



Unveiling the DNA Code: Delving into the World of Single Nucleotide Polymorphisms

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Abstract

Single Nucleotide Polymorphisms (SNPs), pervasive in the human genome, represent minute yet impactful variations that intricately shape individual genetic profiles. Acting as unique genetic markers, these single-base substitutions contribute to the rich diversity observed across populations. The Human Genome Project's groundbreaking efforts have unveiled millions of SNPs, categorizing them into types such as synonymous and non-synonymous, each with distinct functional implications. SNPs play a pivotal role in disease susceptibility, with Genome-Wide Association Studies uncovering their links to conditions ranging from cardiovascular diseases to cancer, neurological disorders, autoimmune diseases, and metabolic disorders. Moreover, SNPs exert profound effects on drug response, influencing drug metabolism, transporter function, and drug target interactions. As the field of personalized medicine advances, the integration of SNP data holds promise for tailored treatment plans, but ethical considerations surrounding privacy and genetic discrimination necessitate careful navigation in this genomic era.

Keywords: SNPs, genome, genetic diversity, disease susceptibility, personalized medicine

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1. Introduction

Within the intricate tapestry of our genetic makeup lies a hidden realm of diversity, a symphony of variations that shape our unique identities. These variations, known as single nucleotide polymorphisms (SNPs), are the most common type of genetic variation among humans, representing a single-letter change in our DNA code. While these seemingly insignificant alterations may appear trivial, they hold immense power, influencing our susceptibility to diseases, our response to medications, and the very essence of our individuality [1-3].

2. Defining Single Nucleotide Polymorphisms

SNPs, often pronounced as "snips," represent a single-base substitution within the DNA sequence. Imagine a vast library of books, each representing an individual's genome. While the overall content of these books remains largely similar, certain letters may be replaced at specific locations, creating a unique genetic fingerprint. These subtle alterations, often involving the replacement of one nucleotide (A, C, G, or T) with another, are the essence of SNPs.

3. Prevalence and Distribution of SNPs

SNPs are ubiquitous in the human genome, scattered throughout our DNA like scattered stars in the night sky. It is estimated that there exists approximately one SNP for every 1,000 base pairs of DNAs, amounting to millions of variations across the human population. This remarkable abundance of SNPs underscores their significance in shaping human diversity and influencing individual traits.

The prevalence and distribution of Single Nucleotide Polymorphisms (SNPs) constitute a complex and intricate landscape within the realm of human genetics, providing profound insights into the diversity of our species. SNPs, which involve variations at a single nucleotide level, serve as crucial markers of genetic variation. The Human Genome Project (HGP) marked a pivotal milestone in unraveling the human genome, contributing significantly to the identification and cataloging of millions of SNPs. This vast array of genetic variations offers a rich tapestry of information that holds the key to understanding individual differences, susceptibilities to diseases, and the evolutionary history of populations [4].

Various methodologies have been instrumental in the discovery and analysis of SNPs. High-throughput sequencing technologies have enabled the efficient and cost-effective identification of SNPs across entire genomes. Genome-Wide

Association Studies (GWAS) have facilitated the exploration of associations between specific SNPs and traits or diseases, unraveling the genetic underpinnings of complex phenotypes. As a result, our understanding of the genomic landscape has expanded, revealing not only the prevalence of SNPs but also their functional significance.

The global distribution patterns of SNPs exhibit both shared characteristics and population-specific variations. Ethnic and regional groups often harbor distinct sets of SNPs, reflecting historical migration patterns, founder effects, and local selective pressures. Factors such as natural selection and genetic drift have played pivotal roles in shaping the prevalence and distribution of these genetic variations. Functionally, SNPs can be categorized as synonymous or non-synonymous, with non-synonymous SNPs having the potential to alter the amino acid sequence of proteins, thus influencing their structure and function. This functional diversity underscores the importance of SNPs in the regulation of gene expression and the molecular basis of various diseases.

