarkers, functional biomarkers and impact biomarkers.
3. Determining the translational potential of this knowledge for human health.

2. Micronutrients in Antioxidant Defense

The antioxidant defence is the first line of defense against genetic toxicity. It involves neutralizing free radicals such as ROS before they damage the DNA. This antioxidant defense network comprises both direct free radical scavengers as well as enzymatic systems, both essentially reliant on sufficient micronutrient supply

2.1 Vitamins E and C in Direct Radical Scavenging

Vitamin E encompasses a family of lipophilic compounds that partition into lipid membranes and lipoproteins, where they function as chain-breaking antioxidants. Vitamin E terminates the chain reaction of lipid peroxidation by intercepting lipid peroxyl radicals, thereby protecting membrane-associated DNA from secondary damage induced by lipid-derived electrophiles. Recent clinical report have shown that vitamin E supplementation can significantly decrease markers of oxidative DNA damage, specifically 8-hydroxy-2'-deoxyguanosine (8-OHdG) as well as modulate the inflammatory microenvironment that can indirectly promote DNA damage (Sharif et al., 2025). Vitamin E's genoprotective role is particularly critical in tissues exposed to high oxidative loads, where lipid peroxidation products such as 4-hydroxynonenal and malondialdehyde can form exocyclic DNA adducts with mutagenic potential (Dinu et al., 2026).

Vitamin C (ascorbate) serves as the primary water-soluble antioxidant in plasma and cytoplasm, directly neutralizing superoxide, hydroxyl radicals, and singlet oxygen (Figueroa-Méndez et al., 2015). Vitamin C also regenerates oxidized vitamin E to its active form (Packer et al., 1987; Xu et al., 2025). This synergy is particularly relevant at membrane-cytoplasm interfaces, where oxidative damage to membrane lipids is most effectively contained.

2.2. Enzymatic Antioxidant Support

While direct scavengers provide immediate but stoichiometric protection, enzymatic antioxidant systems such as Superoxide Dismutases(SOD) and glutathione peroxidase (GPx), offer catalytic, sustained defense. These enzymes incorporate micronutrients such as Zinc, Copper, Manganese and selenium as essential cofactors.

The SOD family is the first enzymatic line of defense against the superoxide radical ($O_2^{-}\bullet$) to produce hydrogen peroxide. Humans have 3 isoforms of SOD each with unique subcellular localizations and metal co-factor requirement: cytoplasmic SOD1 requires copper and zinc; mitochondrial SOD2 requires manganese; and extracellular SOD3 requires copper and zinc (Wong, 2025).

Selenium is incorporated as selenocysteine into the active site of GPx enzymes (Kunwar & Nayak, 2026). The selenium-dependent GPx family represents a vital enzymatic system for detoxifying hydrogen peroxide and organic hydroperoxides, including lipid hydroperoxides that can propagate DNA damage.

2. Micronutrients as Cofactors for DNA Repair

When antioxidant defenses are overwhelmed and DNA damage occurs, DNA repair systems must identify and correct the lesions (Fig 1).

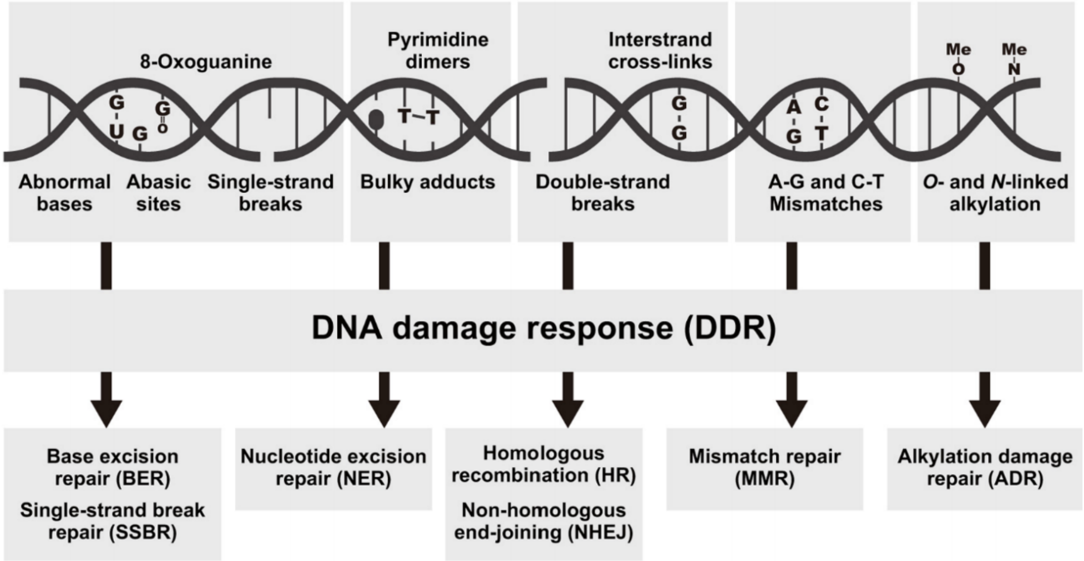

Figure 1. Types of DNA damage and the associated repair pathways. Examples of DNA lesions (top), activation of the DNA damage response (DDR, middle), and the most relevant DNA repair pathways responsible for the removal of the lesions (bottom). Tasaki et al., 2018.

