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MICRO-SATELLITE DNA ASSOCIATE WITH DISEASES AND CANCERS

Hozan I. Ibrahim Rwandzy
Medical Laboratory Science Department, Health Science College, Lebanese French University Erbil, Kurdistan Region Iraq.
hozan.rwandzy@lfu.edu.krd

Hazha Jamal Hidayat
Biology Department, Education College, Salahaddin University, Erbil, Kurdistan Region Iraq.
hazha.hidayat@su.edu.krd

Seerwan Hamadameen Sulaiman
Medical Laboratory Science Department, Health Science College, Lebanese French University, Erbil, Kurdistan Region Iraq.
serwan.sulaiman@lfu.edu.krd

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ABSTRACT

Most of the human genome is comprised of non-coding DNA. Satellite DNA (satDNA) is a non-coding region, and it is one of the DNA types that contains repeated sequences. Microsatellite (MS) DNA is one of the satDNAs. MS has a tiny percentage of satellite DNA, and several repeat sequences of it have been identified as significant participants in genome structure. MS is correlated with frequent mutations, epigenetic alterations, and changes in gene expression. MS may significantly affect phenotypes. Many genetic diseases and cancer forms have microsatellite instability, which is a significant feature. The context of disease-focused research for many types of mental disabilities has shifted because of the revelation that the expansion of unstable repeats can induce a range of neurological diseases and cancers. This review's goal is to summarize how MS affects humans through genetic

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disorders, neurological diseases, developmental disorders, and cancers.

1.Background

Satellite DNA (satDNA) sequence consistently arrange in arrays of tandem repeats (Garrido-Ramos, 2017). Satellite DNA, also known as "tandem repeated sequences," is one of the DNA types that contains repeated sequences (Rich et al., 2014). Several repeats families have been identified as significant participants in genome structure, evolution, and diversity, although repeats have historically been thought of as junk DNA because their role was obscure (Bowen & Jordan, 2002; Dumbovic *et al*., 2017). Identical satellite DNA repeats on several chromosomes have been shown to be crucial for the development of the chromocenter and the maintenance of the entire genome in the nucleus. Satellite repeats are often found on all chromosomes (Jagannathan *et al*., 2018). Per-centromeric and sub-telomeric heterochromatin are where it is most frequently found (Garrido-Ramos, 2017). However, single repeats and short arrays of satellite repeats are also dispersed throughout the euchromatin, frequently close to genes or inside introns *(Feliciello et al*., 2021). Regarding both coding and non-coding regions of DNA, the satDNA distribution is not random across both (Samara et al., 2006).

The majority of the components of the human genome are non-coding DNA, transposons, and elements derived from transposons, whereas just a small portion of the DNA codes for proteins (Goldenfeld & Woese, 2011). Many diverse kinds of repeated DNA sequences, mostly transposons and retrotransposon, are scattered throughout eukaryotic genomes (Biscotti, Olmo, & Heslop-Harrison, 2015). It was only in the 1970s of the previous centuries that this truth was first discovered. Later, the Human Genome Project efforts led to the estimation that 98–99% genome of human are non-coding DNA (Rich *et al*., 2014). A sizable percentage of the human genome can be composed of SatDNAs (Lopes *et al*, 2021). According to the most recent projections based on the Human Genome Project's results, the human genome contains roughly 70% of repetitive and repeat-derived DNA components

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(de Koning *et al*., 2011). Transposable elements (TE), such as the short and long interspersed retro-transposable elements (SINE and LINE), and human endogenous retroviruses (HERVs), are among the types of DNA repeats. DNA methylation and histone silencing markers permanently mute the majority of transposable elements (Ganesan, 2022). The genomic satDNA is connected to notable mutation rates compared to rates at coding gene loci (Samara *et al*., 2006). Changes in DNA sequences or repetitive unit copy counts are typically assumed to have no impact on human phenotype, and they are especially not thought to be linked to diseases (Lee *et al*, 2019), while sense genes and associated repetitive DNA have a crucial impact on several human diseases and cancers (Zhou *et al,* 2021).

This review's aim is to show repetitive DNA and show potential effects on health, sickness, and cancer. Recent researches have shown that satellite repeat and their transcription have a crucial impact in several biological processes at the cellular level. The satDNA mis-regulation transcription, show to be linked to genomic instability and human diseases.

2.Categories of Satellite DNA

Satellite DNA is divided into groups based on its size, structure, and location (Garrido-Ramos, 2017). The three classes of satellite DNA are as follows (Liehr, 2019; Picardo *et al*, 2009; Rich *et al*., 2014; Richard *et al*., 2008; Tremblay *et al*, 2010):

1.1 Microsatellites

The range of repetitive microsatellite (MS) DNA is less than 10 bp per repeat (Liehr, 2021). The simplest repeat is simple sequence repeats (SSR), which are referred to as short tandem repeats (STR), frequently referred to as short sequence repeats (SSRs), are widely distributed across the chromosome and make up most of human satellites (Forster *et al*., 2015; Remya *et al*., 2010; Wyner *et al*,, 2020). SSR may significantly affect phenotypes. For instance, a significant amount of research

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has connected variations in regulating microsatellite composed of the motif found in human phenotypes (Domart *et al*., 2012).

