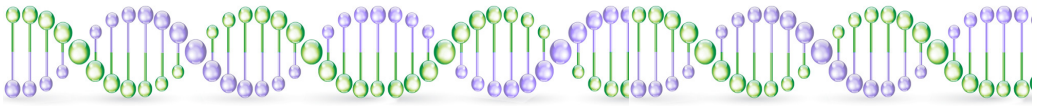
Information Sheet



Hereditary Mixed Polyposis syndrome and the GREM1 gene

As the name suggests, Hereditary Mixed Polyposis syndrome results in an increased risk of polyps occurring in the bowel (colon) including adenoma, hyperplastic, hamartoma, juvenile and serrated. These polyps, over time, can become cancerous.

Hereditary Mixed Polyposis syndrome is very rare. It is caused by mutations affecting the GREM1 gene. The best known mutation is a large duplication that occurs in less than 1% of individuals with Ashkenazi heritage.

And yes, in case you were wondering, the gene, GREMLIN1, was named after the movie Gremlins.

What is the cancer risk in Hereditary Mixed Polyposis syndrome?
Because GREM1 mutations are rare, the lifetime colon cancer risk for someone with Hereditary Mixed Polyposis syndrome is not known. The risk is believed to be moderate. That is, a 10 to 25% lifetime risk of colon cancer compared to the average risk of 6 to 12% lifetime.

Who should have a genetic test for Hereditary Mixed Polyposis syndrome?
Specific testing of GREM1 is not usually performed unless a pathogenic mutation has already been detected in a blood relative. Instead, GREM1 is usually including on a panel of 9 to 12 known polyposis genes.

Anyone who meets the clinical criteria for polyposis should consider genetic testing. This would Medicare funded if the individual had:

- a total of 10 or more adenomatous polyps in the colon before age 30
- a total of 10 or more adenomatous polyps in the colon and a colon cancer
- a total of 20 or more adenomatous polyps in the colon before age 60
- a juvenile polyp and has signs of hereditary haemorrhagic telangiectasia or has a relative who has had juvenile polyps
- more than one juvenile polyp in the small and large intestine or more than 5 in total
- a hamartomatous polyp and other signs of Cowden syndrome

What is special about the GREM1 40 kb duplication?
A particular mutation occurs upstream of the actual GREM1 gene in 1% of individuals with Ashkenazi Jewish heritage. It is a very large (40 kilobases) duplication of DNA code. It involves another gene and a region upstream of GREM1. This mistake results in increased GREM1 expression.

In a large study comparing Ashkenazi Jewish individuals with and without GREM1 mutations, the colon cancer risk (in the absence of screening) was doubled.

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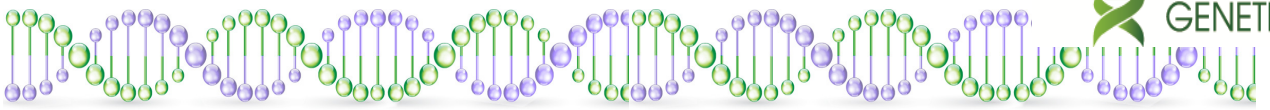

How is Hereditary Mixed Polyposis syndrome managed?
The key to reducing cancer risk in Hereditary Mixed Polyposis syndrome is to remove the polyps before they become a cancer. Screening usually starts at age 25 or 30 with colonoscopies performed every 3 years or as directed by polyp load.

Is Hereditary Mixed Polyposis syndrome inherited?
Yes. Hereditary Mixed Polyposis syndrome is a hereditary cancer syndrome caused by a mutation in the GREM1 gene.

There is a 50% chance of a person who carries a germline GREM1 mutation, whether male or female, passing the mutation to their son or daughter. If a mutation is identified, then predictive testing is available for blood relatives.

Does this sound like you or your family?
Has a GREM1 mutation been detected in a blood relative? Genetic testing is available.
Make an appointment with Dr Hilda High at Sydney Cancer Genetics. It is a confidential opportunity to discuss your personal and family history of cancer and genetic testing can be organised, if needed.

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