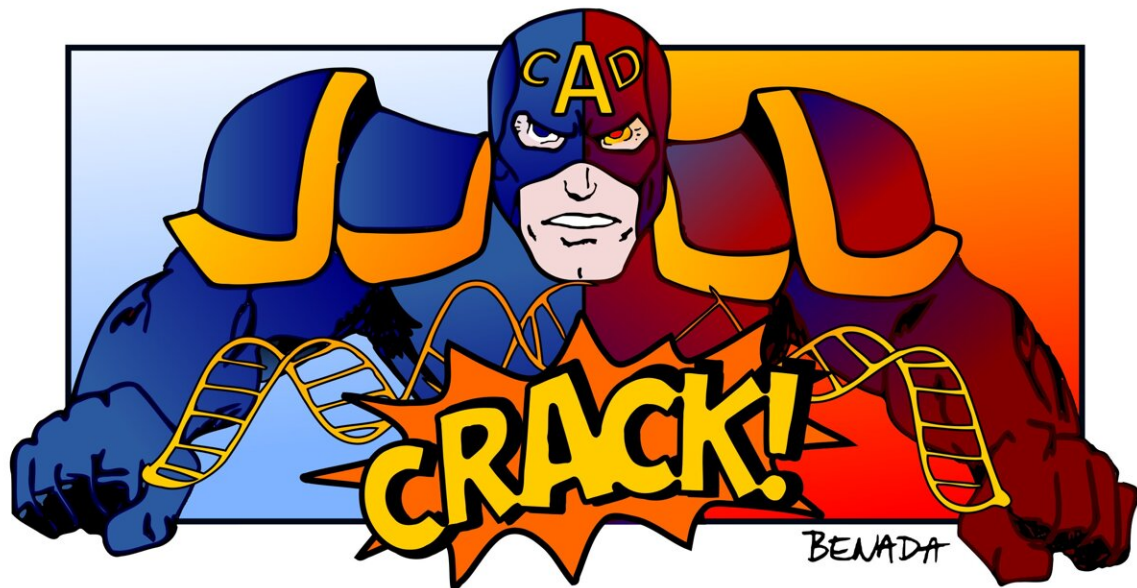


Tumor cells activate DNA breaks, protecting them from death due to treatment-induced damage

April 29 2022, by Bob Yirka



CAD, normally a guardian that eliminates unwanted cells of the body, is turned by cancer cells into a villain protecting them against radiotherapy. Credit: Jan Benada

An international team of researchers has found that some tumor cells are able to set off a caspase-activated DNase (CAD) that promotes breaks in DNA strands after exposure to genotoxic treatments. In their paper

published in the journal *Science*, the group suggests the broken strands help the tumors overcome the treatment by preventing their own cell death.

Prior research has shown that firing a beam of radiation at [cancerous tumors](#) can kill the cells that comprise them, but quite often, some of the cells survive the onslaught, allowing the tumor to begin growing again. Prior research has also shown that non-[cancerous cells](#) often activate the G₁ cell cycle checkpoint as a means of self-protection when exposed to radiation, but this mechanism does not work with cancer cells. That has left researchers wondering how some [tumor cells](#) are able to survive after such treatment.

In their work, the researchers were conducting screening efforts with bone [cancer cells](#) when they noticed that CAD appeared to play a role in preventing tumor [cell death](#). After firing radiation at tumor cell samples, they found what they described as "mysterious nicks" in strands of their DNA, arising approximately 12 to 18 hours after the radiation had been applied. Suspecting that CAD might be the factor responsible for the nicks, they disabled the enzyme in some samples, and the cells became more sensitive to the radiation—the cells also tended to enter mitosis earlier than normal. Next, the researchers transplanted human tumor cells into mice and tested the impact of adding CAD to the mix. This led to cells that were better able to withstand radiation treatment.

The work does not prove that CAD is the only player involved in preventing cell death in tumors after radiation exposure, but it does suggest that it plays a major role. It also did not explain how tumor cells breaking their own DNA strands prevents cell death, though they suggest it might be tied to the way the immune system responds.

More information: Brian D. Larsen et al, Cancer cells use self-inflicted DNA breaks to evade growth limits imposed by genotoxic

stress, *Science* (2022). [DOI: 10.1126/science.abi6378](https://doi.org/10.1126/science.abi6378)

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