In the realm of medical genetics, SNPs have emerged as key players in personalized medicine and disease susceptibility. Pharmacogenomics, a field dedicated to understanding how genetic variations influence drug response, relies heavily on the analysis of SNPs. Additionally, SNPs have been linked to the susceptibility and progression of various diseases, including cancer, diabetes, and cardiovascular disorders. The identification of disease-associated SNPs holds significant promise for the development of targeted therapies and precision medicine approaches. Technological advances in genotyping have propelled the field forward. Microarrays and next-generation sequencing technologies have enabled large-scale genotyping, allowing researchers to analyze thousands to millions of SNPs simultaneously. This high-throughput approach has facilitated the identification of genetic markers associated with complex traits and diseases on a genomic scale.

However, the increasing availability of genetic information, including SNP data, raises ethical and social considerations. Privacy concerns, genetic discrimination, and the potential misuse of genetic data underscore the importance of responsible practices in genomic research and healthcare. Informed consent and genetic counselling become critical components in navigating the ethical landscape of SNP analysis. In conclusion, the prevalence and distribution of SNPs represent a dynamic and multifaceted field within human genetics. As research progresses, the integration of SNP data into personalized medicine and public health initiatives holds the promise of revolutionizing healthcare strategies. This nuanced understanding of human genetic variation not only advances scientific knowledge but also raises important societal and ethical questions that warrant careful consideration as we navigate the genomic era.

4. Types of SNPs

The impact of SNPs varies depending on their location within the genome. SNPs can reside within genes, regulatory regions that control gene expression, or intergenic regions between genes. SNPs within genes can directly alter the amino acid sequence of the resulting protein, potentially affecting its function. Such SNPs are termed non-synonymous SNPs. On the other hand, synonymous SNPs do

not alter the amino acid sequence and are less likely to have a direct functional impact [5].

4.1. Synonymous SNPs (sSNPs)

Synonymous SNPs are variations in the DNA sequence that do not result in a change in the amino acid sequence of the encoded protein. This is because the genetic code is redundant, with multiple codons coding for the same amino acid. Synonymous SNPs were traditionally considered silent mutations with no functional consequences. However, recent research suggests that they can influence mRNA splicing, stability, and translation efficiency [6].

4.2. Non-Synonymous SNPs (nsSNPs)

Non-synonymous SNPs result in a change in the amino acid sequence of the protein product, potentially altering its structure and function [7]. Depending on the nature of the amino acid change, nsSNPs can have diverse effects. They may be benign, confer a selective advantage, or contribute to the development of diseases.

4.3. Missense SNPs

Missense SNPs are a subtype of nsSNPs where a single nucleotide change results in a different amino acid. The functional consequences of missense SNPs depend on the nature of the substituted amino acid and its location in the protein structure. They can affect protein folding, stability, and enzymatic activity [8].

4.4. Nonsense SNPs

Nonsense SNPs introduce a premature stop codon, leading to the truncation of the protein. The resulting truncated protein is often nonfunctional. Nonsense SNPs are frequently associated with genetic disorders and can lead to loss-of-function mutations [9].

4.5. Frameshift SNPs

Frameshift SNPs result from insertions or deletions of nucleotides, causing a shift in the reading frame of the mRNA. Frameshift mutations typically lead to a completely different amino acid sequence downstream of the mutation, often resulting in a nonfunctional protein [10].

4.6. Intronic SNPs

Intronic SNPs are located within introns, non-coding regions of genes. While introns were traditionally considered nonfunctional, intronic SNPs can influence splicing patterns, mRNA stability, and gene regulation [11].

4.7. Intergenic SNPs

Intergenic SNPs are located in regions between genes. While not directly influencing protein-coding regions, intergenic SNPs can affect the regulation of nearby genes, including promoters, enhancers, and non-coding RNAs [12].

4.8. Splice Site SNPs

Splice site SNPs occur at the junctions between exons and introns, influencing mRNA splicing. Alterations in splice sites can lead to aberrant splicing patterns, affecting the stability and functionality of the mRNA [13].

5. Role of SNPs in Disease Susceptibility

SNPs play a crucial role in determining an individual's susceptibility to various diseases. While SNPs rarely cause

diseases directly, they can contribute to disease risk by influencing an individual's genetic predisposition. For instance, certain SNPs have been linked to an increased risk of developing complex diseases such as heart disease, diabetes, and cancer.

