UT Southwestern Harold C. Simmons Comprehensive Cancer Center | NCI Designated Comprehensive Cancer Center

POLD1 Mutations

What you should know about *POLD1* mutations

Individuals with a *POLD1* mutation have polymerase proofreading-associated polyposis syndrome (PPAP), which means they have an increased chance to develop early onset colorectal cancer and polyps of the GI tract. Exact cancer risks for individuals with one mutation in this gene are not fully understood, but more specific information becomes available with ongoing research.

Individuals with a *POLD1* mutation may also have autosomal dominant mandibular hypoplasia, deafness, early aging, and lipodystrophy (MDPL) syndrome. MDPL is a rare, systemic disorder that is characterized by the loss of subcutaneous fat, distinctive facial features, and metabolic abnormalities including insulin resistance and diabetes.

Cancer risks associated with a *POLD1* mutation

- Individuals with a *POLD1* mutation may have an increased risk to develop adenomatous polyps of the GI tract and colorectal cancer. The specific lifetime risk for colorectal cancer is not currently known, but is thought to be increased compared to the general population risk of ~5%.
- Other cancers may be associated with *POLD1* mutations, but additional evidence is needed.

Risks to family members

Mutations in the *POLD1* gene are inherited in an autosomal dominant manner. This means that children, brothers, sisters, and parents of individuals with a *POLD1* mutation have a 1 in 2 (50%) chance of having the mutation as well. Both males and females can inherit a familial *POLD1* mutation and can pass that it on to their children.

Managing cancer risks

The following surveillance is recommended by the National Comprehensive Cancer Network (v3.2019).

- Colonoscopy starting at age 25-30
    - Repeat every 2-3 years if colonoscopy is negative
    - Repeat every 1-2 years if polyps found
- Consider surgery if the polyp burden becomes unmanageable by colonoscopy

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