1.2 Minisatellites

Jeffreys's group was the first to describe the range of repeating minisatellite DNA between 10 and 60 bp per repetition (Jeffreys *et al*., 1985). It is one family of repetitive DNA families scattered across the genome is variable number tandem repeats (VNTR), commonly known as mini-satellites (Eslami *et al*., 2021). They are typically described as the repetition in tandem with a short (6-100 bp) (Lang *et al.*, 2019; Vergnaud *et al*., 2000). a, b, and g-satellite repeats serve as a representation of this type of satellite DNA (Rudd *et al*., 2003). Several disorders have been linked to minisatellite VNTRs (Antwi-Boasiako *et al*., 2018; Ksiazek *et al*., 2019).

1.3 Macrosatellites

Repeating macrosatellite DNA is many kb per repeat (Dumbovic *et al*., 2017; Richard *et al*., 2008). The sole satellite DNA is the macrosatellite repeat (MSR), that can produce protein-coding RNA and include open reading farm (ORF) in each repetition unit (Geng *et al*., 2012). The quantity of macrosatellite repeats in a tandem array differs between individuals. There is a major copy number variation (CNV), which may be connected to disease (Schaap *et al*., 2013).

2 Some Common Human Diseases Correlate with Microsatellite DNA

There are instances of variations in repetitive DNA that cause diseases and/or phenotype changes because of repetitive DNA changes (Liehr, 2021). Repetitive DNA affect genomes and may support essential biological processes like cell proliferation during embryogenesis (Lopez-Pajares, 2016), disease-related to aging (Zheng *et al*., 2021),and tumorigenesis (Zheng *et al*., 2021). Many neurological disorders have been linked to sequence expansions (Abecasis *et al*., 2012). Several human diseases, and cancer, are linked to epigenetic and/or genetic changes in microsatellite (Steinke et al., 2013).

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2.1 Polyglutamine (PolyQ) Diseases

The primary cause of this genetic disorder is the CAG repeat expansion; it is the basic cause of polyglutamine diseases, often known as triplet repeat disorders (Donaldson *et al*., 2021). A string of continuous glutamine residues created by the translation of extended CAG sequences is prone to accumulating and causing cellular damage and toxicity (Massey & Jones, 2018). Types 1, 2, 3, 6, 7, and 17 of Spinocerebellar Ataxia (SCA) are polyglutamine (polyQ) diseases (McIntosh *et al*., 2021), as well as the disease of Machado – Joseph (MJD/SCA3) (Paulson, 2012), Huntington's disease (HD) (Mueller *et al*., 2019), Spinal Muscular Atrophy X- Linked Type 1 (SMAX1), and Dentatorubral Pallidoluysian Atrophy (DRPLA) (La Spada & Taylor, 2003; Orr & Zoghbi, 2007).

2.1.1 Spinocerebellar Ataxias (SCA)Types 1,2,3,6,7 & 17

The neurological disorder Spinocerebellar Ataxia (SCA), which is autosomal dominant, both men and women are affected equally, and the central nervous system (CNS) is the major target of attack *(*Ashizawa *et al*., 2018; Rüb *et al*., 2013). The autosomal dominantly transmitted of Spinocerebellar Ataxias (SCA) is a subset of inherited cerebellar ataxias (Jayadev & Bird, 2013). Ataxia symptoms, which emerge from the cerebellum's gradual deterioration but may also impact other related areas, such as the brain stem, are shared by many progressive neurodegenerative illnesses (de Silva *et al*., 2019). Characteristic of this are executive dysfunctions, respiratory failure, gaze palsy, dysarthria, dysphagia, peripheral neuropathy, slowness of saccades, pyramidal and extrapyramidal motor symptoms, progressive loss of balance and coordination, decreased cognition dysphagia and dysarthria (Sullivan *et al*., 2019).

2.1.2 Huntington's disease (HD)

Huntington's disease (HD) is a rare deteriorating neurological condition that appears at adult-onset and is autosomal dominant (Nopoulos, 2022). It is characterized by development of chorea, it ultimately affected all muscles and was frequently seen along with other aberrant movement patterns, such as dystonia, bradykinesia, and

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motor incoordination (Walker, 2007). Other typical behavioral or mental health symptoms include personality changes, trouble paying attention, cognitive impairment, impatience, and dementia (Dumbovic *et al*., 2017).

2.1.3 Dentatorubal Pallidoluysian Atrophy (DRPLA)

Haw River syndrome and Naito-Oyanagi disease are additional names for the rare autosomal dominant disorder known as dentatorubral pallidoluysian atrophy (DRPLA). (Chaudhry et al., 2021). It is distinguished by signs, including choreoathetosis, ataxia, myoclonus, and epilepsy (Tsuji, 2012). According to the age of onset, it was categorized into three DRPLA groups: less than 20 years, the juvenile-onset group exhibits ataxia and signs consistent with myoclonus epilepsy; early adult-onset group, whose ages range from 20 to 40, may exhibit myoclonus and seizures; and Ataxia is a characteristic of the late adult onset group, which has an age greater than 40 years (Carroll *et al*., 2018), Choreoathetosis, dementia, and autism, are the symptoms, besides these symptoms, patients with DRPLA frequently have surgery-resistant obstructive sleep apnea, cervical dystonia, and corneal endothelial degradation (De Jesus, 2020).

