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Dear Doctor:

I am sharing this information with you about a genetic test for the *KRAS*-variant, a recently discovered inherited genetic marker with significant implications in cancer.

The *KRAS*-variant is an inherited mutation in a microRNA control center, and is not a tumor acquired *KRAS* mutation, which you may be most familiar with. This mutation has been shown to be a genetic marker of increased risk of developing cancer, primarily in women, including premenopausal triple negative breast cancer [1], post-menopausal ovarian cancer [2, 3], and non-small cell lung cancer (NSCLC) [4]. The *KRAS*-variant is a genetic marker of increased risk of NSCLC for men, as well. In an independent validation study, women with this mutation were found to be significantly more likely to develop both breast and ovarian cancer, as well as bilateral breast cancer and additional cancers in their lifetime [5].

In addition, the *KRAS*-variant has been shown to be a predictive biomarker of treatment response, across numerous cancer types, including colon cancer [6], head and neck cancer [7], ovarian cancer [8] and NSCLC [9]. Specifically, there appears to be resistance to cisplatin, and sensitivity to cetuximab across these cancer types.

I may be interested in testing for this mutation because I am a woman or a man with a family history of breast and ovarian cancer, or because I am a woman with one of these cancers myself. If I am positive for this mutation, it could be important for my daughters to be tested. If I am a woman with this mutation, it may impact how you follow me for early cancer or second cancer detection and prevention. Women who carry this mutation have a > 20% lifetime risk of developing breast cancer [1] and are at significantly higher risk of developing a second primary breast cancer [5]. Based on these findings and American Cancer Society (ACS) guidelines women qualify for breast MRI screening for surveillance (<http://www.cancer.org/cancer/breastcancer/moreinformation/breastcancerearlydetection/breast-cancer-early-detection-acs-recs>). In addition, because *KRAS*-variant patients have a genetic risk of ovarian cancer [2, 3, 5], based on US Preventive Task Force guidelines these women should qualify for ovarian cancer screening (<http://www.uspreventiveservicestaskforce.org/Page/Topic/recommendation-summary/ovarian-cancer-screening>).

I may also be interested in testing for this mutation because I am a cancer patient, and am making decisions about the best type of therapy for me. Based on the data showing that individuals with the *KRAS*-variant respond uniquely to cancer therapies, I think it might be good additional data to have in hand when we make these choices. There is additional data on both the MiraDx as well as the MiraKind websites about testing. You can order testing through MiraDx for me, or I can join a study at MiraKind and results will be returned directly to you.

I look forward to discussing this with you.

Sincerely,

Your patient

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