Base excision repair (BER) handles small, non-helix-distorting lesions such as oxidized bases, alkylated bases and uracil; nucleotide excision repair (NER) eliminates bulky adducts; double-strand break repair via homologous recombination (HR); non-homologous end joining (NHEJ) deals with the most dangerous lesions; and mismatch repair (MMR) corrects replication errors (Fig 1). Numerous proteins make up each repair pathway and many of them need micronutrients such as zinc, magnesium and iron, for catalytic activity or structural integrity.

2.1. Zinc in Zinc Finger Proteins

One of the most prevalent structural motifs in proteins is the zinc finger.

Zinc fingers are critical for DNA-binding proteins such as p53 and BER enzymes involved in damage identification, repair and cell cycle control.

p53

The p53 tumor suppressor protein (guardian of the genome)(Efeyan and Serrano, 2007), coordinates cellular responses to DNA damage, including cell cycle arrest, apoptosis, and DNA repair. p53 functions as a transcription factor that controls hundreds of target genes, and its ability to bind DNA is solely dependent on the structural integrity of its core DNA-binding domain, which contains a zinc ion tetrahedrally coordinated by cysteine and histidine residues. Zinc deficiency compromises p53 function (Wong, 2025). Loss of zinc from the DNA-binding domain disrupts the protein's three-dimensional structure, hindering its ability to bind consensus DNA sequences and transactivate target genes. This functional compromise shows p53 is very sensitive to zinc status and occurs at zinc concentrations that have little effect on cell survival (Wong, 2025).

Base Excision Repair Enzymes

Zinc finger motifs are also necessary for the operation of certain BER enzymes. 8-Oxoguanine DNA glycosylase (OGG1), which excises the common oxidative lesion 8-oxo-dG, contains a zinc finger motif critical for substrate recognition and catalysis. Recent animal studies have shown that zinc deficiency increases age-related DNA damage by reducing OGG1 catalytic activity (Wong et al., 2025). Similarly, zinc is necessary for the structural stability of apurinic/apyrimidinic endonuclease 1 (APEX1), which breaks down abasic sites produced by glycosylases. A bottleneck in the repair of oxidative DNA damage is created by the combined effect of zinc shortage on several BER enzymes, allowing lesions to persist and potentially get fixed as mutations during replication.

Iron in the form of Iron-Sulfur Clusters

Iron (Fe) in the form of iron-sulfur (Fe-S) clusters is an essential cofactor for some enzymes involved in DNA replication and repair. Fe-S clusters are prosthetic groups that help a variety of proteins with substrate binding, electron transfer, and structural stabilization. Fe-S clusters are necessary for the unwinding activity of key DNA helicases involved in telomere maintenance, interstrand crosslink repair, and nucleotide excision repair (Bharti et al., 2013).

3. Folate, Vitamin B12, and Vitamin B6 - in Epigenetic Maintenance

Micronutrients such as folate, B12 and B6 are essential for maintaining the epigenetic marks that regulate gene expression, silence transposable elements, and ensure proper chromosome architecture. Disruption of epigenetic patterns can itself promote genomic instability (Russo et al., 2021). Vitamin B9(folate), B12, and B6 are essential cofactors in one-carbon metabolism, the metabolic pathway that supplies methyl groups for all biological methylation reactions, including DNA methylation - a cornerstone of epigenetic regulation.

Folate, in its active form as 5-methyltetrahydrofolate, donates methyl groups for the remethylation of homocysteine to methionine a reaction absolutely dependent on Vitamin B12 as a cofactor for methionine synthase. Methionine is then adenylated to form S-adenosylmethionine (SAM), the universal methyl donor for DNA methyltransferases, which establish and maintain methylation patterns at CpG sites across the genome. Vitamin B6 serves as an essential cofactor for serine hydroxymethyltransferase, which generates 5,10-methylenetetrahydrofolate - the form of folate required for thymidylate synthesis.

