Biochemists identify new genetic code repair tool

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Clemson University researchers recently reported finding a new class of DNA repair-makers.

Clemson biochemist Weiguo Cao studies how cells repair damaged DNA. The finding from Cao's lab in the Clemson Biosystems Research Complex in collaboration with computational chemist Brian Dominy appeared in the Sept. 9 issue of *The* Journal of Biological Chemistry*:* "A new family of deamination repair enzymes in the uracil DNA glycosylase superfamily by Hyun-Wook Lee, Brian N. Dominy and Weiguo Cao."

"DNA is a string of a long molecule composed of four building blocks: A for adenine, T for thymine, G for guanine and C for cytosine. The heredity of all organisms is determined by the pairing of A with T and G with C," said Cao, a professor in the genetics and biochemistry department.

DNA is constantly assaulted by various stresses. A common type of damage is modification of three out of the four building blocks for genetic code, A, G, C by a chemical process called deamination. The genetic consequence of deamination is that it will change the pairing of the genetic code. For example, the deamination of C (cytosine) will generate U (uracil). Instead of pairing with G as C will do, U pairs with A. In so doing, it changes the genetic program inside the cell and may cause dangerous mutations resulting in disease.

To ensure the integrity of the genetic material, cells are equipped with a "molecular toolkit" for repairing DNA damage. The toolkit is comprised of a variety of different molecules — called enzymes — that have evolved to repair different types of DNA damage. One of the DNA repair enzymes the Cao lab studies is called uracil DNA glycosylase (UDG). As it's name indicates, it is traditionally known as an enzyme that removes uracil from DNA. Because deamination of C (cytosine) is a very common type of damage found in DNA, UDG has been found in many organisms and researchers have grouped them into five families in the so-called UDG superfamily.

In their most recent work, Cao and his colleagues discovered a new class of enzymes in that superfamily that lack the ability to repair uracil. A further study showed that this class of enzymes, instead, is engaged in the repair of deamination on the different building block adenine. This caught them by surprise because all known UDG enzymes are capable of uracil repair.

To further understand how this new class of enzymes works as a tool for repair, Cao and Dominy combined computational and biochemical methods to pinpoint the critical part of the repair machine that is responsible.

"What we learned from this work is that DNA repair toolkits have an amazing ability to evolve different repair functions for different kinds of DNA damage," Cao said. "This work also demonstrates how a combination of research approaches from different disciplines makes the discovery possible."

"Collaborative efforts involving computational and experimental investigative methods can greatly enhance the efficiency of scientific discovery, as well as provide more thorough answers to very important scientific questions," Dominy said. "In my opinion, the collaborative

efforts between our two groups have demonstrated the substantial value of such interactions."

Provided by Clemson University