2.1.4 Spinal Bulbar Muscular Atrophy X-Linked 1 (SMAX1 OR SBMA)

Spinal and bulbar muscular atrophy (SBMA) is another name for Kennedy's disease (Breza & Koutsis, 2019). It is an uncommon X-linked disease that typically manifests in adult males (in the fourth or fifth decade) and is clinically characterized by progressively progressing muscle weakening and atrophy. Muscle cramps may precede the onset of weakness by several years (Grunseich *et al*., 2014). SBMA is characterized by weakness, with difficulties walking and a propensity to fall among its earliest symptoms. Atrophy of the tongue with fasciculations, inadequate uvula, soft palatal movements, and weakening in both sides of the masseter muscles are also common symptoms (Fan *et al*., 2014). Face weakness, speaking difficulties, and coarse fasciculation are symptoms associated with both spinal and bulbar motor neuron involvement (Sheila *et al*., 2019).

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2.1.5 Machado – Joseph Disease (MJD)

It a group of dominant autosomal disorders of motor coordination known as spinocerebellar ataxias 3 (SCA3). It is brought on by the degeneration of the cerebellum, and is the most common inherited SCA (Ashizawa *et al*., 2018). Some signs of this disorder include memory problems, spasticity, swallowing, difficulty speaking, weakness in the arms and legs, clumsiness, frequent urination, and uncontrollable eye movements. Early adolescence is when symptoms can start, and they can get worse with time. While MJD eventually results in paralysis, mental abilities rarely change (Donis *et al*., 2016).

2.2 X-Fragile Syndrome

A common inherited condition caused by a triplet repeat, the mild-to-moderate intellectual disability that characterizes fragile X syndrome (FXS) (Dumbovic *et al*., 2017). Alternately, the loss of function mechanism is brought on by the microsatellite expansion's inhibition of gene transcription. For instance, the *FMR1* gene, which causes fragile X-mental retardation 1. It is linked to the expansion of the CGG satellite, resulting in the transcription silencing and losing FMRP, this protein product of *FMR1* gene (Tabolacci et al., 2016). Physical characteristics such as a long narrow face, huge ears, flexible fingers, and large testicles. About one-third of individuals affected also display characteristics of autism, including difficulty interacting with others and speech delays (Garber *et al*., 2008). 10% of people get seizures, and hyperactivity is prevalent. Typically, men are more affected than women (Santoro *et al*., 2012).

2.3 Myotonic dystrophy

A chronic hereditary condition that impairs muscles work and is called myotonic dystrophy; it's a specific form of muscular dystrophy (Meola & Cardani, 2015). The disorders of triplet repeat expansion include prevalent genetic conditions like myotonic dystrophy (Dumbovic *et al*., 2017) It has two types; Steinert's disease, commonly known as myotonic dystrophy type 1 (DM1), and myotonic dystrophy type 2 (DM2), is also referred to as proximal myotonic myopathy, both of which

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have an autosomal dominant inheritance pattern (Soltanzadeh, 2022). The dystrophy myotonic protein kinase (DMPK) gene 3' untranslated region has a CTG expansion, which causes DM (Llamusí & Artero, 2008). Symptoms include progressively worsening weakness and muscle loss, muscles frequently contract and cannot relax, cataracts, intellectual impairment, and issues with cardiac conduction are examples of further symptoms. Males may experience early baldness and infertility because of these conditions (Meola & Cardani, 2015).

2.4 Friedreich's Ataxia

Most Caucasians with early-onset hereditary ataxias have Friedreich ataxia (FRDA), an autosomal recessive condition. It typically results from a significant increase of an intronic GAA repeat, which lowers the expression of the target frataxin gene (Pandolfo, 2008). Alongside causing a progressive neurological handicap, FRDA also raises the risk of developing diabetes mellitus and hypertrophic cardiomyopathy (Klockgether, 2011). Skeletal defects like pescavus and kyphoscoliosis are frequent. Typically, the earliest signs appear around the time of puberty (Indelicato *et al*., 2020).

3.Cancers Correlate with Microsatellite DNA

Variable number tandem repeats (VNTRs) have been connected to numerous cancers (Ramírez-Patiño et al., 2013), and it is related to the prognosis and outcome of cancer (Xia et al., 2013). Minisatellite VNTR-based commercial cancer detection kits have been produced (Leem *et al*., 2011). And some suggest that cancer-related VNTRs be used in targeted sequencing for tailored therapeutics (Rose, 2015). Multiple cancers have been of TE and satellite repeats are abnormally expressed repeating RNAs, which is frequently accompanied by DNA demethylation and maybe a kind of epigenetic instability linked to carcinogenesis (Hall *et al*., 2017; Pappalardo & Barra, 2021).

A protein that is immunogenic can be produced from transposable elements that have complete ORF, innate immune activation and interferon signaling have been

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linked to abnormal repetitive RNA expression in cancers (Chen *et al*., 2021). The mutations can take the form of changes in the number of repeat units (increase or decrease), single nucleotide substitutions, deletions, and insertions, among other events (Paulson, 2018). Changes in reading frames could result from an increase or decrease in repeat units of micro satellites in coding areas, which would alter the protein product (Li *et al*., 2004), and in non-coding areas are recognized to influence the regulation of genes (Pagni *et al*., 2022). Because of the high rate of mutations in microsatellites' tracts, they are known to be extremely polymorphic (Kelkar *et al*., 2010). The genetic complexity of many cancers is influenced by microsatellites , according to recent studies (Fonville *et al*., 2015).

The DNA mismatch repair (MMR) system, which is governed by *MMR* genes, prevents genomic instability in cells (Kim et al., 2022). Mismatch repair (MMR) is a natural process that checks for and maintains DNA repeats in microsatellite loci during cell division (Strand *et al*., 1993). Genetic and epigenetic modifications to the MMR genes are expected to reduce mismatch repair, resulting in a greater mutation rate that promotes carcinogenesis (Shilpa *et al*., 2014). Microsatellites are now recognized as hereditary risk factors for a number of diseases (Velmurugan *et al*., 2017).

