Researchers create model of cancer-preventing enzyme, study how it works

Researchers at the University of Missouri-Columbia recently created a model of proline dehydrogenase, an important cancer-preventing enzyme in the human body, and analyzed how it works. A paper detailing their results was published today in the *Journal of Biological Chemistry*.

Proline dehydrogenase is important because it plays a role in apoptosis, the process of cell death, by enabling the creation of superoxide, a highly reactive electron-rich oxygen species. Superoxide is involved in the destruction of damaged cells and therefore is important in preventing the development and spread of cancer. The protein proline dehydrogenase "opens up to allow oxygen to ‘steal’ electrons" and create a superoxide, said Tommi A. White, an MU doctoral student in biochemistry.

White worked with John J. Tanner, professor of chemistry and biochemistry in MU’s College of Arts and Science, and Navasona Krishnan, a doctoral student at the Unviersity of Nebraska-Lincoln, and Donald F. Becker, an associate professor at the University of Nebraska-Lincoln, to create the first model of proline dehydrogenase. Because the human form of this enzyme is difficult to work with, the team studied proline dehydrogenase from the bacteria Thermus thermophilus. They used bioinformatics and biochemical studies to show that this enzyme is functionally similar to the human version, so their results can be generalized to the human version, as well as the bacterial version.

Using X-ray crystallography and biochemical analysis, the team created a model of proline dehydrogenase that can tell scientists more about the molecule’s structure and functions.

"The three-dimensional model tells us a lot about the structure of the molecules and helps us understand how they work," Tanner said. "This protein is important in cancer prevention because it enables the creation of superoxide, which aid in cell death. Cells aren’t meant to live forever, and at some point, they need to die and be destroyed. Cells that are damaged or diseased are usually destroyed in this process. Our structure tells us how oxygen gets access to electrons stored in the enzyme. We think we've identified a gate that opens to let oxygen into the enzyme where the electrons are stored."

In this way, proline dehydrogenase is important in preventing cancer. White said it’s unusual for proline dehydrogenase to be involved in such a process because the usual job of this type of enzyme is to transfer electrons to the mitochondrial membrane, not allow them to be attached to oxygen to create highly reactive superoxides.

Tanner and White said they hope to continue to study proline dehydrogenase and the molecules that can inactivate it. They also plan to examine another protein they suspect works in collaboration with proline dehydrogenase to understand how that protein affects the cancer-preventing abilities of proline dehydrogenase.

Source: University of Missouri-Columbia