Deficiency of these B vitamins creates a dual threat to epigenetic stability (Russo et al., 2021):

1. DNA Hypomethylation: Reduced SAM availability leads to genome-wide hypomethylation, which can activate transposable elements, promote chromosomal instability, and dysregulate gene expression patterns that favor carcinogenesis.

2. Uracil Misincorporation: When folate is limiting, thymidylate synthesis is compromised, causing uracil to be misincorporated into DNA. The attempted repair of uracil by base excision repair creates transient strand breaks - genetic damage visible as micronuclei. Also the resulting reduced thymidine level leads to stalled replication forks and replication Collapse (Adolph et al., 2024).

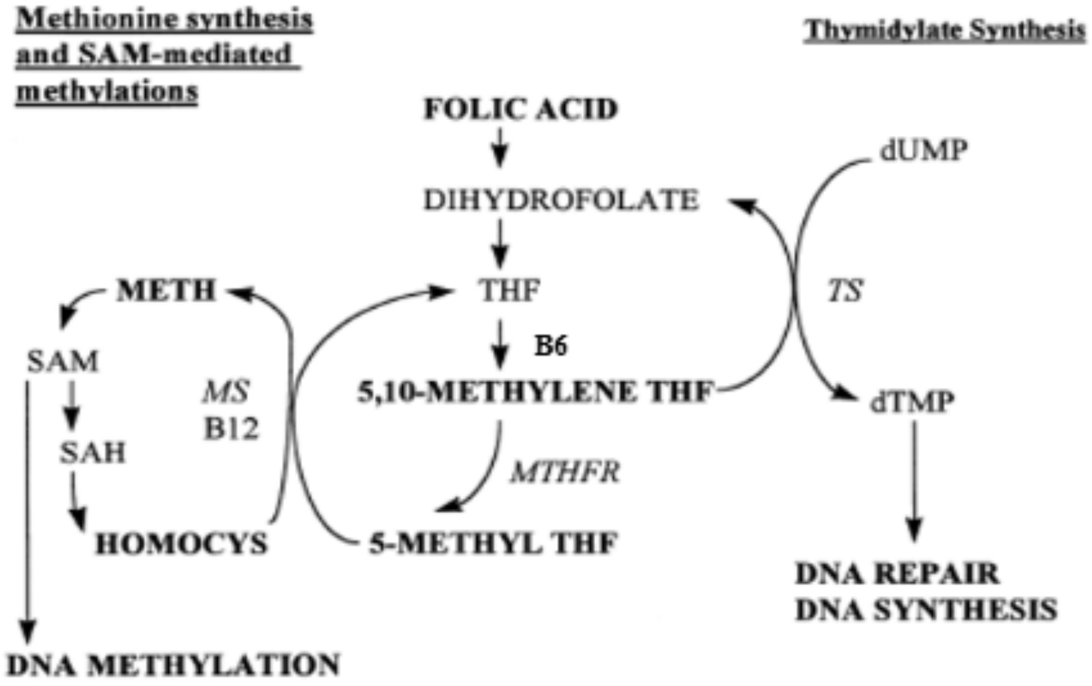

Fig. 2. The main metabolic pathways in folate and homocysteine (homocys) metabolism. B12: Vitamin B12; B6: Vitamin B6; meth: methionine; THF: tetrahydrofolate; TS: thymidylate synthase; MS: methionine synthase; MTHFR: methylenetetrahydrofolate reductase; SAM: S-adenosyl methionine; SAH: S-adenosyl homocysteine.

5. Assessement of Micronutrient Status and Genetic Damage in Clinical Practice

5.1. Assessment of Micronutrient Status

No single measurement approach can effectively capture micronutrient status. (Zambrano-Villacres et al., 2026).

Direct Biomarkers of Status

Traditional micronutrient assessments rely on direct measurement of nutrient concentrations in blood compartments (serum, plasma, or erythrocytes). These measures provide an indication of circulating levels (Wang et al., 2026). However, circulating levels may not accurately reflect tissue state. This is an important factor when comparing micronutrient status to functional outcomes such as genomic stability.(Zambrano-Villacres et al., 2026).

Functional Biomarkers

Functional biomarkers provide a more dynamic picture of nutritional status by assessing the biological activity of micronutrients rather than their availability. These tests provide comprehensive information on nutrient availability and metabolic function by assessing enzyme activity reliant on specific micronutrient cofactors. The erythrocyte glutathione reductase activation coefficient (EGRAC) is an example of this method for determining vitamin B2 (riboflavin) levels. By assessing the activity of glutathione reductase, a flavin adenine dinucleotide (FAD)-dependent enzyme, before and after adding FAD to the test, EGRAC provides a riboflavin status index that reflects long-term availability rather than current dietary intake. Similarly, functional assessment of vitamin B6 can be achieved through measurement of erythrocyte aspartate aminotransferase activation, while thiamine (vitamin B1) status is reflected in transketolase activity. These functional assays are particularly useful for nutrients involved in antioxidant defense and DNA repair pathways because they capture the physiologically relevant fraction of the nutrient pool.

