Short bacterial protein is surprisingly versatile

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MIT researchers have discovered why an unusually short bacterial protein can have many more interactions than would normally be expected of something its size.

The team, led by biology professor Graham Walker, found that the protein, UmuD, belongs to a recently discovered class of proteins called intrinsically disordered proteins.

Proteins, which consist of chains of amino acids, locally fold themselves into one of two structures--a helix or a pleated sheet. In contrast, intrinsically disordered proteins lack such well-defined local structures.

The lack of formal structure probably allows such proteins to bind to a wider variety of proteins, Walker said.

"They have some structure, but not the way we're used to thinking about it," said Walker, senior author of a paper on the work, which appeared in the *Proceedings of the National Academy of Sciences* the week of Jan. 14.

Normally, proteins form a specific structure with binding sites where other proteins can attach. The larger the protein, the more binding sites it can have. A protein like UmuD, which is made of fewer amino acids, would not be expected to have enough binding sites to interact with very many other proteins.

"If you think of it as two jigsaw puzzle pieces, it's hard to see how you

could fit much more than one or two pieces together," said Walker, American Cancer Society Professor of Biology.

Previous structural studies carried out at high concentrations had shown that UmuD predominantly folds into sheets. However, the MIT researchers used a technique called circular dichroism spectroscopy to reveal that at concentrations similar to those in living bacteria, UmuD appears as a random coil.

As the intrinsically disordered proteins bind with other proteins, they may change their shape, allowing them to then interact with different proteins, potentially creating a chronological sequence of interactions as proteins bind and then are cast off.

UmuD usually is found in groups of two, which implies that it must have some kind of stable protein structure, said Sharotka Maria Simon, lead author of the paper and an MIT Ph.D. recipient now at Brandeis University.

"Even though we call it disordered, UmuD must have enough structure to consistently form a pair," she said.

The new finding sheds light on UmuD's role in the bacterial SOS system, which is called into action when DNA is damaged. In a paper published in Molecular Cell in December, Walker and others reported that UmuD had an unexpected role involving yet another protein in the SOS system.

The SOS system helps activate and control translesion polymerases, enzymes that copy damaged DNA. The system, which is called upon as a last resort, when DNA has lesions that regular repair mechanisms can't fix, keeps the cell alive by maintaining its DNA, at the cost of preserving potentially harmful mutations.

UmuD's ability to interact with multiple partner proteins allows it to control the function of two translesion polymerases, coordinating their action with DNA replication.

Other authors of the PNAS paper are F.J.F. Sousa and R. Mohana-Borges of the Universidade Federal do Rio de Janeiro. The research was funded by the National Cancer Institute and a Cleo and Paul Schimmel Fellowship.

Source: MIT