Chromosome 1

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Humans normally have 46 chromosomes in each cell, divided into 23 pairs. Two copies of chromosome 1, one copy inherited from each parent, form one of the pairs.

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1. Introduction

Chromosome 1 is the largest human chromosome, spanning about 249 million DNA building blocks (base pairs) and representing approximately 8 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 1 likely contains 2,000 to 2,100 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. 1p36 deletion syndrome

1p36 deletion syndrome is caused by a deletion of genetic material from a specific region in the short (p) arm of chromosome 1. The signs and symptoms of this disorder, which include intellectual disability, distinctive facial features, and structural abnormalities in several body systems, are probably related to the loss of multiple genes in this region. The size of the deletion varies among affected individuals.

2.2. 1q21.1 microdeletion

1q21.1 microdeletion is a chromosomal change in which a small piece of the long (q) arm of chromosome 1 is deleted in each cell. Most commonly, affected individuals are missing about 1.35 million DNA building blocks (base pairs), also written as 1.35 megabases (Mb), in the q21.1 region. However, the exact size of the deleted region varies. The loss of multiple genes from this region probably contributes to the various signs and symptoms that can be associated with a 1q21.1 microdeletion. Related features can include delayed development, intellectual disability, physical abnormalities, and neurological and psychiatric problems; however, some individuals with a 1q21.1 microdeletion have no obvious signs or symptoms.

2.3. 1q21.1 microduplication

A 1q21.1 microduplication is a copied (duplicated) segment of genetic material at position q21.1 on one of the two copies of chromosome 1 in each cell. Some people with a 1q21.1 microduplication have developmental delay, intellectual disability, or features of autism spectrum disorders characterized by impaired communication and socialization skills. Affected individuals may also have psychiatric disorders such as schizophrenia, malformations of the heart, or other neurological or physical features. Other individuals with 1q21.1 microduplications have no identified physical, intellectual, or behavioral problems.

1q21.1 microduplications most often involve the same segment of about 1.35 million base pairs that is missing in 1q21.1 microdeletions (described above). In other cases, individuals have a shorter or longer duplicated segment within the q21.1 region of chromosome 1. Extra copies of genes in the duplicated segment likely contribute to the signs and symptoms that occur in some individuals with 1q21.1 microduplications; researchers are working to determine which specific genes are

involved and how they relate to these features. Because some people with a 1q21.1 microduplication have no apparent features of the condition, additional genetic or environmental factors are thought to be involved in the development of signs and symptoms.

2.4. Neuroblastoma

Deletions within region 1p36 have also been associated with another condition called neuroblastoma. Neuroblastoma is a type of cancerous tumor composed of immature nerve cells (neuroblasts). These deletions are somatic mutations, which means they occur during a person's lifetime and are present only in the cells that become cancerous. About 25 percent of people with neuroblastoma have a deletion of 1p36.1-1p36.3, which is associated with a more severe form of neuroblastoma. Researchers believe the deleted region could contain a gene that keeps cells from growing and dividing too quickly or in an uncontrolled way, called a tumor suppressor gene. When tumor suppressor genes are deleted, cancer can occur. Researchers have identified several possible tumor suppressor genes in the deleted region of chromosome 1, and more research is needed to understand what role these genes play in neuroblastoma development.

2.5. Thrombocytopenia-absent radius syndrome

A deletion in the 1q21.1 region of chromosome 1 is involved in most cases of thrombocytopenia-absent radius (TAR) syndrome. TAR syndrome is characterized by the absence of a bone called the radius in each forearm and a shortage (deficiency) of blood cells involved in clotting (platelets).

The deletion in chromosome 1 involved in TAR syndrome eliminates at least 200,000 DNA building blocks (200 kilobases, or 200 kb) from the long (q) arm of the chromosome, including a gene called *RBM8A*. Most people with TAR syndrome have the deletion in one copy of chromosome 1, which removes one copy of the *RBM8A* gene, and a mutation in the other copy of the *RBM8A* gene in each cell. The *RBM8A* gene provides instructions for making a protein called RNA-binding motif protein 8A. This protein is believed to be involved in a number of important cellular functions involving the production of other proteins.

RBM8A gene mutations that cause TAR syndrome reduce the amount of RNA-binding motif protein 8A in cells. The deletion on chromosome 1 eliminates one copy of the *RBM8A* gene in each cell and the RNA-binding motif protein 8A that would have been produced from it. The reduced total amount of RNA-binding motif protein 8A is thought to cause problems in the development of certain tissues, but it is unknown how it causes the specific signs and symptoms of TAR syndrome. No cases have been reported in which individuals have deletions on both copies of chromosome 1 that include both copies of the *RBM8A* gene; studies indicate that the complete loss of RNA-binding motif protein 8A is not compatible with life.

