Chromosome 5

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Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 5, one copy inherited from each parent, form one of the pairs.

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1. Introduction

Chromosome 5 spans about 181 million DNA building blocks (base pairs) and represents almost 6 percent of the total DNA in cells.

Identifying genes on each chromosome is an active area of genetic research. Because researchers use different approaches to predict the number of genes on each chromosome, the estimated number of genes varies. Chromosome 5 likely contains about 900 genes that provide instructions for making proteins. These proteins perform a variety of different roles in the body.

2. Health Conditions Related to Chromosomal Changes

2.1. 5q minus syndrome

Deletion of a region of DNA from the long (q) arm of chromosome 5 is involved in a condition called 5q minus (5q-) syndrome. This deletion occurs in immature blood cells during a person's lifetime and affects one copy of chromosome 5 in each cell. 5q- syndrome is a type of bone marrow disorder called myelodysplastic syndrome (MDS), in which immature blood cells fail to develop normally. Individuals with 5q- syndrome often have a shortage of red blood cells (anemia) and abnormalities in blood cells called megakaryocytes, which produce platelets, the cells involved in blood clotting. Affected individuals also have an increased risk of developing a fast-growing blood cancer known as acute myeloid leukemia (AML).

Most people with 5q- syndrome are missing a sequence of about 1.5 million DNA base pairs, also written as 1.5 megabases (Mb). This region of DNA contains 40 genes. Research suggests that the loss of one copy of multiple genes in this region contribute to the features of 5q- syndrome. In particular, loss of the *RPS14* gene leads to the problems with red blood cell development characteristic of 5q- syndrome, and loss of *MIR145* or *MIR146A* contributes to the megakaryocyte abnormalities. Scientists are still determining how the loss of other genes in the deleted region might be involved in the features of 5q- syndrome and the development of AML.

2.2. 5q31.3 microdeletion syndrome

5q31.3 microdeletion syndrome is caused by a chromosomal change in which a small piece of chromosome 5 is deleted in each cell. This rare condition is characterized by severely delayed development of speech and walking, weak muscle tone (hypotonia), breathing problems, seizures, and distinctive facial features. The deletion occurs on the long (q) arm of the chromosome at a position designated q31.3. The size of the deletion can range from several thousand to several million DNA building blocks (base pairs). The deleted region typically contains at least three genes. The loss of one of these genes, *PURA*, is thought to lead to most of the characteristic features of the condition.

The protein produced from the *PURA* gene, called Pur-alpha (Purα), is especially important for normal brain development. Purα helps direct the growth and division of nerve cells (neurons). It may also be involved in the formation or maturation of myelin, the protective substance that covers nerves and promotes the efficient transmission of nerve impulses. A loss of one copy of the *PURA* gene is thought to alter normal brain development and impair the function of neurons, leading to developmental delay, hypotonia, seizures, and other neurological problems in people with 5q31.3 microdeletion syndrome.

Some studies suggest that loss of another nearby gene on chromosome 5, called *NRG2*, increases the severity of the signs and symptoms. It is unclear how the loss of other genes in the deleted region contributes to the development of 5q31.3 microdeletion syndrome.

2.3. Cri-du-chat syndrome

Cri-du-chat (cat's cry) syndrome is caused by a deletion of the end of the short (p) arm of chromosome 5. This chromosomal change is written as 5p- (5p minus). The signs and symptoms of cri-du-chat syndrome are probably related to the loss of multiple genes in this region. Researchers are working to determine how the loss of these genes leads to the features of the disorder. They have discovered that in people with cri-du-chat syndrome, larger deletions tend to result in more severe intellectual disability and developmental delays than smaller deletions. Researchers have also defined regions of the short arm of chromosome 5 that are associated with particular features of cri-du-chat syndrome. A specific region designated 5p15.3 is associated with a cat-like cry, and a nearby region called 5p15.2 is associated with intellectual disability, small head size (microcephaly), and distinctive facial features.

2.4. PDGFRB-associated chronic eosinophilic leukemia

Translocations involving chromosome 5 are involved in a type of blood cell cancer called *PDGFRB*-associated chronic eosinophilic leukemia. This condition is characterized by an increased number of eosinophils, a type of white blood cell. The most common translocation that causes this condition fuses part of the *PDGFRB* gene from chromosome 5 with part of the *ETV6* gene from chromosome 12, written as t(5;12)(q31-33;p13). Translocations fusing the *PDGFRB* gene with one of more than 20 other genes have also been found to cause *PDGFRB*-associated chronic eosinophilic leukemia, but these other genetic changes are relatively uncommon. These translocations are acquired during a person's lifetime and are present only in cancer cells. This type of genetic change, called a somatic mutation, is not inherited.