A DNA repair failure resulting from a mutation in the *MMR* gene underlies the autosomal dominant genetic disease known as hereditary nonpolyposis colorectal cancer (HNPCC, also known as Lynch syndrome), and it significantly raises the risk for several types of cancer, especially endometrial and colon cancer (Steinke *et al*., 2013). In addition, it has been determined that microsatellites are genetic risk factors for breast cancer (Hause *et al*., 2016). Information about ovarian cancer is caused by modifications to the mismatch repair gene (Shilpa *et al*., 2014). MS was identified in thymomas, hepatic, and small intestinal cancers (Matsubayashi *et al*., 2022). Also, MS has been connected to the development of gastric, endometrial, and sporadic colon cancers (Pal *et al.*, 2008). According to these earlier discoveries, microsatellites could be involved in the genetics of lung cancer (Hause *et al*., 2016).

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MS loci variants for glioblastoma, lower-grade glioma, kidney, prostate, breast cancer, and ovarian cancer (McIver *et al*., 2014; Thakur *et al*., 2021). Additionally, the existence of minor alleles and MS variability can serve as clinical indicators for liver cancer (Vaksman & Garner, 2015). MSs have demonstrated the ability to stratify risk, enhance clinical decision-making, and serve as prospective therapeutic targets through the use of MS loci and their repeat length variations (Karunasena *et al*., 2014).

4.Conclusion:

In conclusion, the present study reveals the knowledge on the microsatellites that has a relation with genetic variation, diseases, and cancers by preparing a broad summary of data. A variety of cancers and other disorders are characterized by satellites dysregulation. Microsatellite DNA repeats are among the most varied and adaptable genomic sequence groups, contributing to several essential biological processes. This study's findings showed that there are many phenotypic characteristics connected to MS. Several human diseases, and cancer, are linked to epigenetic and/or genetic changes in microsatellites. Numerous neurological disorders have been linked to MS sequence expansions, such as Polyglutamine diseases group (Spinocerebellar Ataxias (SCA) Type 1, 2, 3, 6, 7, and 17, Huntington's disease (HD), Dentatorubral Pallidoluysian Atrophy (DRPLA), Spinal Bulbar Muscular Atrophy X-Linked type 1 (SMAX1/ SBMA), Machado–Joseph Disease (MJD), X-Fragile Syndrome, Myotonic dystrophy, and Friedreich's Ataxia. As well as being related to cancers of hereditary nonpolyposis colorectal cancer, breast, thymomas, hepatic, small intestinal, gastric, endometrial, glioblastoma, lower-grade glioma, liver, and immunodeficiency, microsatellites are hyper-transcribed in cancers of the lung, kidney, ovary, colon, and prostate. Through the utilization of MSs loci and their repeat length variations, MSs have shown the capacity to stratify risk, improve clinical decision-making, and serve as potential therapeutic targets.

3 References:

1. Abecasis, G., Auton, A., Brooks, L., DePristo, M., Durbin, R., & Handsaker, R. (2012). An integrated map of genetic variation from 1,092 human genomes. Nature [Internet]. In: Nature Publishing Group, a division of Macmillan Publishers Limited. All ….
2. Antwi-Boasiako, C., Dzudzor, B., Kudzi, W., Doku, A., Dale, C. A., Sey, F., . . . Ahenkorah, J. (2018). Association between eNOS gene polymorphism (T786C and VNTR) and sickle cell disease patients in Ghana. Diseases, 6(4), 90.
3. Ashizawa, T., Öz, G., & Paulson, H. L. (2018). Spinocerebellar ataxias: prospects and challenges for therapy development. Nature Reviews Neurology, 14(10), 590-605.
4. Biscotti, M. A., Olmo, E., & Heslop-Harrison, J. (2015). Repetitive DNA in eukaryotic genomes. Chromosome Research, 23, 415-420.
5. Bowen, N. J., & Jordan, I. K. (2002). Transposable elements and the evolution of eukaryotic complexity. Current issues in molecular biology, 4(3), 65-76.
6. Breza, M., & Koutsis, G. (2019). Kennedy's disease (spinal and bulbar muscular atrophy): a clinically oriented review of a rare disease. Journal of neurology, 266(3), 565-573.
7. Carroll, L. S., Massey, T. H., Wardle, M., & Peall, K. J. (2018). Dentatorubral-pallidoluysian atrophy: an update. Tremor and Other Hyperkinetic Movements, 8.
8. Chaudhry, A., Anthanasiou-Fragkouli, A., & Houlden, H. (2021). DRPLA: understanding the natural history and developing biomarkers to accelerate therapeutic trials in a globally rare repeat expansion disorder. Journal of neurology, 268, 3031-3041.
9. Chen, R., Ishak, C. A., & De Carvalho, D. D. (2021). Endogenous retroelements and the viral mimicry response in cancer therapy and cellular homeostasis. Cancer discovery, 11(11), 2707-2725.
10. De Jesus, O. (2020). Dentatorubral Pallidoluysian Atrophy.
11. de Koning, A. J., Gu, W., Castoe, T. A., Batzer, M. A., & Pollock, D. D. (2011). Repetitive elements may comprise over two-thirds of the human genome. PLoS genetics, 7(12), e1002384.
12. de Silva, R. N., Vallortigara, J., Greenfield, J., Hunt, B., Giunti, P., & Hadjivassiliou, M. (2019). Diagnosis and management of progressive ataxia in adults. Practical neurology, 19(3), 196-207.
13. Domart, M. C., Benyamina, A., Lemoine, A., Bourgain, C., Blecha, L., Debuire, B., . . . Saffroy, R. (2012). Association between a polymorphism in the promoter of a glutamate receptor subunit gene (GRIN2A) and alcoholism. Addiction biology, 17(4), 783-785.