Researchers sometimes refer to the deletion in chromosome 1 associated with TAR syndrome as the 200-kb deletion to distinguish it from another chromosomal abnormality called a 1q21.1 microdeletion (described above). People with a 1q21.1 microdeletion are missing a different, larger DNA segment in the chromosome 1q21.1 region near the area where the 200-kb deletion occurs. The chromosomal change related to 1q21.1 microdeletion is often called the recurrent distal 1.35-Mb deletion.

2.6. Other chromosomal conditions

Other changes in the number or structure of chromosome 1 can have a variety of effects, including delayed growth and development, distinctive facial features, birth defects, and other health problems. Changes to chromosome 1 may include an extra segment of the short (p) or long (q) arm of the chromosome in each cell (partial trisomy 1p or 1q), a missing segment of the short or long arm of the chromosome in each cell (partial monosomy 1p or 1q), or a circular structure called ring chromosome 1. 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

Changes in the structure of chromosome 1 are associated with other forms of cancer and conditions related to cancer. These changes are typically somatic, which means they are acquired during a person's lifetime and are present only in tumor cells.

Deletions in the short (p) arm of the chromosome have been identified in tumors of the brain and kidney. Duplications in the long (q) arm of the chromosome have been reported in a disorder called myelodysplastic syndrome, which is a disease of the blood and bone marrow. People with this condition have a low number of red blood cells (anemia) and an increased risk of developing leukemia.