The protein produced from the *ETV6-PDGFRB* fusion gene, called ETV6/PDGFRβ, functions differently than the proteins normally produced from the individual genes. The ETV6 protein normally turns off (represses) gene activity and the PDGFRβ protein plays a role in turning on (activating) signaling pathways. The ETV6/PDGFRβ protein is always turned on, activating signaling pathways and gene activity. When the *ETV6-PDGFRB* fusion gene mutation occurs in cells that develop into blood cells, the growth of eosinophils (and occasionally other white blood cells, such as neutrophils and mast cells) is poorly controlled, leading to *PDGFRB*-associated chronic eosinophilic leukemia. It is unclear why eosinophils are preferentially affected by this genetic change.

2.5. Periventricular heterotopia

In a few cases, abnormalities in chromosome 5 have been associated with periventricular heterotopia, a disorder characterized by abnormal clumps of neurons around fluid-filled cavities (ventricles) near the center of the brain. In each case, the affected individual had extra genetic material caused by an abnormal duplication of part of this chromosome. It is not known how this duplicated genetic material results in the signs and symptoms of periventricular heterotopia.

2.6. Other chromosomal conditions

Other changes in the number or structure of chromosome 5 can have a variety of effects, including delayed growth and development, distinctive facial features, birth defects, and other health problems. Changes to chromosome 5 include an extra segment of the short (p) or long (q) arm of the chromosome in each cell (partial trisomy 5p or 5q), a missing segment of the long arm of the chromosome in each cell (partial monosomy 5q), and a circular structure called ring chromosome 5. Ring chromosomes occur when a chromosome breaks in two places and the ends of the chromosome arms fuse together to form a circular structure.

2.7. Other cancers

Deletions in the long (q) arm of chromosome 5 frequently occur in AML and MDS. While deletions in a specific segment of chromosome 5 are associated with a form of MDS called 5q minus syndrome (described above), other deletions are related to other forms of these blood disorders. These changes are typically somatic, which means they are acquired during a person's lifetime and are present only in tumor cells.

Studies suggest that some genes on chromosome 5 play critical roles in the growth and division of cells. When segments of the chromosome are deleted, as in some cases of AML and MDS, these important genes are missing. Without these genes, cells can grow and divide too quickly and in an uncontrolled way. Researchers are working to identify the specific genes on chromosome 5 that are related to AML and MDS.

