

# [Studying chromosome 11 of the human genome](https://assignbuster.com/studying-chromosome-11-of-the-human-genome/)

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In this paper I will be studying chromosome 11 of the human genome. Specifically, I will be researching some of the diseases that occur when there are mutations in the genes on chromosome 11. Five specific diseases will be looked at and studied in detail: the Sickle Cell Anemia gene, the MLL gene which causes Trisomy 11, the H19 gene which causes Beckwith-Weideman Syndrome, the WT1 and PAX6 genes which causes Wilm's Tumor syndrome, and finally, the work being done on the genes of Chromosome 11q22-q24 regarding cervical carcinoma. The following research was all acquired from the NCBI online database.

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The HBB gene which causes Sickle Cell Anemia, is found on chromosome 11p15. This gene causes an inherited blood disorder, mainly effecting people from the African continent (1/500), but also people from the Mediterranean and South Asian countries. (NCBI Online, 24 June 2003) Approximately 8% of the African American population are carriers; often, this gene is associated with malaria occurrence, as carriers are somewhat protected against malaria. (NCBI Online, 24 June 2003) Sickle cell anemia is an autosomal (not sex related) recessive disease caused by a mutation in the hemoglobin beta gene.

When a mutation occurs, the HBB gene produces a structurally abnormal hemoglobin (Hb), called HbS. (NCBI Online, 24 June 2003) Hb is a protein which carries oxygen and gives red blood cells their distinctive color. In individuals who are homozygous for HbS, the abnormal HbS can bunch together, distorting the red blood cells into sickled shapes [as shown in Figure 1]. These clusters can only occur if the HbS is placed under certain circumstances or conditions, such as high hemoglobin concentrations or low oxygen levels. NCBI Online, 24 June 2003)

When the mutated and rigid red blood cells become trapped within small blood vessels, they block the vessels causing pain and eventual damage to the organs in the body. (NCBI Online, 24 June 2003) Although a cure has not yet been found, medical advancements have allowed for the treatment of symptoms and complications associated with Sickle Cell Anermia. Hydroxyurea, an antitumor drug, has been used to induce the formation of fetal Hb (HbF), which is normally found in the fetus or newborn.

When fetal Hb is present in persons with Sickle Cell Anemia, Hydrozyurea can prevent sickling from occuring. NCBI Online, 24 June 2003) The MLL gene which causes Trisomy 11 is located on chromosome 11q23. A mutation in this gene is a " very rare chromosomal disorder caused by a duplication (trisomy) of the end (distal) portion of the long arm of chromosome 11. " (Genetic Information and Patient Services, November 2003) This disorder is most often noticeable at birth; some characteristic features of the disorder are " delayed mental and physical development, retarded growth of the fetus during pregnancy and of the child after birth, an unusually small brain (microencephaly), and/or distinctive facial features. (Genetic Information and Patient Services, November 2003) The MLL gene can produce a type of leukemia which effects both sexes and mainly adults at an average age of 60. (Dessen & Huret, 2002)

In general terms, trisomy refers to " the condition of having three copies of a given chromosome in each somatic cell rather than the normal number of two. " (Dictionary. com) The leukemia is specifically acute myeloid leukemia or AML. This syndrome is caused by only a partial tandem duplication of the MLL gene on chromosome 11. Dessen & Huret, 2002) A recent study has shown that " MLL tandem duplications are less common than previously reported. " (Schnittger, October 2003) Also, the MLL tandem duplications " are preferentially observed in AML with normal karyotypes, but can also be found in the presence of chromosome alterations. " (Schnittger, October 2003) Two scientists, Cheryl Shuman and Rosanna Weksberg studied the Beckwith-Wiedemann Syndrome, also referred to as BWS syndrome. The information for BWS syndrome is from their reports on their studies.

Their studies show that " chromosome abnormalities involving 11p15 are found in 1% or less of cases. " (Shuman, 10 April 2003) This syndrome can occur with mutations of many different genes on chromosome 11: mutations in genes IGF2 and H195, 5-10% of sporadic cases and 40% of familial cases had mutations in the CDKNIC gene, 50% of cases had a loss of methylation at the KCNQIOT1 gene, and in 10-20% of patients, " paternal uniparental disomy for chromosome 11p15 [was] observed. " (Shuman, 10 April 2003) In diagnosing BWS, two major and one minor characteristic must be obvious out of a list of possible criteria.