5.2. Biomarkers of Genetic Damage

The true integrity of the genome is revealed by measuring biomarkers of genetic damage.These effect biomarkers serve as early warning signals of genomic instability and can be used to monitor the effectiveness of nutritional interventions. These biomarkers include; Comet Assay, Cytokinesis-Block Micronucleus Cytome Assay, Urinary 8-oxo-dG.

The Comet Assay (Single-Cell Gel Electrophoresis)

One of the most dependable biomarkers for identifying the early biological effects of genotoxic exposures is the comet assay, sometimes referred to as single-cell gel electrophoresis (Najafzadeh et al., 2026). The assay's relative simplicity, speed, sensitivity, and cost-effectiveness are what make it appealing. In a standard protocol, isolated single cells are embedded in agarose and lysed in high-salt solutions to remove all cellular contents except DNA attached to a nuclear scaffold. After further electrophoresis, broken DNA sequences move toward the anode whereas intact sequences accumulate close to the nuclear scaffold. These migrating DNA pieces resemble a comet tail when viewed with fluorochromes, and they may be measured for intensity and form using globally developed parameters (Najafzadeh et al., 2026). The assay is accepted as a reliable indicator of early biological effects and genetic damage following exposure to environmental, occupational, or lifestyle toxicants and has been widely adopted by governmental regulatory agencies for human biomonitoring (Najafzadeh et al., 2026; Møller et al., 2026).

The Cytokinesis-Block Micronucleus Cytome Assay

The micronucleus cytome assay represents one of the most comprehensive tools for assessing genomic instability. When cells undergo division in the presence of cytochalasin-B (which blocks cytokinesis but not nuclear division) binucleated cells accumulate, allowing selective scoring of damage that occurred during the preceding cell cycle. The assay captures multiple biomarkers of genomic instability such as Micronuclei, Nucleoplasmic bridges and Nuclear buds (Boutin et al., 2026; Boutin et al., 2026).

Urinary 8-oxo-dG Assay

The most extensively studied biomarker of oxidative DNA damage is 8-oxo-dG. 8-oxo-dG is created when hydroxyl radicals attack the C8 position of guanine in DNA. It is removed during base excision repair and eliminated unaltered in urine, where it may be quantified as an integrated index of oxidative DNA damage and repair throughout the body (Guetens et al., 2002).

Table 1: Assessing the Micronutrient Status and Genetic Damage

Assessment Domain	Examples	What They Communicate
Direct nutrient status	Serum/plasma Zn, Se, folate; multinutrient panels	Current circulating levels; identifies overt deficiency or excess
Functional nutrient status	EGRAC (B2), erythrocyte SOD activity (Zn, Cu, Mn), GPx activity (Se)	Biologically active nutrient fraction; integrated over longer time
Genetic damage (early effect)	Comet assay (strand breaks), 8-oxo-dG (oxidative damage)	Current damage load; reversible with intervention
Genetic damage (fixed effect)	Micronucleus frequency, chromosomal aberrations	Damage that survived cell division; more stable endpoint

6.0 Genetic Susceptibility in Micronutrient-Mediated Genoprotection

Genetic susceptibility is inherited predisposition of an individual to respond differently to nutritional factors based on variations in genes encoding proteins involved in micronutrient metabolism, antioxidant defense, and DNA repair. These genetic polymorphisms which are naturally occurring DNA sequence variations can significantly modify the relationship between micronutrient status and genomic stability. This explains why people with comparable dietary intakes may display varying degrees of genetic damage and disease risk (Fenech, 2016). Examples include of genetic polymorphisms include; MTHFR C677T, SOD2 Ala16Val and GPx1 Pro198Leu.

MTHFR C677T

The methylenetetrahydrofolate reductase (MTHFR) gene encodes a critical enzyme in folate metabolism that irreversibly converts 5,10-methylenetetrahydrofolate to 5-methyltetrahydrofolate - the primary circulating form of folate required for homocysteine remethylation to methionine. The C677T polymorphism results in an alanine-to-valine substitution at codon 222, producing a thermolabile enzyme with 30-40% reduced activity in individuals homozygous for the T allele (TT genotype). TT homozygotes require higher folate intake to maintain normal homocysteine levels and optimal DNA methylation patterns. Population-wide dietary recommendations may not be sufficient for these genetically sensitive subpopulation since TT homozygotes need increased folate consumption to maintain normal homocysteine levels and appropriate DNA methylation patterns (Raghubeer & Matsha, 2023).