14. Donaldson, J., Powell, S., Rickards, N., Holmans, P., & Jones, L. (2021). What is the pathogenic CAG expansion length in Huntington's disease? Journal of Huntington's Disease, 10(1), 175-202.
15. Donis, K. C., Saute, J. A. M., Krum-Santos, A. C., Furtado, G. V., Mattos, E. P., Saraiva-Pereira, M. L., . . . Jardim, L. B. (2016). Spinocerebellar ataxia type 3/Machado-Joseph disease starting before adolescence. neurogenetics, 17, 107-113.
16. Dumbovic, G., Forcales, S.-V., & Perucho, M. (2017). Emerging roles of macrosatellite repeats in genome organization and disease development. Epigenetics, 12(7), 515-526.
17. Eslami Rasekh, M., Hernández, Y., Drinan, S. D., Fuxman Bass, J. I., & Benson, G. (2021). Genome-wide characterization of human minisatellite VNTRs: population-specific alleles and gene expression differences. Nucleic acids research, 49(8), 4308-4324.
18. Fan, H.-C., Ho, L.-I., Chi, C.-S., Chen, S.-J., Peng, G.-S., Chan, T.-M., . . . Harn, H.-J. (2014). Polyglutamine (PolyQ) diseases: genetics to treatments. Cell transplantation, 23(4-5), 441-458.
19. Feliciello, I., Pezer, Ž., Sermek, A., Bruvo Mađarić, B., Ljubić, S., & Ugarković, Đ. (2021). Satellite DNA-mediated gene expression regulation: Physiological and evolutionary implication. Satellite DNAs in Physiology and Evolution, 145-167.
20. Fonville, N. C., Vaksman, Z., McIver, L. J., & Garner, H. R. (2015). Population analysis of microsatellite genotypes reveals a signature associated with ovarian cancer. Oncotarget, 6(13), 11407.
21. Forster, P., Hohoff, C., Dunkelmann, B., Schürenkamp, M., Pfeiffer, H., Neuhuber, F., & Brinkmann, B. (2015). Elevated germline mutation rate in teenage fathers. Proceedings of the Royal Society B: Biological Sciences, 282(1803), 20142898.
22. Ganesan, S. (2022). Breaking satellite silence: human satellite II RNA expression in ovarian cancer. Journal of Clinical Investigation, 132(16), e161981.
23. Garber, K. B., Visootsak, J., & Warren, S. T. (2008). Fragile X syndrome. European journal of human genetics, 16(6), 666-672.
24. Garrido-Ramos, M. A. (2017). Satellite DNA: an evolving topic. Genes, 8(9), 230.
25. Geng, L. N., Yao, Z., Snider, L., Fong, A. P., Cech, J. N., Young, J. M., . . . Tawil, R. (2012). DUX4 activates germline genes, retroelements, and immune mediators: implications for facioscapulohumeral dystrophy. Developmental cell, 22(1), 38-51.
26. Goldenfeld, N., & Woese, C. (2011). Life is physics: evolution as a collective phenomenon far from equilibrium. Annu. Rev. Condens. Matter Phys., 2(1), 375-399.
27. Grunseich, C., Rinaldi, C., & Fischbeck, K. (2014). Spinal and bulbar muscular atrophy: pathogenesis and clinical management. Oral diseases, 20(1), 6-9.

28. Hall, L. L., Byron, M., Carone, D. M., Whitfield, T. W., Pouliot, G. P., Fischer, A., . . . Lawrence, J. B. (2017). Demethylated HSATII DNA and HSATII RNA foci sequester PRC1 and MeCP2 into cancer-specific nuclear bodies. Cell reports, 18(12), 2943-2956.
29. Hause, R. J., Pritchard, C. C., Shendure, J., & Salipante, S. J. (2016). Classification and characterization of microsatellite instability across 18 cancer types. Nature medicine, 22(11), 1342-1350.
30. Indelicato, E., Nachbauer, W., Eigentler, A., Amprosi, M., Matteucci Gothe, R., Giunti, P., . . . Klopstock, T. (2020). Onset features and time to diagnosis in Friedreich's Ataxia. Orphanet journal of rare diseases, 15(1), 1-8.
31. Jagannathan, M., Cummings, R., & Yamashita, Y. M. (2018). A conserved function for pericentromeric satellite DNA. Elife, 7, e34122.
32. Jayadev, S., & Bird, T. D. (2013). Hereditary ataxias: overview. Genetics in Medicine, 15(9), 673-683.
33. Jeffreys, A. J., Wilson, V., & Thein, S. L. (1985). Hypervariable 'minisatellite'regions in human DNA. Nature, 314(6006), 67-73.
34. Karunasena, E., McIver, L. J., Rood, B. R., Wu, X., Zhu, H., Bavarva, J. H., & Garner, H. R. (2014). Somatic intronic microsatellite loci differentiate glioblastoma from lower-grade gliomas. Oncotarget, 5(15), 6003.
35. Kelkar, Y. D., Strubczewski, N., Hile, S. E., Chiaromonte, F., Eckert, K. A., & Makova, K. D. (2010). What is a microsatellite: a computational and experimental definition based upon repeat mutational behavior at A/T and GT/AC repeats. Genome biology and evolution, 2, 620-635.
36. Kim, H., Lim, K. Y., Park, J. W., Kang, J., Won, J. K., Lee, K., . . . Choi, S.-H. (2022). Sporadic and Lynch syndrome-associated mismatch repair-deficient brain tumors. Laboratory Investigation, 102(2), 160-171.
37. Klockgether, T. (2011). Update on degenerative ataxias. Current opinion in neurology, 24(4), 339-345.
38. Ksiazek, K., Blaszczak, J., & Buraczynska, M. (2019). IL4 gene VNTR polymorphism in chronic periodontitis in end-stage renal disease patients. Oral diseases, 25(1), 258-264.
39. La Spada, A. R., & Taylor, J. P. (2003). Polyglutamines placed into context. Neuron, 38(5), 681-684.
40. Lang, T., Li, G., Yu, Z., Ma, J., Chen, Q., Yang, E., & Yang, Z. (2019). Genome-wide distribution of novel Ta-3A1 mini-satellite repeats and its use for chromosome identification in wheat and related species. agronomy, 9(2), 60.