The intricate relationship between genetics and disease susceptibility has entered a new era with the discovery and exploration of Single Nucleotide Polymorphisms (SNPs). Representing the most prevalent form of genetic variation, SNPs have become integral in unraveling the complexity of human health and disease. This detailed exploration aims to elucidate the multifaceted role of SNPs in disease susceptibility, spanning their discovery, functional implications, and their impact on various pathological conditions.

5.1. Discovery of Disease-Associated SNPs

Genome-Wide Association Studies (GWAS) have redefined our understanding of the genetic basis of diseases by enabling a systematic exploration of the entire genome for associations with various conditions. Pioneering efforts, such as those conducted by the International HapMap Consortium, have laid the groundwork for the identification of disease-associated SNPs. These studies, coupled with advancements in high-throughput sequencing technologies, have facilitated the detection of millions of SNPs linked to diverse diseases, ranging from common complex disorders to rare genetic syndromes.

5.2. Functional Implications of Disease-Associated SNPs

The functional consequences of disease-associated SNPs are crucial in comprehending their impact on disease pathogenesis. Non-Synonymous SNPs (nsSNPs), particularly missense SNPs, play a pivotal role as they directly influence protein structure and function. An illustrative example is the rs662 polymorphism in the PCSK9 gene, which has been associated with increased low-density lipoprotein cholesterol levels and heightened risk of coronary heart disease. Furthermore, SNPs in regulatory regions, such as promoters and enhancers, exert influence on gene expression levels, thus affecting key physiological pathways associated with disease susceptibility.

5.2.1. Cardiovascular Diseases

Cardiovascular diseases (CVDs), as the leading cause of global morbidity and mortality, exemplify the intricate interplay between genetic variations, particularly SNPs, and disease susceptibility. The rs1333049 SNP near the CDKN2A/B gene locus has been implicated in coronary artery disease, underscoring the genetic contributions to atherosclerosis. Additionally, the genetic landscape of dyslipidemia involves SNPs in lipid metabolism genes, including APOE and LDLR, further emphasizing the genetic underpinnings of CVD risk. The study found that the rs1333049 polymorphism was associated with the expression of the ANRIL gene, which is located near the CDKN2A/B gene locus. ANRIL is a long non-coding RNA that has been implicated in a number of diseases, including coronary artery disease, stroke, and cancer [14]. Another study found that the rs1333049 polymorphism was associated with an increased risk of coronary atherosclerosis in Japanese patients [15].

5.2.2. Cancer Susceptibility

The landscape of cancer research has been transformed by the identification of SNPs influencing susceptibility to various malignancies. The BRCA1 and BRCA2 genes, housing numerous disease-associated SNPs, exemplify the genetic predisposition to breast and ovarian cancers. Beyond these, GWAS have unearthed SNPs associated with colorectal, prostate, and lung cancers, providing insights into the genetic factors contributing to tumorigenesis. This study found that the CC genotype of the rs1333049 polymorphism was associated with a poorer prognosis and lower overall survival in patients with esophageal squamous cell carcinoma (ESCC) [16].

5.2.3. Neurological Disorders

From neurodegenerative diseases to psychiatric conditions, neurological disorders exhibit intricate relationships with genetic variations, including SNPs. The APOE ϵ 4 allele, a well-established genetic risk factor, amplifies the likelihood of Alzheimer's disease. Additionally, SNPs in genes related to neurotransmitter pathways, such as COMT in schizophrenia, illuminate the genetic underpinnings of psychiatric disorders. The study by Corder et al found that the APOE ϵ 4 allele was associated with an increased risk of late-onset Alzheimer's disease, while the APOE ϵ 2 allele was associated with a decreased risk [17]. The review article by Poirier et al discusses the role of APOE ϵ 4 in Alzheimer's disease and the potential mechanisms by which it may increase risk [18]. The meta-analysis of 20 studies by Li et al found that the COMT Met/Val polymorphism was associated with an increased risk of schizophrenia [19]. The study by Stefansson et al found that the COMT Met/Val polymorphism was associated with an increased risk of schizophrenia, and also identified novel SNPs in the BDNF and DAAO genes that were also associated with risk [20].