References

1. Albers CA, Paul DS, Schulze H, Freson K, Stephens JC, Smethurst PA, Jolley JD,Cvejic A, Kostadima M, Bertone P, Breuning MH, Debili N, Deloukas P, Favier R,Fiedler J, Hobbs CM, Huang N, Hurles ME, Kiddle G, Krapels I, Nurden P,Ruivenkamp CA, Sambrook JG, Smith K, Stemple DL, Strauss G, Thys C, van Geet C,Newbury-Ecob R, Ouwehand WH, Ghevaert C. Compound inheritance of a low-frequency regulatory SNP and a rare null mutation in exon-junction complex subunit RBM8Acauses TAR syndrome. Nat Genet. 2012 Feb 26;44(4):435-9, S1-2. doi:10.1038/ng.1083.
2. Attiyeh EF, London WB, Mossé YP, Wang Q, Winter C, Khazi D, McGrady PW, SeegerRC, Look AT, Shimada H, Brodeur GM, Cohn SL, Matthay KK, Maris JM; Children'sOncology Group. Chromosome 1p and 11q deletions and outcome in neuroblastoma. NEngl J Med. 2005 Nov 24;353(21):2243-53.
3. Brunetti-Pierri N, Berg JS, Scaglia F, Belmont J, Bacino CA, Sahoo T, LalaniSR, Graham B, Lee B, Shinawi M, Shen J, Kang SH, Pursley A, Lotze T, Kennedy G,Lansky-Shafer S, Weaver C, Roeder ER, Grebe TA, Arnold GL, Hutchison T,Reimschisel T, Amato S, Geragthy MT, Innis JW, Obersztyn E, Nowakowska B,Rosengren SS, Bader PI, Grange DK, Naqvi S, Garnica AD, Bernes SM, Fong CT,Summers A, Walters WD, Lupski JR, Stankiewicz P, Cheung SW, Patel A. Recurrentreciprocal 1q21.1 deletions and duplications associated with microcephaly ormacrocephaly and developmental and behavioral abnormalities. Nat Genet. 2008Dec;40(12):1466-71. doi: 10.1038/ng.279.
4. Chang H, Qi X, Yeung J, Reece D, Xu W, Patterson B. Genetic aberrationsincluding chromosome 1 abnormalities and clinical features of plasma cellleukemia. Leuk Res. 2009 Feb;33(2):259-62. doi: 10.1016/j.leukres.2008.06.027.
5. Dolcetti A, Silversides CK, Marshall CR, Lionel AC, Stavropoulos DJ, SchererSW, Bassett AS. 1q21.1 Microduplication expression in adults. Genet Med. 2013Apr;15(4):282-9. doi: 10.1038/gim.2012.129.
6. Ensembl Human Map View
7. Gajecka M, Mackay KL, Shaffer LG. Monosomy 1p36 deletion syndrome. Am J MedGenet C Semin Med Genet. 2007 Nov 15;145C(4):346-56. Review.
8. Gregory SG, Barlow KF, McLay KE, Kaul R, Swarbreck D, Dunham A, Scott CE, HoweKL, Woodfine K, Spencer CC, Jones MC, Gillson C, Searle S, Zhou Y, Kokocinski F, McDonald L, Evans R, Phillips K, Atkinson A, Cooper R, Jones C, Hall RE, Andrews TD, Lloyd C, Ainscough R, Almeida JP, Ambrose KD, Anderson F, Andrew RW, Ashwell RI, Aubin K, Babbage AK, Bagguley CL, Bailey J, Beasley H, Bethel G, Bird CP,Bray-Allen S, Brown JY, Brown AJ, Buckley D, Burton J, Bye J, Carder C, ChapmanJC, Clark SY, Clarke G, Clee C, Cobley V, Collier RE, Corby N, Coville GJ, DaviesJ, Deadman R, Dunn M, Earthrowl M, Ellington AG, Errington H, Frankish A,Frankland J, French L, Garner P, Garnett J, Gay L, Ghori MR, Gibson R, Gilby LM, Gillett W, Glithero RJ, Grafham DV, Griffiths C, Griffiths-Jones S, Grocock R,Hammond S, Harrison ES, Hart E, Haugen E, Heath PD, Holmes S, Holt K, Howden PJ, Hunt AR, Hunt SE, Hunter G, Isherwood J, James R, Johnson C, Johnson D, Joy A,Kay M, Kershaw JK, Kibukawa M, Kimberley AM, King A, Knights AJ, Lad H, Laird G, Lawlor S, Leongamornlert DA, Lloyd DM, Loveland J, Lovell J, Lush MJ, Lyne R,Martin S, Mashreghi-Mohammadi M, Matthews L, Matthews NS, McLaren S, Milne S,Mistry S, Moore MJ, Nickerson T, O'Dell CN, Oliver K, Palmeiri A, Palmer SA,Parker A, Patel D, Pearce AV, Peck AI, Pelan S, Phelps K, Phillimore BJ, Plumb R,Rajan J, Raymond C, Rouse G, Saenphimmachak C, Sehra HK, Sheridan E, Shownkeen R,Sims S, Skuce CD, Smith M, Steward C, Subramanian S, Sycamore N, Tracey A,Tromans A, Van Helmond Z, Wall M, Wallis JM, White S, Whitehead SL, Wilkinson JE,Willey DL, Williams H, Wilming L, Wray PW, Wu Z, Coulson A, Vaudin M, Sulston JE,Durbin R, Hubbard T, Wooster R, Dunham I, Carter NP, McVean G, Ross MT, Harrow J,Olson MV, Beck S, Rogers J, Bentley DR, Banerjee R, Bryant SP, Burford DC,Burrill WD, Clegg SM, Dhami P, Dovey O, Faulkner LM, Gribble SM, Langford CF,Pandian RD, Porter KM, Prigmore E. The DNA sequence and biological annotation of human chromosome 1. Nature. 2006 May 18;441(7091):315-21. Erratum in: Nature.2006 Oct 26;443(7114):1013. Banerjee, R [added]; Bryant, SP [added]; Burford, DC [added]; Burrill, WDH [added]; Clegg, SM [added]; Dhami, P [added]; Dovey, O[added]; Faulkner, LM [added]; Gribble, SM [added]; Langford, CF [added];Pandian, RD [added]; Porter, KM [added]; Prigmore, E.
9. Heilstedt HA, Ballif BC, Howard LA, Lewis RA, Stal S, Kashork CD, Bacino CA,Shapira SK, Shaffer LG. Physical map of 1p36, placement of breakpoints inmonosomy 1p36, and clinical characterization of the syndrome. Am J Hum Genet.2003 May;72(5):1200-12.
10. Ichimura K, Vogazianou AP, Liu L, Pearson DM, Bäcklund LM, Plant K, Baird K,Langford CF, Gregory SG, Collins VP. 1p36 is a preferential target of chromosome 1 deletions in astrocytic tumours and homozygously deleted in a subset ofglioblastomas. Oncogene. 2008 Mar 27;27(14):2097-108.

