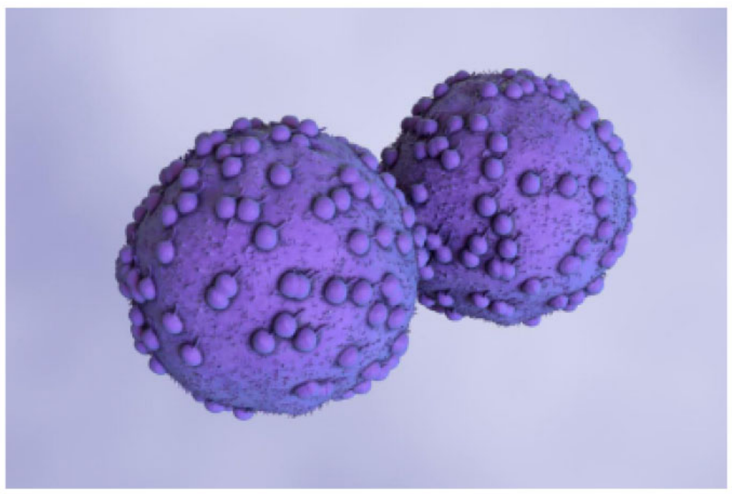
New cancer-causing syndrome uncovered

By Honor Whiteman | Published Monday 25 September 2017

Certain genetic mutations thought to be associated with a rare bone marrow disease may instead predispose individuals to early-onset cancer, two new studies suggest.

The research indicated that mutations in the FANCM gene are not - contrary to current understanding - related to Fanconi anemia, which is an inherited disease of the bone marrow.



Researchers suggest that mutations in the FANCM gene cause early-onset cancer.

However, researchers report that FANCM gene mutations are associated with early cancer development, as well as with toxicity to chemotherapy.

Cancer remains one of the biggest health burdens in the United States, with more than 1.6 million new cases of the disease diagnosed last year.

Genetic mutations are a major cause of cancer; they disrupt the normal processes that control cell growth, causing cells to grow out of control and form tumors.

Identifying cancer-causing gene mutations is crucial for uncovering strategies to prevent, diagnose, and treat cancer. And now, researchers may have added another candidate to the list: FANCM.

The new studies were recently published in the journal *Genetics in Medicine*.

Understanding FANCM mutations

FANCM is a gene that has been linked to the development of Fanconi anemia, after 2005 research identified FANCM gene mutations - known as biallelic mutations - in patients with the disease.

Previous studies have indicated that these biallelic mutations also cause DNA errors that increase cancer - particularly breast cancer - susceptibility. In the new studies, researchers sought to gain a better understanding of the disease outcomes caused by FANCM mutations.

The first study was led by Massimo Bogliolo, of the Centre for Biomedical Network Research on Rare Diseases (CIBERER) and the Universitat Autònoma de Barcelona in Spain.

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Bogliolo and colleagues used genomic sequencing to analyze cells derived from three patients who possessed mutations in the FANCM gene. They found that patients with FANCM gene mutations did not possess any characteristics typical of Fanconi anemia, such as congenital malformations or hematological abnormalities.

However, the study revealed that these patients showed a predisposition for early-onset cancer, including leukemia and head and neck cancer. What is more, these patients experienced high toxicity in response to chemotherapy.

The authors say that their findings indicate that "loss-of-function mutations in FANCM cause a cancer predisposition syndrome clinically distinct from bona fide FA [Fanconi anemia]."

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FANCM mutations and breast cancer

The second study - led by Javier Benítez, also of the CIBERER - included five women with biallelic mutations in the FANCM gene.

Supporting the results of the first study, Benítez and colleagues found that while the women did not develop Fanconi anemia, they did show a high predisposition to breast cancer and toxicity to chemotherapy.

Taken together, the researchers say that the two studies indicate that biallelic mutations in the FANCM gene cause a type of cancer predisposition syndrome, rather than Fanconi anemia.

> **"Until now it was thought that biallelic mutations in the FANCM gene caused Fanconi anemia, but we have now demonstrated that it is not so, given that in the two studies there were eight patients with these mutations and none of them had anemia."**
>
> – Study co-author Jordi Surrallés, CIBERER

Based on their results, the researchers recommend close monitoring of patients with FANCM gene mutations, given their higher cancer susceptibility. Additionally, they caution that care should be taken when treating such patients with chemotherapy, as it could have toxic effects.