SOD2 Ala16Val

The superoxide dismutase 2 (SOD2) gene encodes manganese superoxide dismutase (MnSOD), the primary antioxidant enzyme responsible for dismutating superoxide radicals in mitochondria - the major cellular site of reactive oxygen species production. The Ala16Val polymorphism involves a C-to-T substitution producing an alanine-to-valine change at amino acid 16 within the mitochondrial targeting sequence. This alters the secondary structure of the enzyme's signal peptide, reducing its efficient transport into mitochondria by 30-40%. (Zejnilovic et al., 2009; Zhang, 2011). Importantly, the protective effect of the variant allele is modified by dietary antioxidant intake (Zejnilovic et al., 2009; Zhang, 2011).

GPx1 Pro198Leu

Glutathione peroxidase 1 (GPx1) encodes the most abundant selenium-dependent antioxidant enzyme, which reduces hydrogen peroxide and organic hydroperoxides using glutathione as a cofactor, thereby protecting cells from oxidative DNA damage. The Pro198Leu polymorphism results from a C-to-T substitution causing a proline-to-leucine change at codon 198, located near the selenocysteine active site. This variant affects the enzyme's responsiveness to selenium availability.

Leu/Leu individuals cannot effectively upregulate GPx1 activity in response to increased selenium intake. Their antioxidant enzyme system is less responsive to nutritional intervention, potentially placing them at higher risk of oxidative DNA damage despite adequate selenium status. This underscores the need to consider genetic background when interpreting functional indicators such as GPx1 activity. In Leu/Leu people, GPx1 activity is not considered a reliable indicator of selenium levels (Jablonska et al., 2009).

These insights establish the basis for personalized nutrition strategies that account for individual genetic variation in optimizing micronutrient-mediated genomic protection. For truly personalised interventions, genomic and nutrigenomic approaches are important, including the evaluation of genetic polymorphism that affect nutrient metabolism (Zambrano-Villacres et al., 2026). According to Wang et al. (2026) and Garg et al. (2026), this approach signifies a paradigm change from population-based recommendations to focused, mechanism-driven therapies.

7. Clinical and Public Health Implications:

For clinical practice, the evidence from this review strongly supports that incorporating micronutrient assessment into standard clinical chemistry panels is crucial for optimal genotoxicity testing as this may improve the accuracy and relevance of testing outcomes. Also, assessing the micronutrient status of high-risk individuals particularly from

Table 2: key genes relevant to micronutrient-mediated genoprotection:

Gene	Role in Metabolism	Variant	Personalized Nutrition Implication	References
MTHFR	Folate metabolism, homocysteine methylation	C677T (30-40% reduced enzyme activity)	TT genotype requires higher folate intake (800 µg vs. 400 µg RDA) to maintain normal homocysteine and methylation	Fenech, 2016; Hussain et al., 2026
SOD2	Mitochondrial antioxidant defense (MnSOD)	Ala16Val affects enzyme efficiency	Val variant may benefit from increased manganese intake or targeted antioxidant support	Alsanie, 2026
GPx1	Selenium-dependent glutathione peroxidase	Pro198Leu affects enzyme activity	Leu variant may have altered selenium requirements	Alsanie, 2026

increasingly toxic environment could be a powerful preventive tool against genotoxicity. It is advised that micronutrient status particularly from increasingly toxic environment and molecular markers of risk of genotoxic be incorporated into clinical practice.

Micronutrient status should be a mandatory co-variable in human biomonitoring studies for genotoxicants. This review emphasizes the significance of public health strategies that guarantee adequate micronutrient intake for all individuals through fortification strategies and dietary guidelines (Jain, 2025; Alsanie, 2026). Genetic diversity could explain significant interindividual differences in responsiveness to dietary interventions (Arshad et al., 2026). Hence, personalized nutrition strategies which tailors dietary recommendations to each person's unique genetic factors is advised, in order to maximize health benefits and reduce the risk of chronic diseases particularly cancer (Fenech, 2014; Fenech, 2020; Arshad et al., 2026).

CONCLUSION

Micronutrients are critical biochemical foundation for genome integrity. Linking molecular roles of micronutrients with their application in clinical chemistry appears to be an important arsenal against genotoxic damage thus of great public health significance. Hence, the incorporation of micronutrients into standard clinical chemistry panels and genetic risk assessment protocols is necessary to prevent mutation-driven diseases at the molecular level.

