UT Southwestern
Harold C. Simmons
Comprehensive Cancer Center

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NBN Gene Mutations

What You Should Know About *NBN*-associated Cancer Risk

The information known about single *NBN* gene mutations is based on data derived from a particular mutation found in people of Slavic descent (c.657del5). Current data suggest that cancer risks are not increased for individuals with other mutations in the *NBN* gene. However, women with the Slavic *NBN* mutation have an increased lifetime risk for breast cancer. Individuals who inherit only one mutation in the *NBN* gene are said to have *NBN*-associated cancer risk. Individuals who inherit two mutations in the NBN gene (one from each parent) have a different, more serious condition called Njimegen Breakage Syndrome (NBS).

The Risk for Cancer Associated with a Monoallelic (one) *NBN* Gene Mutation

- Women with the Slavic *NBN* mutation are estimated to have up to a 30% lifetime risk of breast cancer compared to the general population risk of 12%.
- Individuals with single *NBN* mutations may have an increased lifetime risk for other cancers including ovarian, colorectal, pancreatic, blood cancers, or gastric cancer. However, evidence is currently limited and risk is not fully understood.

Managing the Risks

Women with the Slavic mutation in NBN should consider the following screening for breast cancer:

- Annual 3-D mammography at age 40, or 5-10 years earlier than the youngest diagnosis of breast cancer in the family (but no later than 40)

Women with other mutations in the *NBN* gene should discuss their personal and family history with their providers to determine the best screening recommendations. It is not known at this time if men with an *NBN* gene mutation are at an increased risk for cancer.

The Risks to Family Members

First-degree relatives (i.e., parents, siblings, and children) have a 50% chance to have the *NBN* mutation. Second-degree relatives (i.e., nieces/nephews, aunts/uncles, and grandparents) have a 25% chance to have the familial mutation. Rarely, individuals inherit two *NBN* mutation (one from each parent), which causes Nijmegen breakage syndrome (NBS). NBS is a condition characterized by short stature, small head size, distinctive facial features, recurrent respiratory tract infections, an increased risk of cancer, intellectual disability, and other health problems. *NBN* genetic testing for the partner of an individual with an *NBN* mutation may be appropriate to clarify the risk of having children with NBS.

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