UT Southwestern
Harold C. Simmons
Comprehensive Cancer Center

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MSH3 Gene Mutations

What You Should Know About *MSH3* Mutations

Individuals who inherit two *MSH3* mutations, one from each parent (i.e., biallelic mutations), have a condition called *MSH3*-associated polyposis. This means they are at risk to develop numerous colorectal and intestinal polyps, which can become cancerous if left untreated. Individuals who have one *MSH3* mutation (i.e., monoallelic or heterozygous mutations), do NOT have *MSH3*-associated polyposis, and are instead referred to as carriers. Carriers are not known to have features of *MSH3*-associated polyposis but can potentially have children who are affected.

The Risks for Cancer Associated with biallelic (two) *MSH3* Mutations

- Individuals with *MSH3* mutations are thought to have an increased risk to develop adenomatous polyps in the colon and small intestine, as well as colorectal and stomach cancers. The specific lifetime risks of these cancers are currently unknown but are thought to be increased over the general population.
- Individuals with *MSH3* mutations may also have an increased risk of developing brain tumors, but information regarding this association is limited.

The Risks to Family Members

Mutations in the *MSH3* gene are inherited in an autosomal recessive manner. This means that an individual must have two *MSH3* mutations (one mutation inherited from each parent) to have an increased risk for colon polyps, as well as a colorectal and other cancers. Individuals who have only one *MSH3* mutation are referred to as *carriers* and do not appear to be at an increased risk for polyps or cancer compared to the general population. It is not known how many people are *MSH3* mutation carriers in the general population, but the percentage is thought to be low (<1%). When both individuals in a couple have an *MSH3* mutation, their offspring each have a 25% (1 in 4) chance to inherit two *MSH3* mutations, and a 50% (1 in 2) chance to inherit one *MSH3* mutation.

Managing the Cancer Risks

Recommendations for managing these risks typically include:

- Colonoscopy beginning at age 25-30 years, repeating every 2-3 years (or every 1-2 years if polyps are found)
- Surgery to remove the colon can be considered if polyps cannot be managed by colonoscopy

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