ACKNOWLEDGEMENTS

CONFLICT OF INTEREST

FINANCIAL SUPPORT

REFERENCES

Adolph, M. B., & Cortez, D. (2024). Mechanisms and regulation of replication fork reversal. *DNA Repair*, *141*, Article 103731. https://doi.org/10.1016/j.dnarep.2024.103731

Alsanie, S. A. (2026). Integrated omics approaches with non-thermal food fortification: Pathways to personalized nutrition solutions. *Frontiers in Nutrition*. Advance online publication. https://doi.org/10.3389/fnut.2026.1778056

Ames, B. N. (1999). Micronutrient deficiencies: A major cause of DNA damage. *Annals of the New York Academy of Sciences*, *889*(1), 87–106. https://doi.org/10.1111/j.1749-6632.1999.tb08727.x

Ames, B. N. (2010). Prevention of mutation, cancer, and other age-associated diseases by optimizing micronutrient intake. *Journal of Nucleic Acids*, *2010*, Article 725071. https://doi.org/10.4061/2010/725071

Arshad, M. T., Ali, M. K. M., Awlqadr, F. H., Maqsood, S., Ikram, A., Hossain, M. S., Abdullahi, M. A., & Rashed, M. M. (2026). Mitigation of metabolic diseases through personalized nutrition: A critical in-depth review. *Food Science & Nutrition*, *14*(1), Article e71387. https://doi.org/10.1002/fsn3.71387

Bharti, S. K., Sommers, J. A., George, F., Kuper, J., Hamon, F., Shin-ya, K., Teulade-Fichou, M. P., Kisker, C., & Brosh, R. M., Jr (2013). Specialization among iron-sulfur cluster helicases to resolve G-quadruplex DNA structures that threaten genomic stability. *The Journal of biological chemistry*, *288*(39), 28217–28229. https://doi.org/10.1074/jbc.M113.496463

Boutin, J., Fayet, S., Marin, V., Bergès, C., Riandière, M., Toutain, J., Lamrissi-Garcia, I., Thibault, C., Cappellen, D., Dabernat, S., Poulet, A., Francillette, M., Droin, N., Debeissat, C., Brunet de la Grange, P., Moreau-Gaudry, F., & Bedel, A. (2026). Single-cell multiplex approaches deeply map ON-target CRISPR-genotoxicity and reveal its mitigation by palbociclib and long-term engraftment. *Nature Communications*, *17*, Article 1429. https://doi.org/10.1038/s41467-025-68177-3

Collins, A. R., Azqueta, A., & Langie, S. A. S. (2012). Effects of micronutrients on DNA repair. *European Journal of Nutrition*, *51*(3), 261–279. https://doi.org/10.1007/s00394-012-0318-4

DeBenedictis, J. N., Xu, N., de Kok, T. M., & van Breda, S. G. (2025). The role of genetic variation in modulating the effects of blended fruits and vegetables versus fruit- and vegetable-coated food products on antioxidant capacity, DNA protection, and vascular health: A randomized controlled trial. *Nutrients*, *17*(12), Article 2036. https://doi.org/10.3390/nu17122036

Dinu, M., Ristori, S., Pagliai, G., Lotti, S., & Meriggi, N. (2026). Effects of meat-based, meat-based with α-tocopherol, and pesco-vegetarian diets on biomarkers associated with colorectal cancer risk: A randomized behavioral intervention trial. *Scientific Reports*, *16*, Article 1502. https://doi.org/10.1038/s41598-025-31410-6

Efeyan, A., & Serrano, M. (2007). p53: Guardian of the genome and policeman of the oncogenes. *Cell Cycle*, *6*(9), 1006–1010. https://doi.org/10.4161/cc.6.9.4211

Fenech, M. F. (2014). Nutriomes and personalised nutrition for DNA damage prevention, telomere integrity maintenance and cancer growth control. In V. Zappia, S. Panico, G. L. Russo, A. Budillon, & F. Della Ragione (Eds.), *Advances in nutrition and cancer*. Cancer Treatment and Research, Vol. 159. Springer. https://doi.org/10.1007/978-3-642-38007-5_24

Fenech, M., Knasmueller, S., Bolognesi, C., Holland, N., & Bonassi, S. (2016). Molecular mechanisms by which in vivo exposure to exogenous chemical genotoxic agents can lead to micronuclei formation in lymphocytes in vivo and ex vivo in humans. *Mutation Research - Reviews in Mutation Research*, *770*(Pt A), 12–25. https://doi.org/10.1016/j.mrrev.2016.04.008

Fenech, M. (2020). The role of nutrition in DNA replication, DNA damage prevention and DNA repair. In R. Curi, A. de Oliveira Peres, & J. Newsholme, *Principles of nutrigenetics and nutrigenomics* (pp. 27–32). Academic Press. https://doi.org/10.1016/B978-0-12-804572-5.00004-5

