Inhibitors of RAD52 Recombination Protein and Methods Using Same

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Technology description

Overview

PAGE SUMMARY

Drexel University researchers have developed small molecule inhibitors of RAD52 that act as highly specific targeted cancer therapeutics when used against familial breast, ovarian and other cancers. RAD52 is an evolutionary conserved member of the homologous recombination pathway that plays a key role in maintenance of genome integrity in all organisms. RAD52 mutations alone show no significant phenotype in human cells; however, their combinations with mutations in genes like BRCA1, BRCA2, PALB2, and RAD51C that cause hereditary cancers are lethal. This lethality can be reproduced synthetically in cancers carrying such mutations by administering selective RAD52 inhibitors, thus enabling targeted cancer treatments for familial breast cancer, ovarian cancer, pancreatic cancer, prostate cancer, chronic myeloid leukemia (CML) and other cancers.

Researchers in Dr. Mazin’ s laboratory at Drexel’ s College of Medicine have identified several highly specific small molecule inhibitors of RAD52 that suppressed growth in both BRCA-1-deficient and BRCA-2-deficient cell lines, including BRCA-1-deficient CML patient cells. The calculated properties of these inhibitors’ chemotypes fall within the range of drug-like and orally bioavailable. Additionally, one of these inhibitors demonstrated low genotoxicity in human cells.

Institution

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