References

1. Arefi M, García JL, Peñarrubia MJ, Queizán JA, Hermosín L, López-Corral L,Megido M, Giraldo P, de las Heras N, Vanegas RJ, Gutiérrez NC, Hernández-RivasJM. Incidence and clinical characteristics of myeloproliferative neoplasmsdisplaying a PDGFRB rearrangement. Eur J Haematol. 2012 Jul;89(1):37-41. doi:10.1111/j.1600-0609.2012.01799.x.
2. Cornish K, Bramble D. Cri du chat syndrome: genotype-phenotype correlationsand recommendations for clinical management. Dev Med Child Neurol. 2002Jul;44(7):494-7. Review.
3. Cross NC, Reiter A. Fibroblast growth factor receptor and platelet-derivedgrowth factor receptor abnormalities in eosinophilic myeloproliferativedisorders. Acta Haematol. 2008;119(4):199-206. doi: 10.1159/000140631.
4. Eisenmann KM, Dykema KJ, Matheson SF, Kent NF, DeWard AD, West RA, Tibes R,Furge KA, Alberts AS. 5q-myelodysplastic syndromes: chromosome 5q genes direct atumor-suppression network sensing actin dynamics. Oncogene. 2009 Oct1;28(39):3429-41. doi: 10.1038/onc.2009.207.
5. Giagounidis A, Mufti GJ, Fenaux P, Germing U, List A, MacBeth KJ. Lenalidomideas a disease-modifying agent in patients with del(5q) myelodysplastic syndromes: linking mechanism of action to clinical outcomes. Ann Hematol. 2014Jan;93(1):1-11. doi: 10.1007/s00277-013-1863-5.
6. Hunt D, Leventer RJ, Simons C, Taft R, Swoboda KJ, Gawne-Cain M; DDD study,Magee AC, Turnpenny PD, Baralle D. Whole exome sequencing in family trios revealsde novo mutations in PURA as a cause of severe neurodevelopmental delay andlearning disability. J Med Genet. 2014 Dec;51(12):806-13. doi:10.1136/jmedgenet-2014-102798.
7. Kumar MS, Narla A, Nonami A, Mullally A, Dimitrova N, Ball B, McAuley JR,Poveromo L, Kutok JL, Galili N, Raza A, Attar E, Gilliland DG, Jacks T, Ebert BL.Coordinate loss of a microRNA and protein-coding gene cooperate in thepathogenesis of 5q- syndrome. Blood. 2011 Oct 27;118(17):4666-73. doi:10.1182/blood-2010-12-324715.
8. Lalani SR, Zhang J, Schaaf CP, Brown CW, Magoulas P, Tsai AC, El-Gharbawy A,Wierenga KJ, Bartholomew D, Fong CT, Barbaro-Dieber T, Kukolich MK, Burrage LC,Austin E, Keller K, Pastore M, Fernandez F, Lotze T, Wilfong A, Purcarin G, ZhuW, Craigen WJ, McGuire M, Jain M, Cooney E, Azamian M, Bainbridge MN, Muzny DM,Boerwinkle E, Person RE, Niu Z, Eng CM, Lupski JR, Gibbs RA, Beaudet AL, Yang Y, Wang MC, Xia F. Mutations in PURA cause profound neonatal hypotonia, seizures,and encephalopathy in 5q31.3 microdeletion syndrome. Am J Hum Genet. 2014 Nov6;95(5):579-83. doi: 10.1016/j.ajhg.2014.09.014.
9. Mainardi PC, Perfumo C, Calì A, Coucourde G, Pastore G, Cavani S, Zara F,Overhauser J, Pierluigi M, Bricarelli FD. Clinical and molecular characterisationof 80 patients with 5p deletion: genotype-phenotype correlation. J Med Genet.2001 Mar;38(3):151-8.
10. Schafer IA, Robin NH, Posch JJ, Clark BA, Izumo S, Schwartz S. Distal 5qdeletion syndrome: phenotypic correlations. Am J Med Genet. 2001 Sep15;103(1):63-8. Review.
11. Schmutz J, Martin J, Terry A, Couronne O, Grimwood J, Lowry S, Gordon LA,Scott D, Xie G, Huang W, Hellsten U, Tran-Gyamfi M, She X, Prabhakar S, Aerts A, Altherr M, Bajorek E, Black S, Branscomb E, Caoile C, Challacombe JF, Chan YM,Denys M, Detter JC, Escobar J, Flowers D, Fotopulos D, Glavina T, Gomez M,Gonzales E, Goodstein D, Grigoriev I, Groza M, Hammon N, Hawkins T, Haydu L,Israni S, Jett J, Kadner K, Kimball H, Kobayashi A, Lopez F, Lou Y, Martinez D,Medina C, Morgan J, Nandkeshwar R, Noonan JP, Pitluck S, Pollard M, Predki P,Priest J, Ramirez L, Retterer J, Rodriguez A, Rogers S, Salamov A, Salazar A,Thayer N, Tice H, Tsai M, Ustaszewska A, Vo N, Wheeler J, Wu K, Yang J, DicksonM, Cheng JF, Eichler EE, Olsen A, Pennacchio LA, Rokhsar DS, Richardson P, Lucas SM, Myers RM, Rubin EM. The DNA sequence and comparative analysis of humanchromosome 5. Nature. 2004 Sep 16;431(7006):268-74.
12. Shimojima K, Isidor B, Le Caignec C, Kondo A, Sakata S, Ohno K, Yamamoto T. A new microdeletion syndrome of 5q31.3 characterized by severe developmentaldelays, distinctive facial features, and delayed myelination. Am J Med Genet A.2011 Apr;155A(4):732-6. doi: 10.1002/ajmg.a.33891.Am J Med Genet A. 2011 Nov;155A(11):2903.
13. Siddiqi R, Gilbert F. Chromosome 5. Genet Test. 2003 Summer;7(2):169-87.
14. Wu Q, Niebuhr E, Yang H, Hansen L. Determination of the 'critical region' for cat-like cry of Cri-du-chat syndrome and analysis of candidate genes byquantitative PCR. Eur J Hum Genet. 2005 Apr;13(4):475-85.

15. Zhang X, Snijders A, Segraves R, Zhang X, Niebuhr A, Albertson D, Yang H, GrayJ, Niebuhr E, Bolund L, Pinkel D. High-resolution mapping of genotype-phenotyperelationships in cri du chat syndrome using array comparative genomichybridization. Am J Hum Genet. 2005 Feb;76(2):312-26.