41. Lee, H., Zhang, Z., & Krause, H. M. (2019). Long noncoding RNAs and repetitive elements: junk or intimate evolutionary partners? TRENDS in Genetics, 35(12), 892-902.
42. Leem, S. H., Jeong, Y. H., Yoon, S. L., & Seol, S.-Y. (2011). Diagnosis kits and method for detecting cancer using polymorphic minisatellite. In: Google Patents.
43. Li, Y.-C., Korol, A. B., Fahima, T., & Nevo, E. (2004). Microsatellites within genes: structure, function, and evolution. Molecular biology and evolution, 21(6), 991-1007.
44. Liehr, T. (2019). From human cytogenetics to human chromosomics. International Journal of Molecular Sciences, 20(4), 826.
45. Liehr, T. (2021). Repetitive elements in humans. International Journal of Molecular Sciences, 22(4), 2072.
46. Llamusí, B., & Artero, R. (2008). Molecular effects of the CTG repeats in mutant dystrophia myotonica protein kinase gene. Current genomics, 9(8), 509-516.
47. Lopes, M., Louzada, S., Gama-Carvalho, M., & Chaves, R. (2021). Genomic tackling of human satellite DNA: breaking barriers through time. International Journal of Molecular Sciences, 22(9), 4707.
48. Lopez-Pajares, V. (2016). Long non-coding RNA regulation of gene expression during differentiation. Pflügers Archiv-European Journal of Physiology, 468, 971-981.
49. Massey, T. H., & Jones, L. (2018). The central role of DNA damage and repair in CAG repeat diseases. Disease models & mechanisms, 11(1), dmm031930.
50. Matsubayashi, H., Higashigawa, S., Kiyozumi, Y., Oishi, T., Sasaki, K., Ishiwatari, H., . . . Ishikawa, K. (2022). Microsatellite instability is biased in Amsterdam II-defined Lynch-related cancer cases with family history but is rare in other cancers: a summary of 1000 analyses. BMC cancer, 22(1), 1-12.
51. McIntosh, C. S., Li, D., Wilton, S. D., & Aung-Htut, M. T. (2021). Polyglutamine ataxias: our current molecular understanding and what the future holds for antisense therapies. Biomedicines, 9(11), 1499.
52. McIver, L. J., Fonville, N., Karunasena, E., & Garner, H. R. (2014). Microsatellite genotyping reveals a signature in breast cancer exomes. Breast cancer research and treatment, 145, 791-798.
53. Meola, G., & Cardani, R. (2015). Myotonic dystrophies: An update on clinical aspects, genetic, pathology, and molecular pathomechanisms. Biochimica et Biophysica Acta (BBA)-Molecular Basis of Disease, 1852(4), 594-606.
54. Mueller, S. M., Mihaylova, V., Frese, S., Petersen, J. A., Ligon-Auer, M., Aguayo, D., . . . Toigo, M. (2019). Satellite cell content in Huntington's disease patients in response to endurance training. Orphanet journal of rare diseases, 14, 1-5.