11. Kang SH, Scheffer A, Ou Z, Li J, Scaglia F, Belmont J, Lalani SR, Roeder E,Enciso V, Braddock S, Buchholz J, Vacha S, Chinault AC, Cheung SW, Bacino CA.Identification of proximal 1p36 deletions using array-CGH: a possible newsyndrome. Clin Genet. 2007 Oct;72(4):329-38.
12. Klopocki E, Schulze H, Strauss G, Ott CE, Hall J, Trotier F, Fleischhauer S,Greenhalgh L, Newbury-Ecob RA, Neumann LM, Habenicht R, König R, Seemanova E,Megarbane A, Ropers HH, Ullmann R, Horn D, Mundlos S. Complex inheritance patternresembling autosomal recessive inheritance involving a microdeletion inthrombocytopenia-absent radius syndrome. Am J Hum Genet. 2007 Feb;80(2):232-40.
13. Kulikowski LD, Bellucco FT, Nogueira SI, Christofolini DM, Smith Mde A, deMello CB, Brunoni D, Melaragno MI. Pure duplication 1q41-qter: furtherdelineation of trisomy 1q syndromes. Am J Med Genet A. 2008 Oct15;146A(20):2663-7. doi: 10.1002/ajmg.a.32510.
14. Mefford HC, Sharp AJ, Baker C, Itsara A, Jiang Z, Buysse K, Huang S, MaloneyVK, Crolla JA, Baralle D, Collins A, Mercer C, Norga K, de Ravel T, Devriendt K, Bongers EM, de Leeuw N, Reardon W, Gimelli S, Bena F, Hennekam RC, Male A, Gaunt L, Clayton-Smith J, Simonic I, Park SM, Mehta SG, Nik-Zainal S, Woods CG, FirthHV, Parkin G, Fichera M, Reitano S, Lo Giudice M, Li KE, Casuga I, Broomer A,Conrad B, Schwerzmann M, Räber L, Gallati S, Striano P, Coppola A, Tolmie JL,Tobias ES, Lilley C, Armengol L, Spysschaert Y, Verloo P, De Coene A, Goossens L,Mortier G, Speleman F, van Binsbergen E, Nelen MR, Hochstenbach R, Poot M,Gallagher L, Gill M, McClellan J, King MC, Regan R, Skinner C, Stevenson RE,Antonarakis SE, Chen C, Estivill X, Menten B, Gimelli G, Gribble S, Schwartz S,Sutcliffe JS, Walsh T, Knight SJ, Sebat J, Romano C, Schwartz CE, Veltman JA, de Vries BB, Vermeesch JR, Barber JC, Willatt L, Tassabehji M, Eichler EE. Recurrentrearrangements of chromosome 1q21.1 and variable pediatric phenotypes. N Engl JMed. 2008 Oct 16;359(16):1685-99. doi: 10.1056/NEJMoa0805384.
15. Millington K, Hudnall SD, Northup J, Panova N, Velagaleti G. Role ofchromosome 1 pericentric heterochromatin (1q) in pathogenesis of myelodysplastic syndromes: report of 2 new cases. Exp Mol Pathol. 2008 Apr;84(2):189-93. doi:10.1016/j.yexmp.2007.10.003.
16. Morerio C, Rapella A, Tassano E, Lanino E, Micalizzi C, Rosanda C, PanarelloC. Gain of 1q in pediatric myelodysplastic syndromes. Leuk Res. 2006Nov;30(11):1437-41.
17. Murphy WJ, Frönicke L, O'Brien SJ, Stanyon R. The origin of human chromosome 1and its homologs in placental mammals. Genome Res. 2003 Aug;13(8):1880-8.
18. Paner GP, Lindgren V, Jacobson K, Harrison K, Cao Y, Campbell SC, Flanigan RC,Picken MM. High incidence of chromosome 1 abnormalities in a series of 27 renaloncocytomas: cytogenetic and fluorescence in situ hybridization studies. ArchPathol Lab Med. 2007 Jan;131(1):81-5.
19. Rosenfeld JA, Traylor RN, Schaefer GB, McPherson EW, Ballif BC, Klopocki E,Mundlos S, Shaffer LG, Aylsworth AS; 1q21.1 Study Group. Proximal microdeletions and microduplications of 1q21.1 contribute to variable abnormal phenotypes. Eur JHum Genet. 2012 Jul;20(7):754-61. doi: 10.1038/ejhg.2012.6.
20. Schutte BC, Carpten JD, Forus A, Gregory SG, Horii A, White PS. Report andabstracts of the sixth international workshop on human chromosome 1 mapping 2000.Iowa City, Iowa, USA. 30 September-3 October 2000. Cytogenet Cell Genet.2001;92(1-2):23-41.
21. Shaffer LG, Heilstedt HA. Terminal deletion of 1p36. Lancet. 2001 Dec;358Suppl:S9.
22. White PS, Thompson PM, Gotoh T, Okawa ER, Igarashi J, Kok M, Winter C, GregorySG, Hogarty MD, Maris JM, Brodeur GM. Definition and characterization of a regionof 1p36.3 consistently deleted in neuroblastoma. Oncogene. 2005 Apr14;24(16):2684-94.