Dear family members, April 22, 2024

I am writing to inform you that there is a possibility that you could be at increased risk for cancer. I recently was diagnosed with breast cancer, and, because my sister Lynda Leedy died of breast cancer at 40, genetic testing was done to see if it might have a hereditary component. I underwent genetic testing at Ballad Cancer Care in Kingsport, TN, and was found to have a genetic change called a likely pathogenic variant (also known as a mutation) in the CHEK2 gene called c.190G>A that increases the likelihood of certain cancers. This condition often runs in families, so it is possible that other people in our family also have this mutation. It is probably from the mom's side of my family, since there are 4 breast cancers and a few other cancers in the Clay family, (that are known to me). These numbers may seem high, but Mom (Lura Clay Kiser) was from a large family, (one of 12 siblings and a few generations of descendants).

This gene mutation is associated with breast cancer, and possibly colon, thyroid and prostate cancers. If you have it, this mutation could be inherited by your children. See other information attached. Because this is a recently found variant, the number of tests to date is lower than optimum, so it is considered likely pathogenic, and more people need to be tested to clear up uncertainties.

For example, in the table of lifetime risk attached, the range for breast cancer lifetime risk is 20 to 40% with this variant. In the general population, for comparison, the lifetime risk of breast cancer is 13%. More testing could reduce this wide range and provide better estimates of lifetime risk. For lifetime risks of thyroid and prostate cancer the uncertainty is much higher because fewer people have been tested at this time.

Ballad Health is offering **free testing** before August 22, 2024, to any of my adult blood relatives (18+ yrs.) that might carry this gene variant that you could pass on to your children. If you choose to take advantage of this, it can help the researchers gather more data to reduce uncertainty, while assuring you of where you stand and whether more frequent cancer screenings are needed. To find out more information you can contact Holly Mears at Ballad Cancer Care at 423-578-8536 and she would be happy to assist you.

Please let your family members know that this mutation has been found in the Clay family, and that testing is available in this area, **free of charge**. For those outside the area, please consult with your doctor about getting genetic testing. Ballad Health offers referrals in other areas.

I need your help reaching family members: My family information is far from complete because 1.) My Facebook account was hacked, closed, restarted and I am trying to rebuild my contact list; and 2.) My other address information is very out of date and incomplete. I will attach this to the Clay Family blog at https://clayfamilyblog.com. Other family information about ancestors, etc. can be found on this website. Sorry, it is far from complete. Additions are requested. Please pass this information along to as many family members as possible, since many will not know this otherwise.

Sincerely,

Thelma Kay Kiser

423-782-9727

PS. This gene is not one of the worst ones (BRCA1 & BRCA2) for which some people have chosen to have both healthy breasts removed. Although this procedure is mentioned in the attached pages, I would consider it an extreme response unless actual cancers are found (Just my opinion). Because an MRI found spots in both breasts, I expect to have lumpectomy or mastectomy surgery, with some follow up treatment. Please keep me in your prayers. God bless you.

BalladHealth

CHEK2 Medical Management Options

Clinical testing of the *CHEK2* gene is newer compared to other known hereditary cancer genes, such as *BRCA1 & BRCA2*; therefore less is known about the cancer risk associated with having a pathogenic variant or change in the *CHEK2* gene. As we learn more about *CHEK2*, more defined medical management guidelines will be developed. Medical management should be based on personal & family history along with current guidelines regarding the risks associated with carrying a single *CHEK2* mutation. Therefore, it is VERY important that you stay in touch with the Hereditary Cancer Clinic at Ballad Cancer Care for the most up to date information.

CANCER RISKS FOR INDIVIDUALS WITH *CHEK2* MUTATIONS

The risk for breast cancer is increased in women who carry a *CHEK2* mutation, as is shown in the table below. It is important to keep in mind that these risks are spread over the lifetime, and don't refer to any one year or period of time. As we learn more about this gene, the risks listed below may change. in addition, we may learn that there are additional cancers associated with *CHEK2* mutations.