55. Nopoulos, P. C. (2022). Huntington disease: a single-gene degenerative disorder of the striatum. Dialogues in clinical neuroscience.
56. Orr, H. T., & Zoghbi, H. Y. (2007). Trinucleotide repeat disorders. Annu. Rev. Neurosci., 30, 575-621.
57. Pagni, S., Mills, J. D., Frankish, A., Mudge, J. M., & Sisodiya, S. M. (2022). Non-coding regulatory elements: Potential roles in disease and the case of epilepsy. Neuropathology and Applied Neurobiology, 48(3), e12775.
58. Pal, T., Permuth-Wey, J., & Sellers, T. A. (2008). A review of the clinical relevance of mismatch-repair deficiency in ovarian cancer. Cancer: Interdisciplinary International Journal of the American Cancer Society, 113(4), 733-742.
59. Pandolfo, M. (2008). Friedreich ataxia. Archives of neurology, 65(10), 1296-1303.
60. Pappalardo, X. G., & Barra, V. (2021). Losing DNA methylation at repetitive elements and breaking bad. Epigenetics & chromatin, 14(1), 1-21.
61. Paulson, H. (2012). Machado–Joseph disease/spinocerebellar ataxia type 3. Handbook of clinical neurology, 103, 437-449.
62. Paulson, H. (2018). Repeat expansion diseases. Handbook of clinical neurology, 147, 105-123.
63. Picardo, M., Ottaviani, M., Camera, E., & Mastrofrancesco, A. (2009). Sebaceous gland lipids. Dermato-endocrinology, 1(2), 68-71.
64. Ramírez-Patiño, R., Figuera, L. E., Puebla-Pérez, A. M., Delgado-Saucedo, J. I., Legazpí-Macias, M. M., Mariaud-Schmidt, R. P., . . . Zúñiga-González, G. M. (2013). Intron 4 VNTR (4a/b) polymorphism of the endothelial nitric oxide synthase gene is associated with breast cancer in Mexican women. Journal of Korean medical science, 28(11), 1587-1594.
65. Remya, K., Joseph, S., Lakshmi, P., & Akhila, S. (2010). Microsatellites in varied arenas of research. Journal of Pharmacy and Bioallied Sciences, 2(2), 141.
66. Rich, J., Ogryzko, V. V., & Pirozhkova, I. (2014). Satellite DNA and related diseases. Biopolymers and Cell, 30(4), 249-259.
67. Richard, G.-F., Kerrest, A., & Dujon, B. (2008). Comparative genomics and molecular dynamics of DNA repeats in eukaryotes. Microbiology and molecular biology reviews, 72(4), 686-727.
68. Rose, A. M. (2015). Therapeutics and diagnostics based on minisatellite repeat element 1 (msr1). In: Google Patents.
69. Rüb, U., Schöls, L., Paulson, H., Auburger, G., Kermer, P., Jen, J. C., . . . Deller, T. (2013). Clinical features, neurogenetics and neuropathology of the polyglutamine spinocerebellar ataxias type 1, 2, 3, 6 and 7. Progress in neurobiology, 104, 38-66.

70. Rudd, M. K., Mays, R. W., Schwartz, S., & Willard, H. F. (2003). Human artificial chromosomes with alpha satellite-based de novo centromeres show increased frequency of nondisjunction and anaphase lag. Molecular and cellular biology.
71. Samara, K., Zervou, M., Siafakas, N. M., & Tzortzaki, E. G. (2006). Microsatellite DNA instability in benign lung diseases. Respiratory medicine, 100(2), 202-211.
72. Santoro, M. R., Bray, S. M., & Warren, S. T. (2012). Molecular mechanisms of fragile X syndrome: a twenty-year perspective. Annual Review of Pathology: Mechanisms of Disease, 7, 219-245.
73. Schaap, M., Lemmers, R. J., Maassen, R., van der Vliet, P. J., Hoogerheide, L. F., van Dijk, H. K., . . . van der Maarel, S. M. (2013). Genome-wide analysis of macrosatellite repeat copy number variation in worldwide populations: evidence for differences and commonalities in size distributions and size restrictions. BMC genomics, 14, 1-12.
74. Sheila, M., Narayanan, G., Ma, S., Tam, W. L., Chai, J., & Stanton, L. W. (2019). Phenotypic and molecular features underlying neurodegeneration of motor neurons derived from spinal and bulbar muscular atrophy patients. Neurobiology of disease, 124, 1-13.
75. Shilpa, V., Bhagat, R., Premalata, C., Pallavi, V., & Krishnamoorthy, L. (2014). Microsatellite instability, promoter methylation and protein expression of the DNA mismatch repair genes in epithelial ovarian cancer. Genomics, 104(4), 257-263.
76. Soltanzadeh, P. (2022). Myotonic dystrophies: a genetic overview. Genes, 13(2), 367.
77. Steinke, V., Engel, C., Büttner, R., Schackert, H. K., Schmiegel, W. H., & Propping, P. (2013). Hereditary nonpolyposis colorectal cancer (HNPCC)/Lynch syndrome. Deutsches Ärzteblatt International, 110(3), 32.
78. Strand, M., Prolla, T. A., Liskay, R. M., & Petes, T. D. (1993). Destabilization of tracts of simple repetitive DNA in yeast by mutations affecting DNA mismatch repair. Nature, 365(6443), 274-276.
79. Sullivan, R., Yau, W. Y., O'Connor, E., & Houlden, H. (2019). Spinocerebellar ataxia: an update. Journal of neurology, 266, 533-544.
80. Tabolacci, E., Palumbo, F., Nobile, V., & Neri, G. (2016). Transcriptional reactivation of the FMR1 gene. A possible approach to the treatment of the fragile X syndrome. Genes, 7(8), 49.
81. Thakur, J., Packiaraj, J., & Henikoff, S. (2021). Sequence, chromatin and evolution of satellite DNA. International Journal of Molecular Sciences, 22(9), 4309.
82. Tremblay, D. C., Alexander, G., Moseley, S., & Chadwick, B. P. (2010). Expression, tandem repeat copy number variation and stability of four macrosatellite arrays in the human genome. BMC genomics, 11(1), 1-15.