Figueroa-Méndez, R., & Rivas-Arancibia, S. (2015). Vitamin C in health and disease: Its role in the metabolism of cells and redox state in the brain. *Frontiers in Physiology*, *6*, Article 397. https://doi.org/10.3389/fphys.2015.00397

Garg, A., Blume, S. Y., Huynh, H., Barrios, A. M., Karabulut, O. O., Zhao, Q., Midha, A. D., Turner, A. W., Resnick, B. V., Chen, X., Agrawal, A., Kim, J., Chen, L., Ran, Q., Ryan, A. M., Larson, R. C., Negahban, M., Nelson, S. C. K., Yang, A. C., …

Jain, I. H. (2026). Vitamin B2 and B3 nutrigenomics reveals a therapy for NAXD disease. Cell. Advance online publication. https://doi.org/10.1016/j.cell.2026.01.022

Godfrey, K. M., Costello, P., & El-Heis, S. (2025). Nutrition in early life, epigenetics and lifelong health – Evidence from cohort and intervention studies. *Proceedings of the Nutrition Society*. Advance online publication. https://doi.org/10.1017/S0029665125000540

Guetens, G., De Boeck, G., Highley, M., Van Oosterom, A. T., & De Bruijn, E. A. (2002). Oxidative DNA damage: Biological significance and methods of analysis. *Critical Reviews in Clinical Laboratory Sciences*, *39*(4–5), 331–457. https://doi.org/10.1080/10408360290795547

Gujar, V., Li, H., Paull, T. T., Neumann, C. A., & Weyemi, U. (2025). Unraveling the nexus: Genomic instability and metabolism in cancer. *Cell Reports*, *44*(4), Article 115540. https://doi.org/10.1016/j.celrep.2025.115540

Hussain, S. A., Sarker, M. I., Liu, Y., & Jin, T. Z. (2026). DNA methylation and its role in personalized nutrition: Mechanisms, clinical insights, and future perspectives. *International Journal of Molecular Sciences*, *27*(2), Article 566. https://doi.org/10.3390/ijms27020566

Jablonska, E., Gromadzinska, J., Reszka, E., Wasowicz, W., Sobala, W., Szeszenia-Dabrowska, N., & Boffetta, P. (2009). Association between GPx1 Pro198Leu polymorphism, GPx1 activity and plasma selenium concentration in humans. *European journal of nutrition*, *48*(6), 383–386. https://doi.org/10.1007/s00394-009-0023-0

Kunwar, A., & Nayak, M. (2026). Role of selenium-dependent glutathione peroxidases (Seleno-GPxs) in radio-modulation: Lessons for radiation oncology. *Biological Trace Element Research*, *204*, 551–567. https://doi.org/10.1007/s12011-025-04695-x

Milne, E., Greenop, K. R., Ramankutty, P., Miller, M., de Klerk, N. H., Armstrong, B. K., Almond, T., O'Callaghan, N. J., & Fenech, M. (2015). Blood micronutrients and DNA damage in children. *Molecular Nutrition & Food Research*, *59*(11), 2057–2065. https://doi.org/10.1002/mnfr.201500110

Møller, P., Gajski, G., Gerić, M., Haveric, A., Stopper, H., Bankoglu, E. E., Azqueta, A., Giovannelli, L., Collins, A., & Ladeira, C. (2026). The comet assay as a tool in human biomonitoring exposure to combustion-derived air pollution—A systematic review and meta-analysis. *Mutation Research - Reviews in Mutation Research*, *797*, Article 108583. https://doi.org/10.1016/j.mrrev.2025.108583

Najafzadeh, M., Anderson, D., Dhawan, A., & Laubenthal, J. (2025). The comet assay in human biomonitoring. *Methods in Molecular Biology*, 2986, 385–401. https://doi.org/10.1007/978-1-0716-4976-3_17

Nouh, R. A. (2026). Integrative Assessment of Body Composition and Micronutrient Status in an Adult Egyptian Population [Master's Thesis, the American University in Cairo]. *AUC Knowledge Fountain*. https://fount.aucegypt.edu/etds/2761

Packer, J. E., Slater, T. F., & Willson, R. L. (1987). Interaction of ascorbate and α-tocopherol. *Annals of the New York Academy of Sciences*, *498*(1), 104–112. https://doi.org/10.1111/j.1749-6632.1987.tb23761.x

Raghubeer, S., & Matsha, T. E. (2021). Methylenetetrahydrofolate (MTHFR), the One-Carbon Cycle, and Cardiovascular Risks. *Nutrients*, *13*(12), 4562. https://doi.org/10.3390/nu13124562

