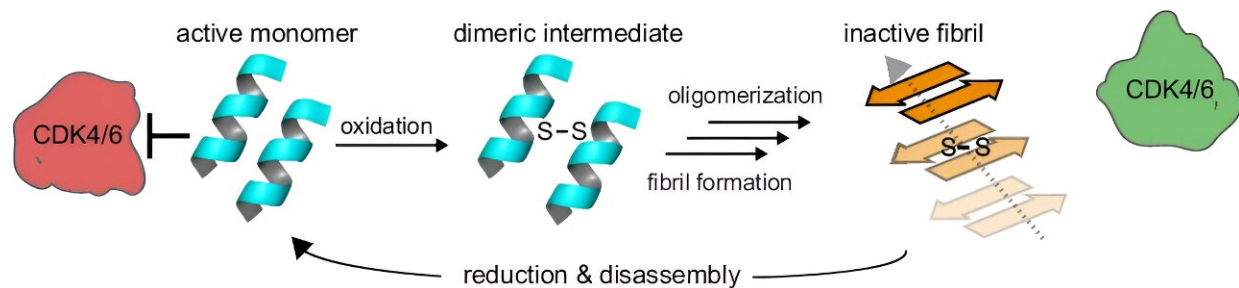


New protein discovery may influence future cancer treatment

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Model of the oxidation-induced amyloid formation and disassembly mechanism of p16. Credit: *Nature Communications* (2024). DOI: 10.1038/s41467-024-49581-7

Researchers from the University of Otago, Christchurch, have spearheaded the discovery of a protein function which has the potential to guide the development of novel cancer treatment options and improve the diagnosis of various cancers.

The research, carried out alongside Dr. Vanessa Morris from the University of Canterbury's School of Biological Sciences as well as researchers in Australia and Denmark, centers on the activity of a tumor-suppressing protein called p16.

The discovery, [published](#) in *Nature Communications* and first authored by University of Otago, Christchurch Ph.D. student Sarah Heath, shows

that p16 has the ability to dramatically alter both its structure and its function.

"This discovery was a real surprise," says senior researcher Dr. Christoph Goebel, a Principal Investigator at Mātai Hāora—the Center for Redox Biology and Medicine, in the campus's Department of Pathology and Biomedical Science.

"We know that some proteins can be modified chemically to impact their structure and functions, but this is the first example of such a dramatic structural and [functional change](#)," Dr. Goebel says.

"We even found that it's fully reversible—such dramatic changes were probably not believed possible until now."

Dr. Goebel says under normal conditions, the protein p16 protects cells from uncontrolled cell division. However, once it changes to what's known as the amyloid (or dysfunctional) state, it loses this protective function.

"We found that the protein does its job perfectly when in the native state but loses all its abilities when in the amyloid state," he explains.

"We currently think that this transition isn't just a [random process](#) but likely a functional switch, and we were very surprised how black and white our results were regarding its function."

Dr. Goebel says his team made the discovery following many years testing p16 in the laboratory, using a combination of molecular and cellular experiments.

He says once the protein is oxidized and in the amyloid state, it can be disassembled and "switched back to normal" by reversing its oxidation.

Therefore, the team was able to discover a redox-based amyloid system which can switch between its normal state and the amyloid state by creating or breaking one chemical bond.

"The data looked almost too good to be true, but the more often we repeated our experiments, also with our collaborators overseas, the more confident we were that what we observed was real."

Dr. Goebel says p16 is among the top five proteins found to be mutated in various cancers, with the ability to actively cause certain types of cancer when damaged.

"Although this will be a future task for us to fully unravel, it could be that this amyloid transition plays a large role in cancer formation, and potentially also plays a role in the response to certain cancer therapies," he says.

"This discovery has the potential to guide the development of novel treatment options and improved diagnostic procedures for various cancers."

The Royal Society Marsden Fund and Health Research Council of New Zealand-backed study took 15 researchers and four years to reach its conclusions. The team are now studying this structural transition and how it works in several different types of cancer cells.

"There are multiple avenues we are exploring, some range from using this novel knowledge to improve diagnostic procedures all the way to the development of new treatments that stabilize the protein in its native and healthy state," Dr. Goebel says.

He says this discovery could not have happened without support too from the people of Ōtautahi Christchurch.

"We are very grateful that so many [cancer patients](#) here in Christchurch are very generously donating their tissues to the He Taonga Tapu Cancer Society Tissue Bank, which has supported our work so far and will continue to do so in future," Dr. Goebel says.

"I am confident that together with our collaborators in the U.S., Canada, Europe and Asia we will be able to understand this new [protein](#) behavior and turn it to our advantage for use in future potential cancer treatments."

More information: Sarah G. Heath et al, Amyloid formation and depolymerization of tumor suppressor p16INK4a are regulated by a thiol-dependent redox mechanism, *Nature Communications* (2024). [DOI: 10.1038/s41467-024-49581-7](#)

Provided by University of Otago

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