Structural Properties of Human CaMKII Ca$^{2+}$/Calmodulin-Dependent Protein Kinase II using X-ray Crystallography

YUMENG MELODY CAO, Smith College, ETHAN MCSPADDEN, JOHN KURIYAN, U.C. Berkeley, DEPARTMENT OF MOLECULAR AND CELL BIOLOGY AND DEPARTMENT OF CHEMISTRY TEAM — To this day, human memory storage remains a mystery as we can at most describe the process vaguely on a cellular level. Switch-like properties of Calcium/Calmodulin-Dependent Protein Kinase II make it a leading candidate in understanding the molecular basis of human memory. The protein crystal was placed in the beam of a synchrotron source and the x-ray crystallography data was collected as reflections on a diffraction pattern that undergo Fourier transform to obtain the electron density. We observed two drastic differences from our solved structure at 2.75 Å to a similar construct of the mouse CaMKII association domain. Firstly, our structure is a 6-fold symmetric dodecamer, whereas the previously published construct was a 7-fold symmetric tetradecamer. This suggests the association domain of human CaMKII is a dynamic structure that is triggered subunit exchange process. Secondly, in our structure the N-terminal tag is docked as an additional beta-strand on an uncapped beta-sheet present in each association domain protomer. This is concrete evidence of the involvement of the polypeptide docking site in the molecular mechanism underlining subunit exchange. In the future, we would like to selectively inhibit the exchange process while not disrupting the other functionalities of CaMKII.

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