Roy, A., & Cisneros, G. A. (2025). Comparison of magnesium and manganese ions on the structural and catalytic properties of human DNA polymerase gamma. *Journal of Chemical Theory and Computation*, *21*(18), 9094–9106. https://doi.org/10.1021/acs.jctc.5c00435 Russo, G., Tramontano, A., Iodice, I., Chiariotti, L., & Pezone, A. (2021). Epigenome chaos: Stochastic and deterministic DNA methylation events drive cancer evolution. *Cancers*, *13*(8), Article 1800.

https://doi.org/10.3390/cancers13081800

Sharif, R., Wai, M. K., Choon, O. T., Abdul Hafid, S. R., & Lee, T. Y. (2025). Tocotrienol-enriched beverage enhances psychological well-being, antioxidant defense, and genomic stability in older adults: A randomized controlled trial. *Nutrients*, *17*(13), Article 2179. https://doi.org/10.3390/nu17132179

Shukla, V., Parvez, S., Fatima, G., Singh, S., Magomedova, A., Batiha, G. E., Alexiou, A., Papadakis, M., Welson, N. N., & Hadi, N. (2024). Micronutrient interactions: Magnesium and its synergies in maternal-fetal health. *Food Science & Nutrition*, *12*(10), 6913–6928. https://doi.org/10.1002/fsn3.4316

Tasaki, E., Mitaka, Y., Nozaki, T., Kobayashi, K., Matsuura, K., & Iuchi, Y. (2018). High expression of the breast cancer susceptibility gene BRCA1 in long-lived termite kings. *Aging*, *10*(10), 2668–2682. https://doi.org/10.18632/aging.101576

Valdiglesias, V., Pásaro, E., Méndez, J., & Laffon, B. (2010). In vitro evaluation of selenium genotoxic, cytotoxic, and protective effects: a review. *Archives of toxicology*, *84*(5), 337–351. https://doi.org/10.1007/s00204-009-0505-0

Wong, C. P., Beaver, L. M., & Ho, E. (2025). Protective role of dietary zinc on DNA damage, oxidative stress, and metal toxicity. *Frontiers in Molecular Biosciences*, *12*, Article 1618318. https://doi.org/10.3389/fmolb.2025.1618318

Wu, M.-T., Ye, W.-T., Wang, Y.-C., Chen, P.-M., Liu, J.-Y., Tai, C.-K., Tang, F.-Y., Li, J.-R., Liu, C.-C., & Chiang, E.-P. I. (2021). MTHFR Knockdown Assists Cell Defense against Folate Depletion Induced Chromosome Segregation and Uracil Misincorporation in DNA. *International Journal of Molecular Sciences*, *22*(17), 9392. https://doi.org/10.3390/ijms22179392

Xu, Y., Zheng, H., Slabu, I., Liehn, E. A., & Rusu, M. (2025). Vitamin C in Cardiovascular Disease: From Molecular Mechanisms to Clinical Evidence and Therapeutic Applications. *Antioxidants*, *14*(5), 506. https://doi.org/10.3390/antiox14050506

Xu, M., Li, J., Hsiao, Y.-C., Kovi, R. C., Li, J.-L., Klimczak, L. J., Riva, L., Adams, D., Bushel, P. R., Merrick, B. A., Gordenin, D., Bucher, J. R., Sills, R. C., & Pandiri, A. R. (2025). Environmental carcinogens often exacerbate endogenous mutagenic processes to enhance tumor promotion. Cell Reports, 44(7), Article 115978. https://doi.org/10.1016/j.celrep.2025.115978

Zambrano-Villacres, R., Arteaga-Pazmiño, C., Guevara Castillo, W. D., Herrera-Fontana, M. E., Domínguez Brito, L. D., Becerra Granados, L. M., Recoba-Obregón, P. E., Rodríguez-Veintimilla, D., Bressi, V., Andrade-Molina, D., Frias-Toral, E., & Duran-Aguero, S. (2026). The Seven Methods for the Evaluation of Nutritional Status—ABCDEFG: Narrative Review. *Applied Sciences*, *16*(2), 845. https://doi.org/10.3390/app16020845

Zejnilovic, J., Akev, N., Yilmaz, H., & Isbir, T. (2009). Association between manganese superoxide dismutase polymorphism and risk of lung cancer. *Cancer genetics and cytogenetics*, *189*(1), 1–4. https://doi.org/10.1016/j.cancergencyto.2008.06.017

Zhang, J., Zhang, X., Dhakal, I. B., Gross, M. D., Kadlubar, F. F., & Anderson, K. E. (2011). Sequence variants in antioxidant defense and DNA repair genes, dietary antioxidants, and pancreatic cancer risk. *International journal of molecular epidemiology and genetics*, *2*(3), 236–244.