Some major criteria include: history of BWS in thefamily, macrosomia, abnormal earlobe pits or creases, an embryonal tumor inchildhood, Hemihyperplasia (an asymmetric overgrowth of a area/areas of the body), and possibly a cleft palate. (Shuman, 10 April 2003) Some minor criteria include: premature birth, Neonatal hypoglycemia, advanced bone aging, and monozygotic twinning (usually in the females). (Shuman, 10 April 2003) If one parent has uniparental disomy (UPD), then prenatal testing is done to test for BWS syndrome in the fetus. Shuman, 10 April 2003) Beckwith-Wiedemann Syndrome is found in approximately 1 out of 13, 700 cases across the world. However, this number is probably slightly low as there are many milder cases that often go undiagnosed.

In children born with BWS, there is a 20% mortality rate due to premature birth. Often, children born with BWS develop Wilms Tumor or other tumors. (Shuman, 10 April 2003) Dr. Alan Gandy summarizes Wilms tumor as an " embryonal renal neoplasm which is characterized usually by an abdominal mass. (Gandy, 1 March 1995) Wilms tumour is caused by the deletion of the gene WT2-1 on chromosome 11p13. Proper function of this gene is to encode a DNA-binding protein that is most often found in the fetal kidney " and in tissue that gives rise to the genitourinary system. " (Gandy, 1 March 1995) The DNA-binding protein is expected to be a " Kruppel-like zinc-finger protein. " (Gandy, 1 March 1995) However, the inactivation of WT2-1 causes the Wilms Figure 2: Wilms Tumor tumor. (Gandy, 1 March 1995) This tumor is prevalent in 1/12 000 live births and is the second most common extra cranial solid tumor in children.

The tumor appears in the kidney soon after birth (6 months-10 years)[as shown in Figure 3] and is related to other cancers. (Gandy, 1 March 1995) Wilms tumor is frequently a symptom of other gene mutations, such as BWS and WAGR syndrome. (Gandy, 1 March 1995) Features of the Primary Wilms tumor include abdominal mass [as shown in Figure 2], abdominal pain, hypertension, and anemia etc. Metastases occurs in the lungs, lymph nodes, liver, brain and other areas to a lesser extent. (Gandy, 1 March 1995) Depending on the stage of the tumor, different actions can be taken to cure the tumor.

Surgery (removal of the kidney and lymph nodes) and chemotherapy are both used as ways to manage the tumor. However, as the stages progress, likelihood of a cure is reduced. (Gandy, 1 March 1995) Studies done by G. M. Hampton et al. show that there are genes or a gene on chromosome 11 that has the ability to "[suppress] tumorigenicity in cell lines derived from different histopathological types of cervical carcinoma, suggesting that aberration of this gene(s) may represent at least one of the additional changes required for tumorigenic progression. ( Hampton, 19 July 1994)

The suppressor gene specified is between 11q22 and q24. A study was performed on 32 patients with cervical carcinoma to conclude which genes were required for tumorigenic progression. " Of the 32 patients examined, 14(44%) demonstrated clonal genetic alterations resulting in loss of heterzygosity for one or more markers. Seven of the clonal genetic alterations on chromosome 11 were specific to the long arm, and the overlap between these and other allelic deletions suggest that a suppressor gene(s) relevant to cervical carcinoma maps to chromosome 11q22-q24. "( Hampton, 19 July 1994)

In conclusion, Chromosome 11 of the Human genome contains over 1000 genes. Of the many, this essay looks at 5 specifically in order to gather information on the genes of this chromosome. Through the closes study of Sickle Cell Anemia, Trisomy 11, Beckwith-Weideman Syndrome, Wilm's Tumor syndrome, and the genes of Chromosome 11q22-q24 regarding cervical carcinoma, one can gather a better understanding of the genes on chromosome 11, and the type of mutations that occur. Although the Humane Genome Project is relatively new, there is already much information that has been revealed and still much more to be discovered.