5.2.4. Autoimmune Diseases

Autoimmune diseases, characterized by an aberrant immune response against self-tissues, often have a substantial genetic component involving SNPs. Immune-related genes, including HLA and PTPN22, harbor SNPs that contribute significantly to autoimmune diseases such as rheumatoid arthritis, type 1 diabetes, and multiple sclerosis. These genetic insights enhance our understanding of disease etiology and offer potential targets for therapeutic interventions. Nejtgaard et al found that the HLA-DRB1* shared epitope alleles were associated with an increased risk of anti-CCP1 antibody positivity and seropositive RA in the Danish population [21]. The study by Plenge et al found that mutations in the TRAF1 gene were associated with an increased risk of RA [22]. Nejtgaard et al reviewed the role of HLA genes and autoantibodies in susceptibility to autoimmune diseases, including T1D [23]. The review article by Kerlero et al discussed the genetic risk factors for MS, including SNPs in the HLA-DRB1 and IL2RA genes.

5.2.5. Metabolic Disorders

Metabolic disorders, including diabetes and obesity, exemplify the intricate interplay between genetic susceptibility and environmental factors. SNPs in genes involved in insulin signaling (e.g., TCF7L2 in type 2 diabetes) and energy homeostasis (e.g., FTO in obesity)

influence an individual's predisposition to these metabolic conditions. The integration of genetic information into risk prediction models holds the potential to refine preventive strategies and personalized treatment approaches.

5.3. Challenges and Future Perspectives

Despite significant advancements, challenges persist in fully harnessing the potential of SNPs in disease susceptibility. The polygenic nature of many diseases, involving the interaction of numerous SNPs with environmental factors, necessitates a nuanced approach. Additionally, the translation of genetic findings into clinical applications, such as risk prediction and targeted therapies, requires careful consideration of ethical, social, and regulatory aspects. In conclusion, SNPs represent a pivotal component in the intricate tapestry of genetics and disease susceptibility. From cardiovascular diseases to cancer, neurological disorders, autoimmune diseases, and metabolic disorders, SNPs offer a window into the genetic basis of diverse pathologies. The synergy of GWAS and advanced genomic technologies has propelled the identification of disease-associated SNPs, providing unprecedented insights into the complex genetic architecture of human health and disease. As research progresses, the integration of genetic information into clinical practice holds the promise of more precise diagnostics, personalized treatment strategies, and a deeper understanding of the intricate web linking genetics and disease susceptibility.

6. SNPs and Drug Response

SNPs can also influence an individual's response to medications. Variations in certain genes can affect drug metabolism, leading to increased or decreased sensitivity to particular drugs. Understanding these pharmacogenetic associations is crucial for personalized medicine, tailoring drug dosage and treatment strategies based on individual genetic profiles.

The field of pharmacogenomics has undergone a transformative shift with the recognition of the profound impact of Single Nucleotide Polymorphisms (SNPs) on drug response. As the precision medicine era unfolds, understanding how genetic variations, particularly SNPs, influence an individual's response to pharmacotherapy has become paramount. This comprehensive exploration delves into the intricate interplay between SNPs and drug response, examining the mechanisms, clinical implications, and the evolving landscape of personalized medicine.

6.1. Genetic Variability in Drug Metabolism

The metabolism of drugs, a complex interplay of enzymes and pathways, is profoundly influenced by genetic variability. SNPs in genes encoding drug-metabolizing enzymes, such as cytochrome P450 (CYP) enzymes, can lead to variations in drug metabolism rates. For instance, the CYP2D6 gene harbors numerous SNPs, impacting the metabolism of a wide range of drugs, including antidepressants and beta-blockers. Understanding these variations is crucial for predicting individual responses and optimizing drug dosages.

6.2. Drug Transporter SNPs

In addition to drug metabolism, the transport of drugs across cell membranes is a critical determinant of drug efficacy. SNPs in genes encoding drug transporters, such as those belonging to the ATP-binding cassette (ABC) transporter family, can influence drug absorption, distribution, and excretion. Notable examples include SNPs in the ABCB1 gene, which encodes P-glycoprotein, impacting the bioavailability of various drugs, including anticancer agents and immunosuppressants.