Lifetime Risk of Cancer *CHEK2* pathogenic variant carriers vs. the General Population

Types of Cancer	*CHEK2* Gene Mutation Carrier	General Population
Female Breast	20-40%	13%
Second breast primary (within 10 years of first diagnosis)	Up to 29%	5-10%
Male Breast	0.4 - 1%	0.1%
Colon	5-10%	5%
Thyroid	Elevated, exact risk not yet defined	1%
Prostate	Elevated, exact risk not yet defined	12%

Now that you have the knowledge of the *CHEK2* mutation in your family, you are empowered to reduce your risk of cancer. The decision of how you should go about managing your risk is personal and can be difficult. You should discuss these options with your doctor(s). We are here to help in any way we can. Presented below are acceptable strategies for you to consider.

FEMALE BREAST CANCER

A) Increased Breast Cancer Surveillance (Screening)

Some women choose to be watched closely rather than remove their breasts surgically, with the hope that if cancer does develop, it will be caught at an early stage when it is more treatable. However, there is no guarantee that a breast cancer will be detected early. If you choose surveillance, it should be performed by experienced providers, and should consist of:

1) Mammogram every twelve months beginning at age 40
2) Clinical breast exams every six-twelve months
3) Breast self-examination monthly
4) Breast MRI every twelve months starting at age 30-35

*Studies have shown that MRI is better than mammograms for detecting cancer in high-risk women. Mammogram and breast MRI can be alternated every six months to allow for more frequent imaging. A breast MRI is typically ordered by your gynecologist or primary care physician, and their office usually pre-certifies the MRI prior to your appointment.

B) Prophylactic bilateral mastectomy (surgical removal of healthy breast tissue)

While this surgery is not a standard recommendation at this time for women with a *CHEK2* mutation, it is a surgery that can be considered for those with a strong family history of breast cancer and discussed with their physicians. The most effective way to reduce the risk of breast cancer is by prophylactic (preventive) mastectomy. While this strategy cannot reduce the risk of cancer completely, it prevents cancer in at least 9 out of 10 women (90%) who opt for the surgery. Breast reconstruction is an option that many women choose as well.

C) Hormonal Treatment

As a group, women considered high risk for developing breast cancer can reduce their risk of breast cancer by about half by taking drugs such as tamoxifen for 5 years. However, these medications can have serious side effects (like a slight increased risk for blood clots and uterine cancer). Its effectiveness also depends on the hormonal characteristics of a breast cancer in an individual. Thus, this is a strategy that should be discussed with your doctor if you are interested in pursuing it. **The use of tamoxifen to reduce risk in women with *CHEK2* mutations has not been evaluated.**

MALES WITH *CHEK2* PATHOGENIC VARIANTS

The cancer risks for males with *CHEK2* mutations are still being researched and determined at this time. Males with a *CHEK2* pathogenic variant may be at a slightly increased risk to develop breast cancer and can consider having yearly clinical breast exams and performing monthly self-breast exams. There is emerging evidence for an association with prostate cancer. Consider prostate cancer screening at age 40.

COLON/RECTAL CANCER

- For patients with a personal history of colorectal cancer and a *CHEK2* variant, surveillance is based on staging of initial cancer and surgical status.

- For patients without a personal history of colorectal cancer, high quality colonoscopy screening every 5 years is recommended beginning at age 40 or 10 years prior to age of first-degree relatives colon cancer diagnosis (whichever comes first).

OTHER CANCERS

Some studies have described a possible increased risk for a wide range of cancers for people with CHEK2 mutations, including prostate cancer, ovarian cancer, thyroid cancer and other malignancies. However, these studies are not conclusive and there are currently no medical management guidelines to address these possible risks.

FAMILY MEMBERS

It is very important that you let all your relatives know of the presence of this gene mutation. They need to know that they may be at increased risk for breast and colon cancer. Genetic testing can sort out who in your family is at risk and who is not. Because *CHEK2* mutations are currently not known to be associated with childhood cancers, we do not test anyone under age 18. We understand that it is a big responsibility to inform relatives. Please let us know if we can assist you. We are happy to either see your relatives in clinic here or we can help make referrals to genetic counselors in other areas.

LIFESTYLE

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It's been shown that leading a healthy lifestyle may reduce the risk of cancer. In particular, exercising regularly and avoiding post-menopausal weight gain, in addition to eating a high-fiber/low-fat diet and limiting alcohol intake may reduce risk.

KEEP IN TOUCH

Please keep in touch with us! We are learning more about cancer prevention every day, and we are here to help you in the future as knowledge grows. Feel free to call us any time at 423-578-8500.

Holly Mears, RN & Jessica Bembry, FNP
Hereditary Cancer Clinic
Ballad Cancer Care