New structural insight into neurodegenerative disease

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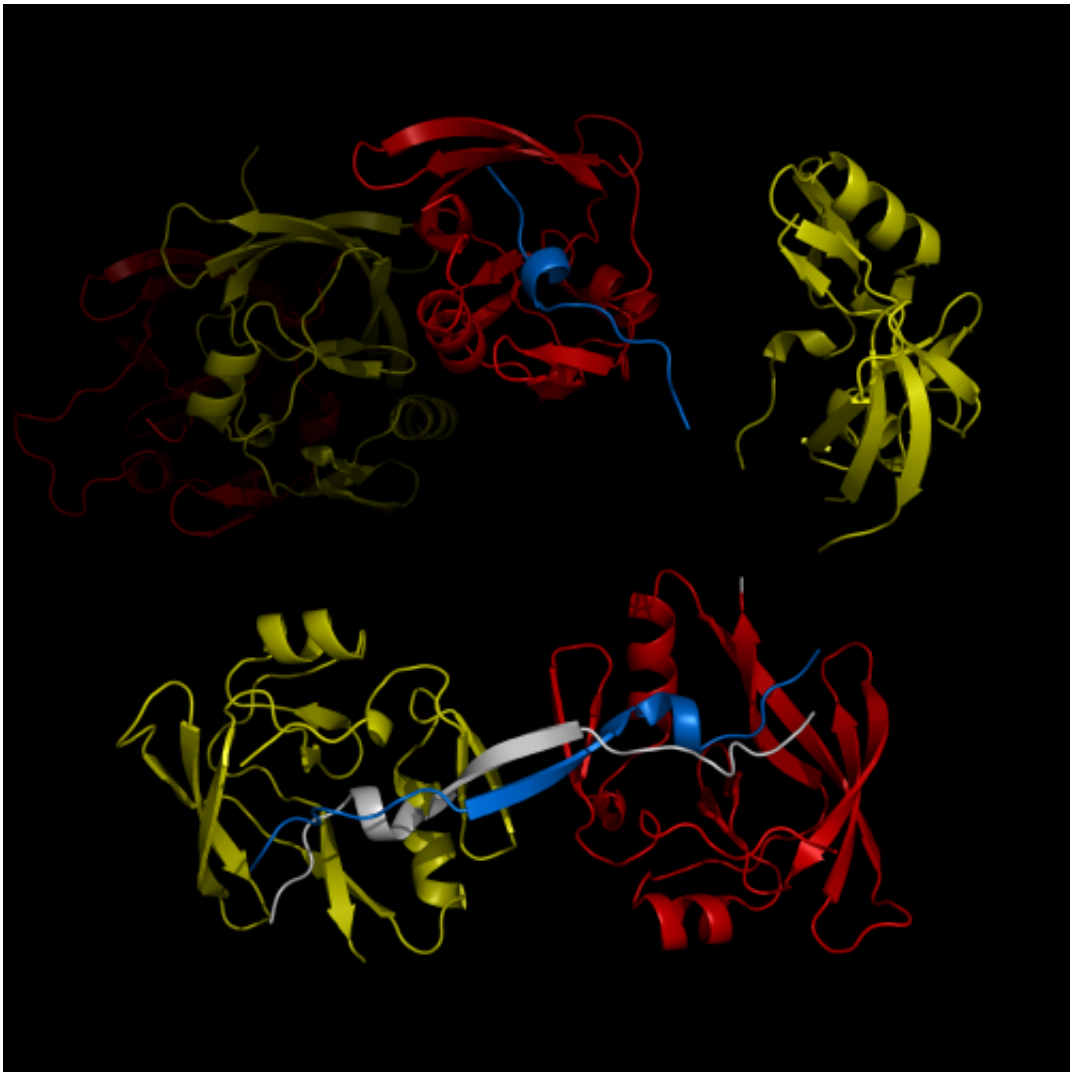

The complex formation between a polyglutamine disease protein, ATXIN-1 and the transcriptional repressor Capicua (CIC) plays a critical role in SCA 1 pathogenesis. The image shows that the homodimerization of ATXIN-1 (yellow and red) is disrupted upon binding of CIC (blue). Furthermore, the binding of

CIC to the ATXIN-1 induces a new form of ATXIN-1 dimerization mediated by CICs (ATXIN-1 AXH domains are shown in yellow and red, and CIC peptides shown in blue and white). Credit: KAIST

A research team from the Korea Advanced Institute of Science and Technology (KAIST) released their results on the structure and molecular details of the neurodegenerative disease-associated protein Ataxin-1. Mutations in Ataxin-1 cause the neurological disease, Spinocerebella Ataxia Type 1 (SCA1), which is characterized by a loss of muscular coordination and balance (ataxia), as is seen in Parkinson's, Alzheimer's, and Huntington's diseases.

SCA1-causing mutations in the ATAXIN1 gene alter the length of a glutamine stretch in the Ataxin-1 protein. The research team provides the first structural insight into the complex formation of ATAXIN-1 with its binding partner, Capicua (CIC). The team, led by Professor Ji-Joon Song from the Department of Biological Sciences at KAIST, solved the structure of Ataxin-1 and CIC complex in atomic level revealing molecular details of the interaction between Ataxin-1 and CIC.

Professor Song explained his recent research work, "We are able to see the intricate process of complex formation and reconfiguration of the two proteins when they interact with each other. Our work, we expect, will provide a new therapeutic target to modulate SCA1 neurodegenerative disease."

Understanding structural and molecular details of proteins at the atomic level will help researchers to track the molecular pathogenesis of the disease and, ultimately, design targeted therapies or treatments for patients, rather than just relieving the symptoms of diseases.

More information: Professor Song's research paper, entitled "Structural Basis of Protein Complex Formation and Reconfiguration by Polyglutamine Disease Protein ATAXIN-1 and Capicua," will be published in the March 15th issue of *Genes & Development*.

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