6.3. Impact of SNPs on Drug Targets

SNPs in genes encoding drug targets, such as receptors or enzymes directly affected by medications, can significantly alter drug efficacy. For instance, variations in the beta-adrenergic receptor gene (ADRB1) have been associated with altered responses to beta-blockers used in cardiovascular therapy. Understanding these genetic variations allows for the customization of treatment plans, ensuring optimal therapeutic outcomes.

6.4. Warfarin and VKORC1/CYP2C9 SNPs

Warfarin, an anticoagulant with a narrow therapeutic index, exemplifies the profound impact of SNPs on drug response. Polymorphisms in the VKORC1 and CYP2C9 genes influence the metabolism and sensitivity to warfarin, necessitating tailored dosing regimens. The integration of genetic testing for these SNPs has become a paradigm for personalized anticoagulant therapy, reducing the risk of adverse events [24-28].

6.5. Clopidogrel and CYP2C19 SNPs

Clopidogrel, a widely prescribed antiplatelet agent, highlights the importance of genetic testing in drug response. Variants in the CYP2C19 gene result in diminished activation of clopidogrel, leading to reduced efficacy in preventing cardiovascular events. Tailoring antiplatelet therapy based on CYP2C19 genotype illustrates the potential for improving outcomes through genotype-guided prescribing.

6.6. Anticancer Therapies and EGFR SNPs

In the realm of oncology, the epidermal growth factor receptor (EGFR) represents a critical drug target. SNPs in the EGFR gene have been linked to variable responses to tyrosine kinase inhibitors (TKIs) used in cancer treatment. Genotyping for EGFR SNPs allows for the identification of individuals likely to benefit from TKIs, enabling a more precise and effective approach to cancer therapy.

6.7. Challenges and Future Directions

While the integration of SNPs into drug response prediction holds immense promise, challenges abound. The complex interplay of multiple SNPs, gene-gene interactions, and the influence of environmental factors necessitate sophisticated computational models for accurate predictions. Furthermore, addressing ethical, legal, and societal implications, including issues of privacy and informed consent, is essential as pharmacogenomic testing becomes more commonplace. The era of personalized medicine is unfolding, driven by a deeper understanding of the role of SNPs in drug response. From influencing drug metabolism and transport to directly impacting drug targets, SNPs play a

pivotal role in determining individual responses to pharmacotherapy. The examples of warfarin, clopidogrel, and anticancer therapies underscore the tangible clinical implications of incorporating genetic information into treatment decisions. As research advances and technological capabilities expand, the prospect of tailoring drug regimens to individual genetic profiles offers unprecedented opportunities for enhancing therapeutic efficacy and minimizing adverse effects in the pursuit of truly personalized medicine.

The analysis of SNPs has emerged as a powerful tool in personalized medicine, enabling healthcare providers to tailor treatment plans based on an individual's genetic makeup. By identifying SNPs associated with specific diseases or drug responses, clinicians can make informed decisions about preventive measures, treatment options, and medication dosages.

8. Ethical Considerations

While the potential benefits of SNP analysis are immense, ethical considerations must be carefully addressed. The privacy and confidentiality of genetic information are paramount, and individuals must have control over the collection, storage, and use of their genetic data. Additionally, the potential for genetic discrimination must be vigilantly guarded against.

9. Future Directions

The field of SNP research is rapidly evolving, with advancements in technology enabling the identification and characterization of SNPs at an unprecedented scale. This surge of information is providing valuable insights into the genetic basis of human diversity, disease susceptibility, and drug response. As research progresses, SNPs are poised to play an increasingly crucial role in shaping personalized medicine and improving human health.

10. Conclusion

SNPs, the subtle yet profound variations within our DNA, hold immense power in shaping our individuality and influencing our health. By understanding the intricacies of SNPs, we unlock new avenues for disease prevention, personalized medicine, and a deeper appreciation of the intricate tapestry of human genetics.

Conflicts of interest

None

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