The document affixed to this article can be used by any qualified bioinformatics professional to verify the fact that calcineurin is the ‘chromosome scanner.’

https://phys.org/news/2019-02-chromosome-scanner-cancer.html

Researchers discover 'chromosome scanner' that protects against cancer

February 26, 2019, University of Copenhagen

In a new study, researchers from the University of Copenhagen have identified one of the main mechanisms behind the repair of serious damage to the human DNA. A 'scanner' inside the cells decides whether or not so-called flawless DNA repair, which protects against cancer, is launched.

Damage to the human DNA can cause unstable genetic material and thus plays a main role in the development of cancer. Therefore, a lot of researchers are trying to learn from the cells' own protection against DNA mutations. Among other things, this is done by quickly and correctly repairing DNA damage and thus avoiding tumour development. Now researchers from the University of Copenhagen have come a step closer to understanding the cells' repair process in a new study published in the scientific journal *Nature Cell Biology*. For these serious damages, there are two basic repair systems, but only one of them is flawless. If this system is out of function, there is increased risk of developing cancer following from the DNA damage to which our cells are constantly exposed. We know from mutations in so-called BRCA genes that this causes hereditary breast and ovarian cancer.

"We have discovered how the cell launches the flawless system for serious DNA damage repair and thus protects against cancer. This is done using a protein you could call a 'scanner,' which scans the histones in the cell and on that basis launches the repair process," says the researcher behind the study, Professor Anja Groth from the Biotech Research & Innovation Centre.

3-D-Printed Copy Rather than Crude Gluing

According to the researchers, the problem with the two repair systems is that one is much easier and faster for the cell to launch than the other, and therefore the former is used more often. However, it does not work as well as the latter. Here the two cut DNA strings are merely glued back together.

"You can imagine that the one repair system somewhat awkwardly tries to glue two DNA strings together, while the other system produces a 3-D-printed copy resembling the DNA before damage completely. The first system produces far more errors than the

latter, and therefore the latter provides far better protection against tumour development," Anja Groth explains.

The protein that acts like a scanner is called BARD1, and the researchers have known for a long time that it works like a so-called tumour suppressor. However, this is the first discovery of BARD1's scanning function, which tells the BRCA1 protein and thus the cell that a flawless repair system can be launched. If possible, it then launches the BRCA1 function that plays such a vital role in cancer protection.

Understanding the Repair Process Is Significant to the Development of Medicine
The flawless repair method is also referred to as a homologous recombination. For part of its lifetime the cell contains two identical DNA strings, as it is getting ready to split. This means that the cell actually holds the solution to its own damage.

"You can say that BARD1 tells the cell that the flawless system can be launched, because BARD determines whether there are signs that the cell contains two identical DNA strings. If so, the 'flawed' repair system is blocked, while the flawless system is launched," Anja Groth concludes.

In connection with this and other discoveries the researchers have founded the company Ankrin Therapeutics, which seeks to utilise DNA repair mechanisms to develop new targeted cancer treatment.

Explore further: **Research explains the role of the gene BRCA1 in DNA repair**
More information: Kyosuke Nakamura et al. H4K20me0 recognition by BRCA1–BARD1 directs homologous recombination to sister chromatids, *Nature Cell Biology* (2019). **DOI: 10.1038/s41556-019-0282-9**

Journal reference: Nature Cell Biology

Read more at: https://phys.org/news/2019-02-chromosome-scanner-cancer.html#jCp

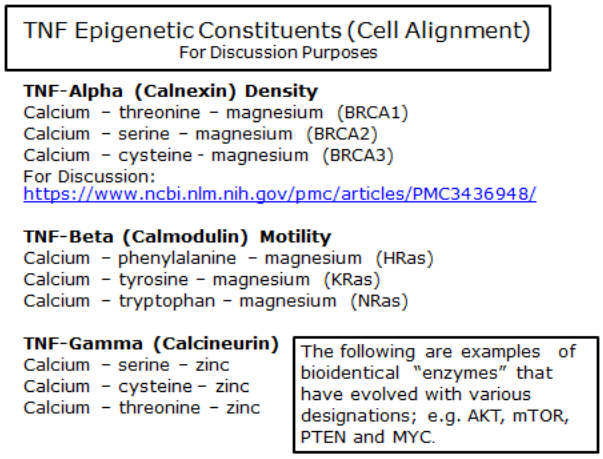
The mystery of BRCA breast cancers is finally being solved; partially.

The following factors can be verified if ample time is allocated to apply physical science based epigenetic modeling to cellular mechanism.

- BRCA 1 - 3 are designations for calcium dependent forms of IL-32 based calnexin; refer to the illustration for discussion.
- BARD 1 - 3 are designations for calcium dependent forms of IL-3 based calcineurin.

- The role of calcineurin is to maintain homeostasis. If BRCA1 - 3 mutations exist, BARD 1 - 3 are activated.

The following illustration depicts interactions between calnexin and calcineurin.



These explanations are provided to initiate discussions with qualified bioinformatics professionals.

https://medicalxpress.com/news/2017-10-mystery-breast-cancer-gene-years.html

Mystery of breast cancer risk gene solved, 20 years after its discovery

October 4, 2017

More than 20 years after scientists revealed that mutations in the BRCA1 gene predispose women to breast cancer, Yale scientists have pinpointed the molecular mechanism that allows those mutations to wreak their havoc.

The findings, reported Oct. 4 in the journal *Nature*, will not only help researchers design drugs to combat breast and ovarian cancers, but also help identify women who are at high risk of developing them, the authors say.

"There have been about 14,000 papers written about BRCA1, and you would think we already know everything about the gene, but we don't," said senior author Patrick Sung,

professor of molecular biophysics and biochemistry and of therapeutic radiology and member of the Yale Cancer Center.

The discovery of BRCA1's role in DNA repair and suppression of tumors was the first evidence that the risk of cancer could be inherited. It was originally thought that mutations in BRCA1 and the related BRCA2 gene might account for 7% to 8% of breast and ovarian cancers, Sung said. However, the cancer risk is likely a lot higher because in many cancer cases the expression of the BRCA genes is silenced even though no mutation can be found, he added.

Sung and colleagues showed in their Nature paper that the interaction of BRCA1 with its partner BARD1 is necessary to recruit the exact genetic sequence needed to repair breaks in DNA caused by endogenous stress and environmental insults such as radiation exposure.

"Defining the mechanism of the BRCA-dependent DNA repair pathway will help scientists design drugs to kill cancer cells more efficiently," Sung said.

"Understanding this mechanism will provide the predictive power for doctors trying to establish a patient's personal risk of developing cancer."

Explore further: **Genetic predisposition to breast cancer due to non-brca mutations in ashkenazi Jewish women**

More information: BRCA1–BARD1 promotes RAD51- mediated homologous DNA pairing, *Nature* (2017). **DOI: 10.1038/nature24060**

Journal reference: Nature