Genetic Counseling Service
75 Claremont Rd Suite 305
Bernardsville, NJ 07924

Dear Family Member,

A member of your family has been identified as having a genetic mutation in the **SMAD4 gene**. Mutations in this gene are known to be associated with an increased risk for certain cancers. This means that other family members are at risk to carry this same gene mutation and hence at an increased risk for certain cancers. This letter has been written to summarize information regarding SMAD4 mutations.

Individuals with mutations in the SMAD4 gene have Juvenile polyposis syndrome (JPS). JPS is characterized by a predisposition to polyps (hamartomatous) in the gastrointestinal tract, specifically in the stomach, small intestine, colon, and rectum. These colon polyps can develop as early as infancy and throughout adulthood, with most affected individuals having polyps by age 20. These benign polyps have the potential to develop into cancer if not removed. The risk for colon cancer is reported to range from 9%-50%; the risk for gastric (stomach) cancer is 21%. SMAD4 mutations are associated with a more aggressive gastrointestinal phenotype than other types of JPS. As a result, individuals with an SMAD4 mutation have higher incidences of colonic adenomas and carcinomas and more frequent upper gastrointestinal polyps and gastric cancer than those with mutations in other JPS-associated genes. Pancreatic and small bowel cancer is rare but elevated in individuals with pathogenic mutations. Hereditary hemorrhagic telangiectasia (HHT) is present in most individuals with SMAD4 mutations, resulting in vascular abnormalities that may require additional monitoring.

Understanding risk is an important tool in prevention and management of cancer. It is important to note that many individuals with *SMAD4* mutations will never develop cancer over their lifetime. When one inherits an *SMAD4* mutation, he/she is not inheriting cancer; rather they are inheriting a predisposition to cancer.

When an individual has one copy of the *SMAD4* gene mutation they have an increased risk for cancer as outlined above. Because everyone has two copies of the gene for *SMAD4,* this means that a parent who carries an *SMAD4* mutation has a 50% chance of passing the mutation onto each of their children. It also means that if a person carries such a mutation, their siblings have a 50% chance to carry the same mutation. Extended family members may also be at risk for having the same mutation. If a person does not carry the mutation, they cannot pass it onto their children.

We strongly recommend that you and all persons in your family who are at risk for carrying the *SMAD4* gene mutation consider scheduling an appointment for cancer genetic counseling to discuss the benefits and limitations of genetic testing. To pursue cancer genetic testing, it is helpful if you have a copy of your family member's genetic testing report indicating that they have an *SMAD4* mutation.

GeneScreen is available to discuss this information in more detail with you and coordinate appropriate testing. Please visit the following website to submit your request for genetic counseling: https://hipaa.jotform.com/200926739003048. You can also contact Genescreen directly at 908-766-2800 to schedule a remote consultation with a genetic counselor.

Sincerely,

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Genescreen

Jill Chisholm, APN
President
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