



Inheritance Patterns for Joubert Syndrome & Related Disorders

We all carry the same genes, including all of the genes known for JSRD, and variations within our genes are what make us unique. Someone who has been diagnosed with JSRD has a change in their gene(s), typically referred to as a mutation that prevents it from making its protein or doing its “job” within our body. To learn more about the genetics of JSRD, please visit www.jsrdf.org.

Joubert syndrome is typically inherited in an autosomal recessive manner. Individuals with a recessive form of JSRD have mutations in *both* copies of a gene associated with JSRD, thus they no longer have a working copy of this gene within their body. Parents of an individual diagnosed with an autosomal recessive form of JSRD are both unaffected carriers. Carriers are individuals that “carry” one nonworking copy of the JSRD gene on one chromosome and one working copy on the other. When both parents are carriers for an alteration in the same JSRD gene, there is a 1 in 4 or 25% chance that the child will be an unaffected, non-carrier, a 1 in 2 or 50% chance that the child would be an unaffected carrier (like the parents) and a 1 in 4 or 25% chance that the child would be affected with JSRD, with *each* pregnancy. It is important to note that there could be intrafamilial variability, which means that if two or more individuals in the same family are affected with JSRD, each may be affected in different ways.

When a sibling to a child affected with a recessive form of JSRD is born into a family and found to be unaffected, they would have a 2 in 3 or 67% chance to be an unaffected carrier and a 1 in 3 or 33% chance to be an unaffected non-carrier for JSRD. Unaffected carriers would be at an increased chance to have a child with JSRD, but only if their future spouse was also a carrier for JSRD.

Siblings of parents of children with a recessive form of JSRD (the affected child’s aunts and uncles) would have a 1 in 2 or 50% chance of also being a carrier.

Alterations in the *OFD1* gene are associated with an X-linked pattern of inheritance. The *OFD1* gene is located on the X-chromosome; therefore females have two copies of this gene (XX) while males have one copy (XY – there is no *OFD1* gene on the Y-chromosome). Fathers of a male with JSRD due to an *OFD1* mutation are not affected and are not carriers. Mothers may be unaffected carriers of the *OFD1* mutation or the mutation may be new in the affected male (not inherited from the mother). Mothers who are unaffected carriers would have a 1 in 2 or 50% chance with each pregnancy of passing the *OFD1* alteration to their children. Males that inherit the *OFD1* alteration from their mother would be affected; females would be likely unaffected.

Digenic inheritance has been proposed to be a cause in patients with single mutations in two different genes; however, this is difficult to prove, since it is always possible that a second mutation in one of the genes has been missed. Further research is required to determine if and when digenic inheritance might take place.

Prenatal diagnosis is available through chorionic villus sampling (CVS) or amniocentesis when the gene responsible for JSRD in the family has been identified. In the absence of this specific information, prenatal diagnosis in a family already known to have a child with JSRD is limited to imaging studies (prenatal ultrasound and fetal MRI).

For more information, additional resources, or to find a JSRDF family in your area, please visit www.jsrdf.org

The information presented is intended to summarize this condition as it is presently understood by medical professionals. The statements included in this document are for information only and should not be considered as medical advice. Please always consult your physician for medical advice.