83. Tsuji, S. (2012). Dentatorubral–pallidoluysian atrophy. Handbook of clinical neurology, 103, 587-594.
84. Vaksman, Z., & Garner, H. R. (2015). Somatic microsatellite variability as a predictive marker for colorectal cancer and liver cancer progression. Oncotarget, 6(8), 5760.
85. Velmurugan, K., Varghese, R., Fonville, N., & Garner, H. (2017). High-depth, high-accuracy microsatellite genotyping enables precision lung cancer risk classification. Oncogene, 36(46), 6383-6390.
86. Vergnaud, G., & Denoeud, F. (2000). Minisatellites: mutability and genome architecture. Genome Research, 10(7), 899-907.
87. Walker, F. O. (2007). Huntington's disease. The Lancet, 369(9557), 218-228.
88. Wyner, N., Barash, M., & McNevin, D. (2020). Forensic autosomal short tandem repeats and their potential association with phenotype. Frontiers in genetics, 11, 884.
89. Xia, X., Rui, R., Quan, S., Zhong, R., Zou, L., Lou, J., . . . Zhang, Y. (2013). MNS16A tandem repeats minisatellite of human telomerase gene and cancer risk: a meta-analysis. PloS one, 8(8), e73367.
90. Zheng, D., Huo, M., Li, B., Wang, W., Piao, H., Wang, Y., . . . Liu, K. (2021). The role of exosomes and exosomal microRNA in cardiovascular disease. Frontiers in cell and developmental biology, 8, 616161.
91. Zheng, Q.-X., Wang, J., Gu, X.-y., Huang, C.-H., Chen, C., Hong, M., & Chen, Z. (2021). TTN-AS1 as a potential diagnostic and prognostic biomarker for multiple cancers. Biomedicine & Pharmacotherapy, 135, 111169.
92. Zhou, M., Guo, X., Wang, M., & Qin, R. (2021). The patterns of antisense long non-coding RNAs regulating corresponding sense genes in human cancers. Journal of Cancer, 12(5), 1499.

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پەیوەندی مایکرۆساتەلایتی ناوکە ترشی DNA لەگەڵ نەخۆشییەکا ن و شێرپەنجەکان

پوختە:

زۆربەی جینۆمی مرۆڤ پێکدێت لەو ناوکە ترشی (DNA) یەی کە پەرلە نیە بۆ دروستکردنی پرۆتین. ساتەلایت دی ئێن ئەی (satDNA) یەکێکە لە ناوچەکان کە پەرلە نیە وە جۆرێکە لەو DNAی کە زنجیرەی دوبارەبووەی تێدایە. مایکرۆساتەلایت(MS) ی دی ئێن ئەی جۆرێکە لە satDNA ، وە ڕێژەیەکی کەمی DNAی ساتەلایتی هەیە وەهەروەها چەندین زنجیرەی دووبارەبووەوەی هەیە کە بەشداربووەکی بەرچاوی هەیە لە پێکهاتە و دەستنیشانکردنی جینۆمدا. MS پەیوەندی هەیە لە فرەشێوەی پازدانەکان و گۆڕانکارییە ئێپیجێنێتیکییەکان و دەربڕین لە جینەکاندا. هەر بۆیە MS کاریگەرییەکی بەرچاوی لەسەر ڕوخسارە بابەتەکان هەیە. زۆرێک لە نەخۆشییە بۆماوەییەکان و جۆرە جیاوازەکانی شێرپەنجە ناسەقامگیری لە MSیان هەیە کە ئەمەش تایبەتمەندییەکی بەرچاوە. لە چوارچێوەی توێژینەوەکانی تایبەت بە نەخۆشی لە زۆر جۆری ناتەواوی دەروونی و دەمارەکان ئاشکرابووە کە هۆکارەکەی لە ئەنجامی فراوانبوونی دووبارەبووەوەی و ناجێگیر لە زنجیرەی MS دایە هەروەها دەتوانێت ببێتە هۆی کۆمەڵێک نەخۆشیتری دەمارەکان و شێرپەنجە. ئامانج لەم توێژینەوە پێداچوونەوەیە بریتیە لە کۆکردنەوە و پوختەکردنی زانیاریەکان دەربارەی ئەوەی ئایە چۆن MS کاریگەری لەسەر مرۆڤ هەیە لە ناتاواوی بۆماوەییدا و نەخۆشییە دەماریەکان و تێکچوونی گەشەکردن و شێرپەنجەکاندا.

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العلاقة المايكروساتيلايت الحمض النووي DNA مع الأمراض والسرطانات

الملخص:
يتكون معظم الجينوم البشري من الحمض النووي (DNA) غير مشفرللبروتين. الحمض النووي الساتلي (satDNA) هو منطقة غير مشفرة وهو نوعية من الحمض النووي يحتوي على تسلسلات متكررة. الحمض النووي المايكروساتيلايت (MS) هو احد من satDNA ، يحتوي المتعدد على حد أدنى من الحمض النووي DNA وقد تم تحديد العديد من التسلسلات المتكررة كمشاركين مهمين في بنية الجينوم. MS ارتبط من المتعدد بالطفرات و والتغيرات الابيجينيتيك و في التعبير الجيني. MS قد يؤثر المتعدد بشكل كبير على الأنماط الظاهرية. العديد من الأمراض الوراثية وأشكال السرطان لها عدم استقرار في المايكروساتيلايت ، ان سياق البحث الذي يركز على المرض للعديد من أنواع الإعاقات العقلية والعصبية كشفت بسبب التوسع في تسلسلات متكررة و غير المستقر من MS يمكن أن يؤدي إلى مجموعة من الأمراض العصبية. للحصول على أفضل النتائج وتحديد العلاقة بين مرض التصلب العصبي المتعدد والأمراض الوراثية والسرطان. الهدف من هذه البحث هو تجميع والتلخيص الامعلومات حول كيفية تأثيرMS على البشر في الاضطرابات الوراثية والأمراض العصبية والاضطرابات النمو والسرطانات.